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Towards an increased understanding of physiologic and pathologic multidirectional knee laxity measurements: a small step in the individualisation of care of anterior cruciate ligament injuries

Dissertation

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Contents

Abstract

ACL injuries are an increasing burden both for individuals, for who a return to preinjury quality of life as well as a limitation of long term consequences such as secondary injuries and osteoarthritis cannot yet be ensured, and for the society, which must cover the high direct and indirect costs of ACL injuries. The general purpose of this thesis was therefore to gain knowledge on ACL-injured patients and their knee laxity through the implementation of individualized patient and knee laxity profiles.

One third of ACL-injured patients are estimated to successfully compensate for their injury without surgery. However, current ACL registries rarely include nonoperatively treated patients thus delivering an incomplete picture of the ACL-injured population. ***Chapter 2*** presents data from an intra-hospital registry and helped to identify 8 specific subtypes of ACL-injured patients according to gender, age, previous ACL injury and preinjury level of practice. The percentage of operated patients varied between these subtypes. The consideration of these patient profiles will help in the future for a better understanding of patients at risk for an ACL injury.

In the management of ACL-injured patients, knee laxity can play a role in prevention, diagnosis and follow-up. While anterior knee laxity is common, static rotational knee laxity has recently received an increased interest. Our understanding of the latter is however insufficient as it is much more complex than the former. For the present thesis, anterior knee laxity was evaluated with the GNRB® and rotational knee laxity with the Rotameter. These 2 devices displayed higher precision than previous arthrometers (***Chapter 5).*** Arthrometers measuring rotational knee laxity display highly variable testing procedures (***Chapter 3)*** which may have influenced the reproducibility of previous devices.

In ***Chapter 4 and 5,*** physiological knee laxity revealed to be complex. In healthy controls, anterior knee laxity was not influenced by individual characteristics such as gender, age, height or body mass. However, rotational knee laxity was greater in females compared to males and negatively influenced by body mass. The influence of individual characteristics as well as the high inter-subject variability observed in rotational knee laxity measurements prevented its direct comparison between groups of subjects. The influencing characteristics were thus considered in ***Chapter 5*** to create individualized knee laxity scores. Then, as anterior and rotational knee laxity were poorly related to each other, both were combined to describe knee laxity profiles in healthy subjects. The diversity of identified profiles highlighted the

complexity of multidirectional knee laxity. This finding also suggested the necessity to individualize knee laxity measurements in the care of knee injuries in the future.

Knee laxity profiles of healthy controls were then compared to the healthy contralateral knee of ACL-injured patients in ***Chapter 6***. The healthy contralateral knees of patients with a noncontact ACL injury displayed both increased internal rotation and anterior displacement compared to the healthy controls. This suggests that it may be relevant to identify an individual knee laxity profile for primary and secondary prevention programs of noncontact ACL injuries.

Finally, ***Chapter 7*** focuses on knee laxity in the injured knees. The combination of anterior and rotational knee laxity measurements led to an excellent diagnostic power for ACL injury, provided that the slope of load-displacement curve was considered concomitantly with the final displacement. With this combination, a positive result was correct in all patients regardless of the subtype (complete, partial or healed) of the ACL tear and the associated injuries. Results in anterior knee laxity could partly distinguish between ACL subtypes of tear but requires further investigation.

Finally, ***Chapter 8*** consists of a general discussion, which critically reviews the results from the current thesis and includes recommendations and future perspectives regarding the use of knee laxity measurements. Overall, the recent development of new arthrometers has offered the possibility to improve the understanding of physiological, pathological knee laxity before and after ACL reconstruction.

Figures

Tables

Abbreviations

ACL	Anterior Cruciate Ligament
ALL	AnteroLateral Ligament
AM	Anteromedial
ATD	Anterior Tibial Displacement
BMI	Body Mass Index
CI	Confidence Interval
ER	External Rotation
ICC	Intraclass Correlation Coefficient
IKDC	International Knee Documentation Comitee
IR	Internal Rotation
MDC	Minimum Detectable Change
MRI	Magnetic Resonance Imaging
NPV	Negative Predictive Value
OA	Osteoarthritis
PC	Primary Compliance
PCL	Posterior Cruciate Ligament
PL	Posterolateral
PPV	Positive predictive value
ROC	Receiving Operating Characteristics
RSA	RadioStereometry Analysis
SC	Secondary Compliance
SD	Standard Deviation
SEM	Standard Errors of Measurements
SSD	Side-to-Side Difference
TR	Total range

Chapter 1
Introduction

Between 1988 and 2004, an increase in sport participation of 20% and 80% was observed respectively in males and females (Hootman et al. 2007). Interestingly, the exposure to musculoskeletal injuries has simultaneously been raised (Hootman et al. 2002). Nowadays, 53 to 72 % of sports injuries are reported to involve the lower limb (Agel et al. 2007a, Agel et al. 2007b, Agel et al. 2007c, Dick et al. 2007a, Dick et al. 2007b, Marshall et al. 2007). The knee is the most affected joint, both in males and females, accounting for 23 % of sports injuries (Hootman et al. 2002). It is also the most common body part affected by severe injuries (inducing more than 3 weeks of participation loss) (Darrow et al. 2009) and represents 60 to 64 % of all injuries requiring surgery (Powell et al. 1999, Darrow et al. 2009).

Sports injuries are a burden for both individuals and society. On the one hand, they can lead to failure to start and maintain a physically active lifestyle (Webborn 2012). On the other hand, they induce high direct and indirect costs including medical treatments, lost sporting and working incomes, and costs due to permanent physical damage and disability as well as reduced quality of life. Anterior cruciate ligament (ACL) injuries have been reported to induce the highest direct costs (Cumps et al. 2008) of all sport injuries. Indirect costs are difficult to evaluate and data are still missing.

ACL injuries are a growing burden with an annual average increase of 1.3 % as reported between 1988 and 2004 (Hootman et al. 2007). Their diagnosis requires a strong experience to be efficient. Furthermore, regardless whether the injury is treated surgically or not, a return to preinjury level of activity and/or a safe return to sport after such injuries cannot be ensured. Indeed, it has been reported that only 44% of patients are able to return to competitive sport after an ACL injury (Ardern et al. 2011). Furthermore, patients with an ACL injury display 5.2 times greater risk to have a new ACL injury (Faude et al. 2006) and 40 to 60% of patients will have signs of osteoarthritis (OA) 10 years after the lesion (Myklebust et al. 2005, Lohmander et al. 2007) especially if the ACL tear is associated with a meniscus tear (Oiestad et al. 2009, Oiestad et al. 2010).

Further investigations are needed to improve the care of ACL injuries as well as patient's quality of life. Amongst all measurements (*i.e.* muscle force, hop tests, …) that should be considered in the care of ACL injuries (Triston et al. 2004), knee laxity may be the only one to have a role on their prevention, their diagnosis and their long term follow-up. The present thesis will therefore specifically focus on knee laxity measurements in ACL injuries.

1. Anterior cruciate ligament injuries

1.1 Incidence, mechanism and care: variabilities between countries, sex, age and sports

Overall incidence of ACL reconstructions were estimated in the Scandinavian ACL registries to 29 to 38 per 100 000 inhabitants per year (Csintalan et al. 2008, Granan et al. 2008, Granan et al. 2009, Lind et al. 2009). Their distribution is age- and sex-dependent (Table 1.1). The highest incidence was observed for patients aged 15 to 39 years (85 to 91 cases per 100 000 inhabitants) (Granan et al. 2008, Lind et al. 2009). More specifically, females display a greater incidence of ACL reconstruction between 15 and 19 years old and males between 20 and 24 years old (Lind et al. 2009). It must be highlighted that the annual incidence of ACL injuries is certainly underestimated as current registries mainly report ACL injuries treated with surgery while those treated without surgery are often missing (Seil et al. 2015).

Table 1.1: The annual incidence of primary ACL reconstructions per 100,000 citizens in Scandinavia (Granan et al. 2009)

Age	Females			Males		
	Denmark	Norway	Sweden	Denmark	Norway	Sweden
10–19	71	76	88	71	47	59
20–29	85	64	62	191	112	117
30–39	79	42	39	137	77	65
40–49	52	24	27	69	38	31
50–59	10	8	6	15	5	5
60–69	3	0.5	0.2	2	1	0.4

The annual incidence of ACL reconstructions also differs between countries. New Zealand (Gianotti et al. 2009) and the United States (Csintalan et al. 2008, Lyman et al. 2009) have similar incidences than the Scandinavian countries with 38 and 30-33 injuries per 100 000 inhabitants respectively. In Australia, the overall incidence of ACL reconstructions reaches 52 per 100 000 persons per year (Janssen et al. 2011) and has increased by 14% between 2003 and 2008. The maximum annual incidence of ACL reconstructions in Australia was observed in males aged 15 to 24 years (181 per 100 000 males per year). This is more than twice the incidence reported in the Scandinavian registries and may partly reflect differences in sport participation between countries.

In the United States, ACL injuries mainly occurred in basketball (20%), followed by football (17%), American football (14%) and ski (7%) (Magnussen et al. 2010). In Scandinavian registries, ACL injuries mainly occurred in football (40%), followed by handball (15%) and alpine skiing (10%) (Granan et al. 2008). Actually, the distribution of ACL injuries amongst sports is sex-dependent. In the Scandinavian registries, males were more likely to be injured during football (69%), handball (10%) and alpine sport (8%) while females were more likely to be injured in handball (39%), alpine sport (23%) and football (20%) (Lind et al. 2009).

Seventy two to 88% of ACL injuries are sports related (Lind et al. 2009, Magnussen et al. 2010, Janssen et al. 2011) and 63 to 80% are reported to be non-contact injuries (Arendt et al. 1999, Janssen et al. 2011). Several mechanisms of ACL injuries have been described in the literature depending on sports practice. In football, ACL injuries mainly occur during changes of direction or cutting manoeuvres combined with deceleration, with knee near full extension and a planted foot (Alentorn-Geli et al. 2009). In basketball and handball, similar mechanisms were observed (Krosshaug et al. 2007). The ACL injury occurs approximately 40 milliseconds after ground contact after an immediate valgus and internal tibial rotation (Koga et al. 2010). In alpine skiing, during a forward fall when the outer edge of the ski gets caught in the snow, the knee can get hyperextended and internally rotated (Ruedl et al. 2011). During a backward fall, flexion, valgus and external rotation forces can act on the knee and induce an ACL injury (Krosshaug et al. 2007).

Reconstructive surgery has become the standard of care of ACL injuries, aiming at restoring knee stability, reducing joint laxity and avoiding secondary menisci and cartilage injuries. Nevertheless, not all ACL-injured patients require surgical reconstruction as some individuals are able to successfully compensate for an acute ACL injury without surgery (Moksnes et al. 2009). It is however currently well accepted that patients with high risk activities such as heavy work or sport activities should undergo an ACL reconstruction (Daniel et al. 1994) specifically because they present more degenerative changes under a conservative treatment (Fink et al. 2001).

The line of distinction between surgical and nonsurgical treatment has not clearly been drawn yet and no rigid criteria exist to decide whether a patient should be operated or not. To date, it remains unclear how individual characteristics such as gender, age, sport activity and previous ACL injuries, factors that seems to critically influence incidence of ACL injuries as shown above, are actually considered to decide whether the patient requires surgery or not. This question will be addressed in ***Chapter 2*** through the analysis of data from our hospital registry. The aim of this chapter will be to give an overview of the ACL-injured population and its treatment through the identification of patient subtypes with similar characteristics.

1.2 Current diagnosis of ACL injuries

The majority of ACL tears can be diagnosed with a detailed patient history, including the injury mechanism, in association with a thorough clinical examination with side-to-side comparisons. For the latter, a large clinical experience of the examiner is mandatory.

The ACL originates at the medial side of the lateral femoral condyle and runs an oblique course to the anterior tibia (Figure 1.1). It consists of two bundles, the anteromedial (AM) and posterolateral (PL) bundles so named for the orientation of their tibial insertion (Arnoczky 1983, Yagi et al. 2002, Petersen et al. 2007). Antero-medial and posterolateral bundles both have a role to stabilise the anterior translation and the internal rotation (IR) of the tibia (Zantop et al. 2007).

The ACL is the primary restraint to anterior tibial displacement (ATD) (Butler et al. 1980, Fukubayashi et al. 1982). It provides 86 per cent of the total resisting force when an anterior force is applied to the tibia (Butler et al. 1980). At 30° of knee flexion, the anteromedial bundle of the ACL is tighter than the posterolateral bundle (Gabriel et al. 2004) so that the anteromedial bundle might be the primary restraint to the anterior knee laxity at 30°. The ACL is also a secondary restraint to IR and valgus (Table 1.2). The resection of the posterolateral bundle significantly increases rotational range at 30° of knee flexion. Further resection of the ACL does not reveal significant increase in tibial rotation so that the posterolateral bundle may be more important in controlling tibial rotation (Lorbach et al. 2010).

1.2.1 Manual diagnosis

When an ACL injury is suspected, the Lachman test (Torg et al. 1976), the pivot shift test (Slocum et al. 1976, Galway et al. 1980) and the anterior drawer test are usually performed (Galway et al. 1972, Hughston et al. 1976, Losee et al. 1978). These tests relies on the properties of the ACL to restrain anterior translation and internal rotation as explained above.

In the case of an acute injury with a painful and swollen knee, clinical information may be limited. In subacute or chronic injuries, clinical examination is facilitated due to improved knee swelling, less pain or no pain and better joint mobility.

Table 1.2: Static restraint to the tibia provided by the ligaments (Halewood et al. 2015)

Applied displacement (to the tibia)	Flexion angles (°)	Primary restraints	Secondary restraints
Anterior drawer	0	ACL	ITB, dMCL, LCL, Menisci, PT
	30	ACL	Menisci, dMCL, PT
	60–120	ACL	
Posterior drawer	0–40	POL, OPL	aPCL, LCL, PFL, MFLs
	40–120	aPCL	pPCL, PFL, MFLs
	120–140	pPCL, aPCL	Posterior calf impingement
Varus rotation	0–60	LCL, PLC, ITB, ALL	PCL, PT
Valgus rotation	0	sMCL, POL, OPL	ACL
	30	sMCL	ACL
	60	dMCL	
External rotation	0	LCL	Menisci, dMCL, PFL
	30–90	sMCL, LCL, PT	PCL, Menisci, PFL
Internal rotation	0–30	POL, ITB	ACL, sMCL, Menisci, PT, ALL
	60	dMCL, ITB	ACL, Menisci, PT, ALL
Hyperextension	<0	OPL	ACL, POL, pPCL, PFL

ACL anterior cruciate ligament, *ITB* iliotibial band, *dMCL* deep fibres of the medial collateral ligament, *sMCL* superficial fibres of the medial collateral ligament, *LCL* lateral collateral ligament, *aPCL* anterior bundle of the PCL, *pPCL* posterior bundle of the PCL, *MFL* meniscofemoral ligaments, *ALL* anterolateral ligament, *POL* posterior oblique ligament, *OPL* oblique popliteal ligament, *PT* popliteal tendon, *PFL* popliteofibular ligament complex, *PLC* posterolateral corner structures

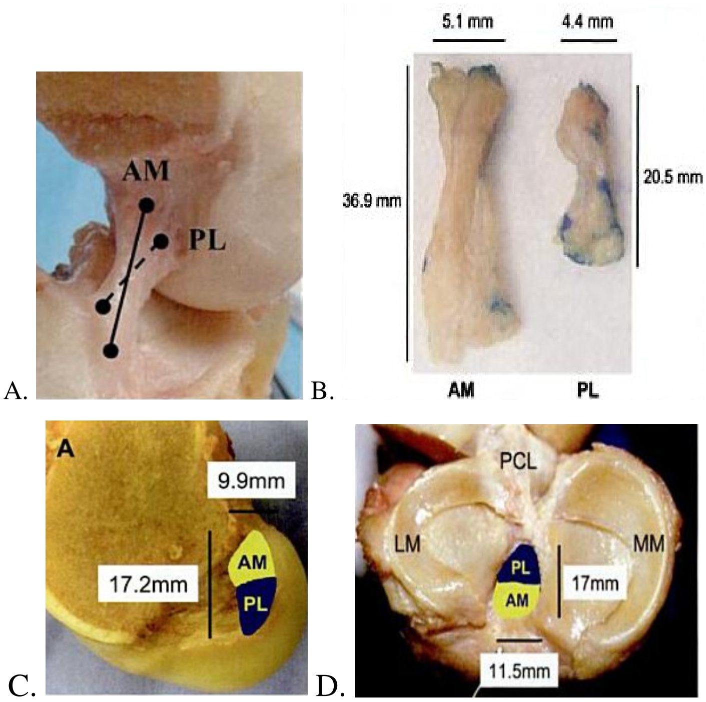


Figure 1.1: ACL anatomy . A. Antero-medial and postero-lateral bundles of the anterior cruciate ligament with the knee flexed and medial femoral condyle and PCL removed. B. Antero-medial and postero-lateral bundles of the anterior cruciate ligament excised from their femoral and tibial insertion. C. Femoral insertions of the anterior cruciate ligament. The medial femoral condyle has been removed. D. Tibial insertion of the anterior cruciate ligament. AM: antero-medial. LM: Lateral Meniscus. MM: Medial meniscus. PCL: Posterior Cruciate Ligament. PL: postero-lateral. Adapted from (Freddie H. Fu 2008)

- ***Lachman test***

Figure 1.2: The Lachman test for anterior stability (Lubowitz et al. 2008)

To realise the Lachman test, the knee is flexed at 20-30° and the tibia is stabilised in neutral rotation. The femur is held distally by the non-dominant hand of the examiner and an anterior force is applied to the upper part of the tibia with the other hand (Figure 1.2). The position of the hand used to apply the force on the tibia is crucial. Examiners with a proximal placement of their hand are more likely to correctly assess the Lachman test than examiners with a more distal position (Hurley et al. 2003). Anterior displacement of the Lachman test is estimated in millimeters and the endpoint feeling is described (firm, delayed or soft). An ATD less than 5 mm is defined as grade I, from 5 to 10 mm as grade II and superior to 10 mm as grade III. An asymmetry with the healthy knee and/or a soft endpoint are signs in favour of an ACL lesion (Torg et al. 1976). To avoid a false positive, the examiner should make sure that the tibia is not subluxated posteriorly before starting the test which would indicate a posterior cruciate ligament (PCL) lesion. False negatives could be caused by bucket handle meniscus tear and the ACL scarring on the PCL (Torg et al. 1976, Donaldson et al. 1985).

- ***Pivot shift test***

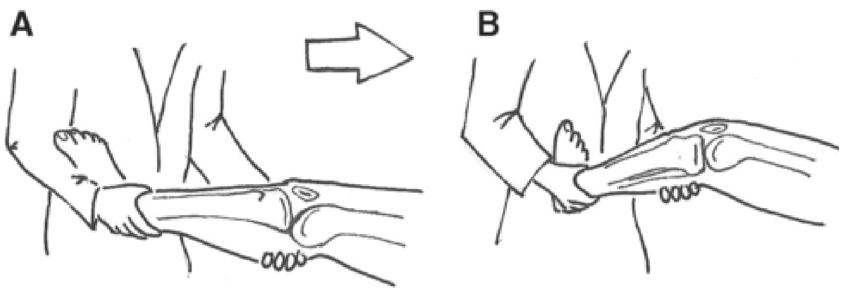


Figure 1.3: The pivot shift test (Lubowitz et al. 2008)

The pivot shift test is a dynamic test. The knee is extended and the foot held in a forced internal rotation while a valgus force is applied to the tibia by the examiner. The knee is progressively flexed and the tibia, which is at the beginning anteriorly subluxated at the level of the lateral femorotibial compartment when the ACL is absent, reduced posteriorly spontaneously between 20 and 30 degrees of knee flexion (Figure 1.3). This reduction is usually unpleasant for the patient who associates it to a feeling of instability or a giving way episode. The test is objectivated in a semi quantitative manner in 4 grades: grade 0, I, II and III (Jakob et al. 1987). In acute ACL injuries, the pivot shift test is less valid and often not possible because of pain, swelling and hamstrings contraction. It is also one of the most difficult orthopaedic clinical tests to reproduce and requires several years of experience before it can be used and interpreted routinely (Galway et al. 1972, Galway et al. 1980). The pivot shift test is also highly dependent of the individual osseous, tendinosus and capsuloligamentary anatomic configuration (Musahl et al. 2010a, Tanaka et al. 2012). In the case of hyperlax patients, the test can be positive without being associated to a structural lesion but is rarely above grade I. This shows the importance of systematically assessing both knees to avoid a false positive.

- ***Anterior drawer test***

The anterior drawer test is realised at 90° of knee flexion with the tibia in neutral rotation. The examiner sits on patient's foot and grasps the proximal tibia with both hands to apply an anterior force (Figure 1.4). A positive test is indicated by a soft endpoint and a grade similar to the Lachman test. As for the Lachman test, the examiner should make sure that the tibia is not subluxated posteriorly at the beginning of the test which would indicate a PCL lesion (Mitsou et al. 1988). He should also encourage the patient to relax his hamstring muscles to minimise the resistance to anterior tibial translation. This test is difficult to assess for acute injuries as the knee is swollen and knee flexion to 90° is difficult.

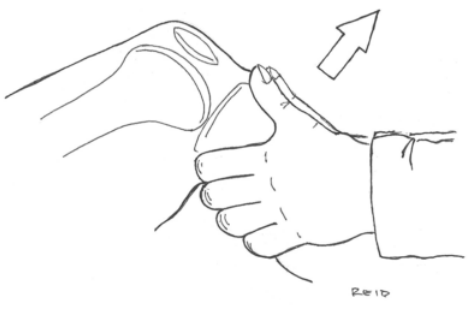


Figure 1.4: Anterior drawer test (Lubowitz et al. 2008)

1.2.2 Diagnostic performance of manual tests

The diagnostic performance of manual tests have been evaluated in the literature by experienced surgeons. As a consequence, the following performance may not be reproducible in less experienced examiners. The Lachman test is the most sensitive (sensitivity >90%) test both in acute and chronic ACL injuries (Benjaminse et al. 2006, van Eck et al. 2013b). Without general anaesthesia, 80% of examined patients have a positive Lachman test which increases to 100% for patients under general anaesthesia (DeHaven 1980). These results have been confirmed by a meta-analysis showing a sensitivity and a specificity for the Lachman test reaching respectively 85% and 94% without anaesthesia and 97% and 93% under anaesthesia (Benjaminse et al. 2006).

The pivot shift test is highly specific: without anaesthesia, 98% of healthy subjects have a negative pivot shift test (Benjaminse et al. 2006). Under anaesthesia, the sensitivity of the pivot shift test is however poor both in acute (32%) and chronic (40%) ACL injuries. The latter increases to 74% under anaesthesia (Benjaminse et al. 2006). These results are consistent with a recent meta-analysis where the sensitivity of the pivot shift test reached 28% without anaesthesia and 73% under anaesthesia (van Eck et al. 2013b). The interpretation of the pivot shift test in ACL injuries has recently been questioned with the description of the anterolateral ligament (ALL) (Claes et al. 2013). In a cadaver study, an isolated section of the ACL never resulted in a grade III (explosive). The highest degree was only reached once the ALL was resected.

Without anaesthesia, the anterior drawer test is positive in 55% of patients (Benjaminse et al. 2006). A recent meta-analysis reported a lower the sensitivity of the anterior drawer test of 38% (van Eck et al. 2013b). The anterior drawer test seems however to be more sensitive in chronic injuries (92%) compared to acute injuries (49%). Under anaesthesia, the sensitivity increased to 77% for both chronic and acute injuries (Benjaminse et al. 2006).

Under experienced hands, the diagnostic performance of manual tests to detect ACL tears thus appears to be adequate. Experienced surgeons are indeed reported to recognise 94% of participants with an ACL injury and to misclassify only 16% of participants with an intact ACL compared to 62 % and 23 % for primary care physicians (Geraets et al. 2015).

In a prospective study in the United Kingdom, only 28% of ACL injuries were reported to be diagnosed at initial medical consultation (Arastu et al. 2015) despite a typical pattern indicating an ACL injury (Figure 1.5). Then, only an additional 11% were diagnosed with the help of Magnetic Resonance Imaging (MRI) (Arastu et al. 2015) although its sensitivity and specificity were reported to reach high values (sensitivity: 81%, specificity: 96%) (Rayan et al. 2009). At the end, the correct diagnosis could only be established after 1 to 6 (median 3) medical visits which represented 0 to 192 weeks (median 6) weeks (Arastu et al. 2015). A delay in the diagnosis superior to 6 months led to an increased medial meniscus tear rate of 72% compared to a rate of only 23% for patients with a diagnosis in the 4 first months after the injury (Arastu et al. 2015).

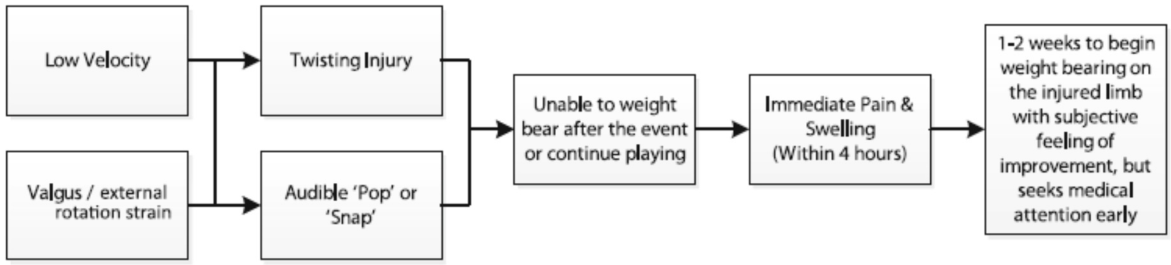


Figure 1.5: Typical pattern indicating an ACL rupture (Arastu et al. 2015)

These results underline that the diagnosis of ACL injuries may not be as efficient as often reported in the scientific literature. Manual clinical tests have the disadvantage to be highly subjective and examiner-dependent (Branch et al. 2010b). MRI is not completely reliable either and is moreover expensive and often requires a waiting period depending on the country. As such, knee laxity devices, also called arthrometers, presented thereafter, may benefit to the diagnosis of ACL injuries as they allow for precise, quick and costless measurements.

2. Knee laxity devices and their reliability

Laxity measurements may be of clinical interest for those cases in which the clinical examination is uncertain. Furthermore, they can help to provide a longitudinal follow up of patients with or without ACL reconstruction.

Arthrometers have specifically been designed to reproduce the manual Lachman or pivot shift tests. They allow for an objective and standardized evaluation of knee laxity. The present section introduces the most commonly reported arthrometers for anterior and rotational knee laxity divided into several categories depending on the type of laxity they measure (static or dynamic, anterior displacement or rotation, etc.). Static laxity is evaluated in a single direction after unidirectional force application. Dynamic laxity measurement techniques considers knee kinematics after the application of a multidirectional force to the knee joint.

2.1 Static anterior knee laxity

Static anterior knee laxity has been studied since the 70's (Kennedy et al. 1971, Sylvin 1971, Volkow 1971). All devices designed to measure anterior knee laxity reproduce the position of the Lachman test: the patient is lying prone and his knee is tested at 20° of flexion. As for the

Lachman test, the patient must be relaxed during the force application. A muscle contraction might indeed limit the ATD (Feller et al. 2000). Furthermore, measurements are influenced by knee rotation so that the tested leg should be placed and tested in neutral rotation (Fiebert et al. 1994).

2.1.1 Non-invasive devices

- ***KT-1000®and KT-2000® (Daniel et al. 1985)***

The KT-1000® was developed in the 1980's and is the most common arthrometer to measure anterior knee laxity (Figure 1.6). However, it seems that the KT-1000® is not commercialised anymore. The device is secured to the anterior proximal and distal tibia by 2 circumferential Velcro® straps. The KT-1000® measures the relative antero-posterior displacement between 2 sensors: one in contact with the patella and the other placed on the anterior tibial tuberosity. Final forces applied on the shank vary from 67 N, 89 N, and 134 N to maximal force. The KT-2000® is identical to the KT-1000® but also plots a graphic representation of the ATD as a function of the magnitude of applied force. Although this arthrometer is widely used, its precision and reproducibility can be questioned. Several authors reported an intraclass correlation coefficient (ICC) above 0.8 (Hanten et al. 1987, Highgenboten et al. 1989, Ballantyne et al. 1995, Myrer et al. 1996). In contrast, some authors reported intra- and inter-rater ICC lower than 0.7 (Berry et al. 1999, Sernert et al. 2001, Wiertsema et al. 2008). The reliability of the KT-1000® diminishes if the examiner is not experienced from 0,9 to 0,65 (Berry et al. 1999). In ACL-injured patients, the inter-examiner ICC even decreases to 0.55 (Sernert et al. 2004). As the force is applied manually, the examiner (Ballantyne et al. 1995) and its hand dominance (Sernert et al. 2007) seem to critically influence laxity measurements. The inter-rater error (calculated as the standard error of measurements (SEM) multiplied by the square root of 2 multiplied by 1.65 to obtain the 90% confidence interval (CI)) was estimated at 2.9 mm for experienced examiners and 3.5 mm for novice examiners (Berry et al. 1999).

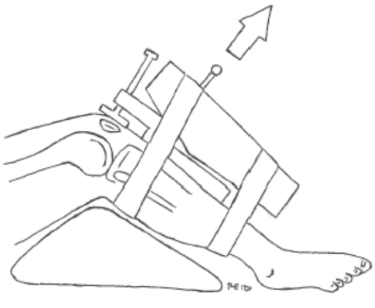


Figure 1.6: The KT-1000® arthrometer (Lubowitz et al. 2008)

- ***Stryker Knee Laxity Tester (Stryker, Kalamazoo, MI) (King et al. 1989)***

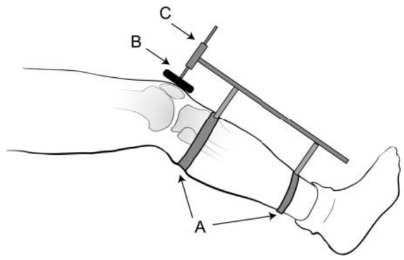


Figure 1.7: The Stryker Knee Laxity Tester (Pugh et al. 2009)

The device consists of a bar placed 4 cm anteriorly from the tibia and secured around the shank with elastics (Figure 1.7). The anterior force application is manual. Comparative studies demonstrated that the Stryker Knee Laxity Tester provides similar reliability than the KT-1000® with an ICC superior to 0.9 (Highgenboten et al. 1989) although the ATD was in average lower with the Stryker Knee Laxity Tester (Highgenboten et al. 1989, Steiner et al. 1990, Anderson et al. 1992). A comparison with radiostereometry analysis (RSA) technique showed that more than 50% of the measured displacement of the Stryker Knee Laxity Tester is due to soft tissues deformation at a load of 180N (Jorn et al. 1998).

- ***Rolimeter (Aircast Europa, Neubeuern, Germany) (Balasch et al. 1999)***

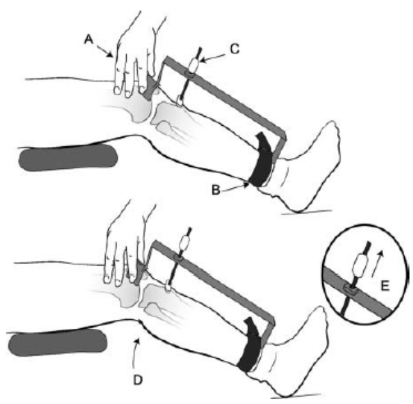


Figure 1.8: The Rolimeter (Pugh et al. 2009)

The Rolimeter is light, easily transportable, cheap and sterilisable (Figure 1.8). Force application is not calibrated and is done manually. This arthrometer is similar to the KT-1000®. The ICC or precision of the device have not been reported in the literature. However, the Rolimeter has been reported to provide similar side-to-side differences (SSD) in the ATD than observed with the KT-1000® in the ACL-injured knee (Balasch et al. 1999, Schuster et al. 2004).

- ***GNRB® (Genourob, Laval, France) (Robert et al. 2009)***

The GNRB® is the first arthrometer to propose a motorized application of the force under standardised and controlled conditions (Figure 1.9). The GNRB® has been reported to have a greater reliability than the KT-1000® regardless of the examiner's experience (Collette et al. 2012). In contrast, Vauhnik et al. calculated an inter-rater ICC lower than 0.4 for the right knee and lower than 0.7 for the left knee (Vauhnik et al. 2013, Vauhnik et al. 2014). The Bland Altman plot 95% limits of agreement showed a relative reliability of 2.0 mm for the right knee and 3.1 mm for the left knee at 134 N (Vauhnik et al. 2013, Vauhnik et al. 2014). Such differences between the left and the right knee could not be explained by the researchers but may have been caused by lack of standardisation in patient installation.

Figure 1.9: The GNRB® (Robert et al. 2009)

The GNRB® will be used in the present thesis to measure anterior knee laxity. This device has many technological advantages. First, the foot can be firmly fixed in neutral rotation with the help of an ankle shell, which allows to avoid the influence of the rotation of the tibia on the ATD (Fiebert et al. 1994). Second, a sensor placed under the thigh indicates the fixation pressure the patella shell which permits to reproduce a similar fixation between legs and tests. Third, the motorised force application allow to standardise the rate of the force which is recognised to influence the slope of the displacement-force curve (Gross et al. 2004). Provided that a standardised protocol is applied, the GNRB® may thus offer a better reproducibility of anterior knee laxity measurements as well as the opportunity to analyse the force-displacement curve in greater details.

2.1.2 Devices combined with imaging

Although the following techniques are more precise, they are invasive, require additional ressources and are time consuming. As a consequence, they will not be considered in the present thesis.

- ***RadioStereometry Analysis (RSA) (Aronson et al. 1974)***

RSA was developed 40 years ago in Sweden by Göran Selvik. This technique is both the most precise and the most invasive method as it requires the surgical implantation of intra osseous tantalum beads of a diameter of 0.8 to 1.6 mm (Aronson et al. 1974). They are implanted into the patient's knee at the distal part of the femur and proximal part of the tibia. Two radiographies are performed simultaneously and the anatomical position of the markers is determined with the help of a calibration cage. This tridimensional technique has a precision of 0.1 mm (Tashman et al. 2004b) and has the advantage to be not influenced by skin movement artefacts (Tashman et al. 2004a). It is more discriminant than the KT-1000® in the post-operative follow-up of ACL patients. The KT-1000® indeed reported lower SSD than the RSA thus probably overestimating the stabilisation brought by the reconstruction of the ACL (Jonsson et al. 1993).

- ***Telos Stress Device (Telos GmbH, Hungen-Obbornhofen, Allemagne)***

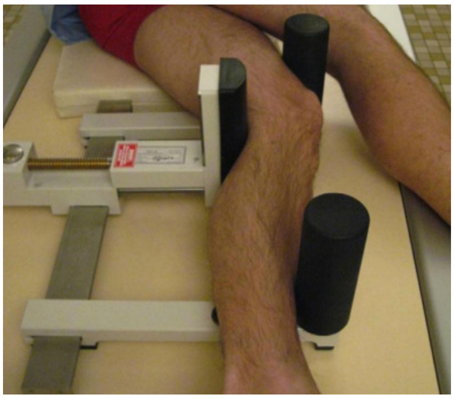


Figure 1.10: Telos device testing anterior knee laxity (Beldame et al. 2012)

The patient is lying on the side to study anterior knee laxity and supine to assess varus-valgus. The tested leg is placed within 2 fixed bars inducing 25° of knee flexion (Figure 1.10). An anterior force is applied at the proximal posterior part of the shank. A dynamometer displays the amount of applied force: 9 or 15 kg, and a lateral radiograph is realised in this constraint position. On the radiograph, the ATD is represented by the distance of 2 parallel lines: the first line is perpendicular to both tibial plateau and tangent to the posterior corner of the medial condyle, the second is perpendicular to both tibial plateau and tangent to the posterior border of the medial tibial plateau. The distance between both lines is measured in millimeters by the radiologist. Reliability of posterior displacement between testers is estimated to reach an ICC of 0.91 and the 95% CI of SEM reached 2.77 mm (Schulz et al. 2005). To the author's knowledge, reliability of the device has not been reported for the ATD.

- ***Lerat's method (Lerat et al. 1993)***

Lerat's method is easy to use and cheap. The patient is lying supine with the hips at the border of a radiological table. The knee is placed on an adapted support inducing 20° of knee flexion. A mass of 9 kg is attached to the patient' thigh above his patella to induce a posterior translation of the femur compared to the tibia (Figure 1.11). This technique seems to be reliable with an intra-tester ICC superior to 0.9 (Lerat et al. 2000).

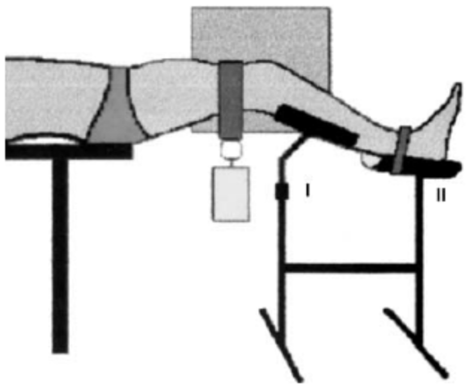


Figure 1.11: Lerat's method (Lerat et al. 2000)

2.2 Static rotational knee laxity

First attempts to measure rotational knee laxity were made in the beginning of the 1980's (Nielsen et al. 1984, McQuade et al. 1989a, Lane et al. 1994). Much more complex than anterior knee laxity measurements, rotational knee laxity measurements are not yet used in the daily clinical practice.

Rotational knee laxity is highly influenced by the patient's position and by the location of rotation measurement. Knee rotation is higher if the knee is flexed at 90° compared to 20° and if the hip is extended compared to flexed at 90° (Shoemaker et al. 1982). Furthermore, if the rotation angle is measured at the foot, the tibiofemoral rotation will be overestimated (Alam et al. 2011). Foot rotation can represent up to 2/3 of the final measure (Shoemaker et al. 1982). To avoid these artefacts, some devices use electromagnetic sensors placed on the tibia (Alam et al. 2011), which is the most precise method.

- ***Rottometer (Almquist et al. 2002)***

The patient sits on a modified chair with knees and hips flexed to 90°. To limit artifacts and target tibiofemoral rotation, the thigh is fixed above the knee with clamps. The ankle is fixed by 2 screws at the calcaneus and 4 screws placed at the medial and lateral malleoli (Figure

1.12). An adjustable spanner is used to apply torque and a stick following the foot plate indicated the resulting degree of rotation. A comparative study using RSA demonstrated that the Rottometer systematically overestimated tibiofemoral rotation by about 100% (Almquist et al. 2002).

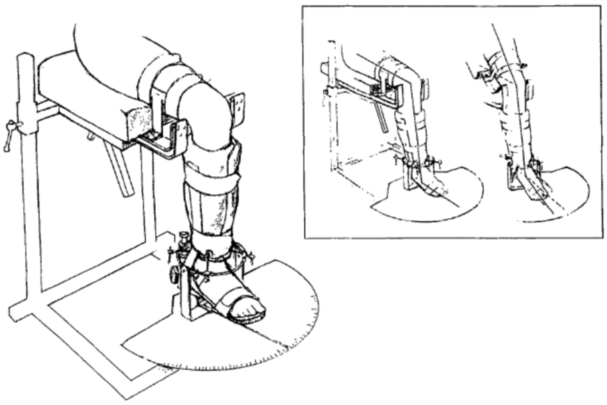


Figure 1.12: The Rottometer (Almquist et al. 2002)

Depending on the amount of torque and degree of knee flexion, the inter-rater ICC varied between 0.49 and 0.85, with the highest ICC obtained for the highest torque (9 Nm) and the higher degree of knee flexion (90°) (Almquist et al. 2011). The 95% CI between measurements of both examiners varied between -7.9° for the lower bound and 3.8° for the upper bound (Almquist et al. 2011).

- ***Device by Musahl et al. (Musahl et al. 2007)***

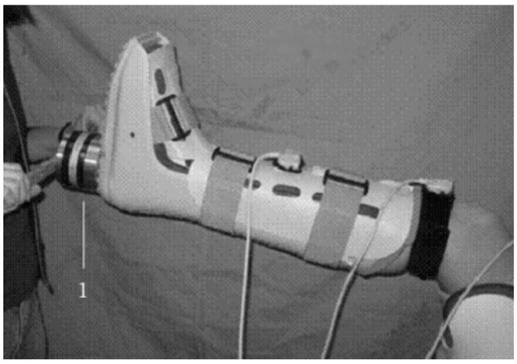


Figure 1.13: Device presented by Musahl et al. (Musahl et al. 2007)

The device consists of an Aircast Foam Walker boot with a 6 degrees of freedom moment sensor fixed on a handle bar attached to the boot. A bubble level is also attached to the handle bar to determine the neutral rotation (Figure 1.13). To measure the relative rotation of the tibia with regards to the femur, magnetic sensors are placed on the boot, on the medial surface of the proximal tibia and on the anterior surface of the thigh. The examiner holds the leg while applying the torque, which may influence muscle relaxation and flexion angles. An initial cadaver study reported a high intra and inter-rater ICC (> 0.94) (Musahl et al. 2007). In 11 healthy subjects, the inter-rater ICC was the greatest at 90° of knee flexion (0.88). The 95% CI of the SEM reached 3.2° for the total range (TR) of rotation at 90° of knee flexion and 5.1° at 30° (Tsai et al. 2008). The average SSD between normal knees was reported to be 3.5° (Tsai et al. 2008).

- ***Device by Park et al. (Park et al. 2008)***

Park et al. (Park et al. 2008) presented the first motorized device to measure knee rotational laxity. The patient sits in a modified chair with the hips flexed at 85° and knees at 60°. The thighs are fixed with clamps (Figure 1.14). Three LED markers were positioned on the anteromedial surface of the tibia to measure the angle of rotation. No data is available on its reproducibility.

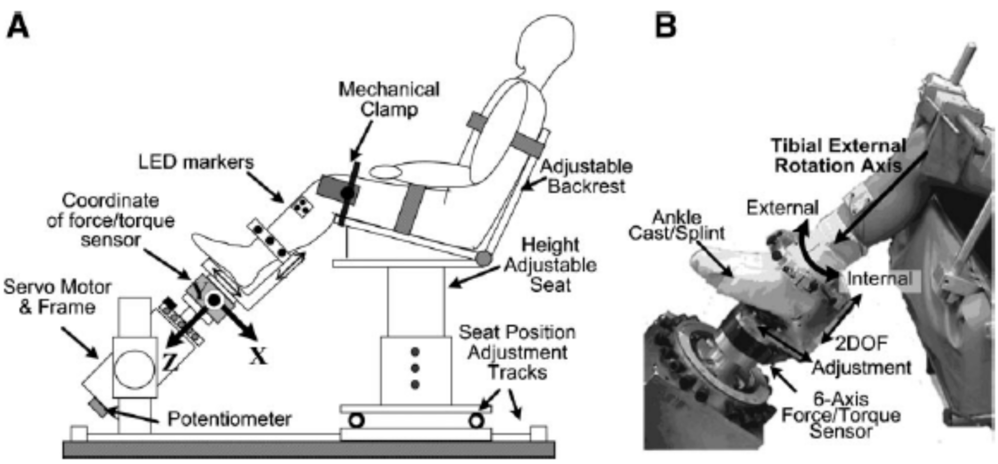


Figure 1.14: Device presented by Park et al. (Park et al. 2008)

- ***Rotameter (Lorbach et al. 2009a)***

Two prototypes of the Rotameter exist. In both versions, the subject is lying prone to reproduce the dial test position. Thighs are fixed in half cones with Velcro strap band. Hips are extended and knees flexed at 30°. The subject is wearing boots (home-made boot in the first version and ski boots of appropriated size in the second version) attached to the handle bar that allows both to apply the torque and measure the degree of rotation (Figure 1.15). A cadaver study showed a high correlation (Pearson r > 0.85) between measurements of the first prototype and knee navigation system (Lorbach et al. 2009a, Lorbach et al. 2010). In vivo, greater ICC were observed for inter-tester reliability (>0.88) compared with intra-rater ICC (>0.67), suggesting that participants were not reinstalled between the measurements undertaken by the two examiners (Lorbach et al. 2009b). The second version of the present device with ski boots will be introduced in the present thesis.

Figure 1.15: The first version of the Rotameter (Lorbach et al. 2009b)

- ***Robotic Knee Testing system (Branch et al. 2010a)***

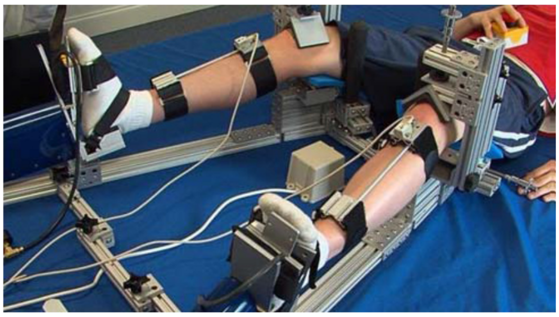


Figure 1.16: Robotic Knee Testing system (Branch et al. 2010a)

Branch et al. developed a custom robotic knee system adjustable to the patient's natural lower limb alignment to avoid pretension in leg anatomical structures. The patient lies supine with knees flexed at 25°. The femur and patella are stabilized with clamps and the ankle is stabilized in pronation and dorsiflexion to limit its rotation during the test. Rotation is measured at the foot with an inclinometer (Figure 1.16). Electromagnetic sensors placed on the proximal tibia showed that tibial rotation represented in average 48.7% of the total rotation measured at the foot (Branch et al. 2010a). The authors corrected their measurements according to these results, which may introduce bias, as this correction may vary between individuals (95% CI: 45.3-52.1%) (Branch et al. 2010a). Inter-rater ICC for TR reached 0.97 at a torque of 5.65 Nm (Branch et al. 2010a).

- ***Rotational Measurement Device (Alam et al. 2013)***

This device consists of 3 parts: (1) a femoral clamp and (2) a tibial splint to which are fixed inclinometers to measure rotation and (3) a boot with a torque wrench (Figure 1.17). Subjects are positioned at 90° of knee flexion. The Rotational Measurement Device allows for a better evaluation of femorotibial rotation compared to a system, which measures the angle of rotation at the foot. Measurement at the foot overestimated rotation in average by 136% (95% CI: -102% to -171%) compared to the device. The latter only slightly overestimated rotation (in average 2°: 95% CI -4.5-0.4°) when compared to electromagnetic sensors placed on the tibia (Alam et al. 2013). Intra-rater ICC of the device reached 0.9 (Alam et al. 2013).

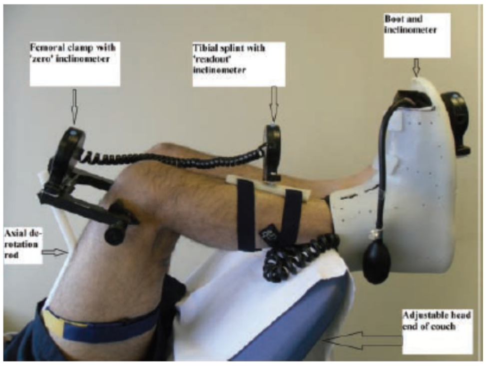


Figure 1.17: The Rotational Measurement Device (Alam et al. 2013)

2.3 Static multiplanar laxity

- ***Genucom Knee Analysis System (FARO Medical Technologies, Montreal, Ontario, Canada)***

This arthrometer was developed in the late 80's and allows to measure antero-posterior laxity and rotational and varus-valgus laxity (Oliver et al. 1987). A 6 degrees of freedom dynamometer indicates to the examiner the force or torque applied to the knee and an electrogoniometer measures the displacement. The ability of the device to measure rotation has been poorly explored. This may be partly explained by a poor reproducibility. Indeed, at 20° of knee flexion, the least significant difference reached 17.5° in tibial rotation; in other words, a change of 17.5° is required to indicate a real change in one subject's laxity (McQuade et al. 1989b).

- ***Vermont Knee Laxity Device (Uh et al. 2001)***

The Vermont Knee Laxity Device measures anterior, rotational and varus-valgus laxity. The subject lies supine with knees flexed at 20° and hips at 10, and the thighs are fixed with clamps at the femoral epicondyles (Figure 1.18). Rotation angle is measured on tibia through electromagnetic sensors. The intraclass correlation coefficient (ICC) is above 0.86 for internal (IR), external (ER) and total range (TR) of rotation (Shultz et al. 2007a). The 95% CI of the absolute measurement errors were evaluated to reach 5 to 7° respectively for internal and external rotation (Shultz et al. 2007a) but was not reported for ATD.

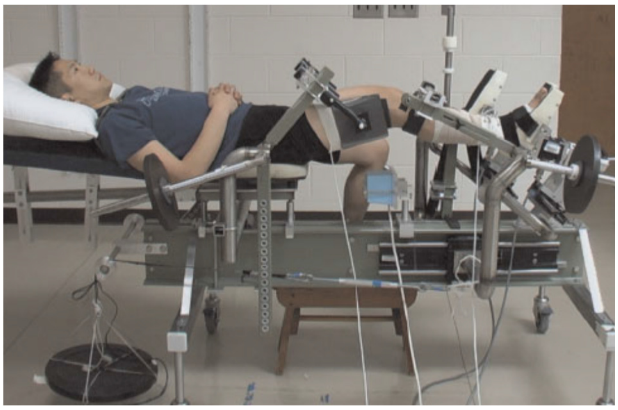


Figure 1.18: Device presented by Shultz et al. (Shultz et al. 2007a)

2.4 Dynamic laxity

Dynamic laxity measurement techniques considers knee kinematics after the application of a multidirectional force to the knee joint. The typical test in ACL injuries to assess dynamic laxity is the pivot shift test. Many efforts are currently made to objective this test with devices (Musahl et al. 2010c, Citak et al. 2011, Colombet et al. 2012, Zaffagnini et al. 2013). None has however yet given expected results due to the task complexity. Devices reporting dynamic laxity *in vivo* still require a manual application of the forces (Hoshino et al. 2007, Kubo et al. 2007, Lopomo et al. 2012). The examiner variabilities in the realisation of the pivot shift test is therefore still an issue for the reproducibility of these device. Indeed, the speed of the procedure, the abduction angle of the hip and the magnitude of the applied force vary between tests and examiners (Lopomo et al. 2013). To date, no device allow for a motorised application of the pivot shift test *in vivo*.

Dynamic knee laxity tests are much more complex to interpret than static laxity measurements. About 25 different parameters have indeed already been studied in the literature (Lopomo et al. 2013). However, to date, no consensus exists on which parameter best quantifies dynamic knee laxity. Because dynamic knee laxity devices are still at their early stage, it was not foreseen to measure it within this thesis.

Finally, laxity can also be assessed with navigation systems (Bull et al. 2002, Plaweski et al. 2006, Colombet et al. 2007, Pearle et al. 2009, Plaweski et al. 2011). They however require to fix sensors to the bones and thus can only be used before and after surgical intervention and they do not allow the standardisation of applied forces. Their use was consequently also not considered within this thesis.

2.5 Laxity measurement protocols, validity and reproducibility

It is commonly accepted that non-invasive arthrometers overestimate displacement due to the soft tissue deformation occurring during the test. They are however easier to use in the clinical practice than devices associated with imaging and also require less time and resources. Dynamic laxity measurements are still in their early stages so that static laxity measurements are nowadays the most confident measurements available. Moreover, static tests induce a less complex movement of the knee in comparison to dynamic tests, which may be easier to standardize and to control with an arthrometer.

While we may have enough hindsight on anterior knee laxity measurements, the same may not be true for static rotational knee laxity measurements. To date, few data report rotational knee laxity measurements *in vivo*. A systematic review reported that in 74 articles where knee rotation was measured under a controlled load, 61 used human cadavers and only 13 using living humans (Lam et al. 2012). From the short description of devices measuring rotational knee laxity in this chapter, it appears that they differ by patient positioning, measurement methods and testing protocols. These different aspects deserve a deeper analysis as proposed in ***Chapter 3***. This will allow to be able to correctly interpret static rotational knee laxity measurements and to set up a strategy to be able to use these arthrometers in the daily clinical practice and provide proper research.

Overall, patient positioning, measurement methods and testing protocols may influence the precision of the device, which remains poorly investigated. The determination of precision is, however, necessary to draw meaningful conclusions from any comparison study as it accounts for the measurement error. It is helpful to detect abnormalities occurring during a subject follow-up and helps to conclude if an observed difference is clinically relevant and meaningful. Studies are often limited to computations of ICCs, which depend strongly on data dispersion and do not provide a clear understanding of device precision. A conservative approach is the use of the minimum detectable change (MDC) (Weir 2005). The MDC represents the minimal required difference with a given instrument in a defined setting to be confident that a true change has indeed occurred. Thus, the precision of the GNRB® and the Rotameter is foreseen in ***Chapter 5***.

3. Knee laxity in the non-injured knee

Physiological laxity has been more extensively studied due to the recent development of specific arthrometers with improved measurement characteristics. It represents the amount of laxity which is considered to lie within the « normal » range. It should not be confused with knee mobility, evaluated by the *genu recurvartum* which is often cited in the context of ACL injuries and hyperlaxity (Uhorchak et al. 2003). Although limited data are available comparing recurvartum and laxity, both seem to be weakly correlated (Lin et al. 2009).

3.1 Physiological laxity, knee function and injuries

Excessive physiological knee laxity is thought to be a risk factor for non-contact ACL injuries. The healthy contralateral knee of ACL-injured patient indeed displays increased anterior laxity compared to healthy knees of a control group (Woodford-Rogers et al. 1994, Uhorchak et al. 2003). This excessive physiological laxity may have place these subjects at risk for an ACL rupture as shown by a 4 year prospective study (Uhorchak et al. 2003). The average anterior physiological laxity at 134N was 3.9 ± 1.5 mm for non-injured subjects (n= 606) and 4.8 ± 1.9 mm for subjects that had a non-contact ACL injury during the 4 years of follow-up (n=19; p=0.03).

The healthy contralateral knee of ACL-injured patients also seem to display greater IR than healthy knees of a control group (Branch et al. 2010a). Surprisingly, the authors found that the former displayed less ER than the latter. As a consequence, the healthy contralateral knee of ACL-injured patients did not display significantly greater total range of knee rotation than healthy control knees. The finding that the healthy contralateral knee of ACL-injured patients have greater rotational knee laxity than healthy subjects thus need to be confirmed.

Excessive physiological laxity may have place subjects at risk for an ACL rupture because of a modified neuromuscular control. It is commonly accepted that knee laxity has no relation to knee function. In fact, the literature specifies that the amount of SSD in knee laxity observed after ACL reconstruction is not linked to clinical outcomes (Higuchi et al. 2003, Kocher et al. 2004, Pollet et al. 2005). Nevertheless, subjects with excessive physiological knee laxity have been reported to have movement patterns associated with non-contact ACL injury mechanisms. They display greater hip and knee movements in the transverse, sagittal and frontal planes during drop landings (Shultz et al. 2009b, Torry et al. 2011).

Even though the influence of physiological knee laxity on knee function has not been clearly established, several studies suggest that it could be related to ACL injury risk and that it could even determine the outcome of ACL reconstructive surgery (Branch et al. 2011, Kim et al. 2011, Kim et al. 2014). After ACL reconstruction with a bone-patella-tendon-bone graft, patients identified with an increased physiological laxity have lower Lysholm (Kim et al. 2011, Kim et al. 2014) and IKDC (International Knee Documentation Committee) subjective (Branch et al. 2011, Kim et al. 2011, Kim et al. 2014) scores. As preoperative scores were not reported, it remains unclear whether this finding is the consequence of the ACL reconstruction or of the injury itself.

More data need to be gathered to confirm these preliminary conclusions. The study of physiological laxity may be of particular interest to detect at-risk subjects for ACL injuries and poor reconstruction outcomes if confirmed that patients with an ACL injury display a greater physiological laxity than healthy subjects. This will be the purpose of ***Chapter 6***.

3.2 Influencing factors

To date, no normative references exists in the literature regarding physiological laxity. Actually, physiological laxity is complex to analyse as it is influenced by several individual parameters which makes it more difficult to establish reference values. As a consequence, it may be problematic to compare absolute values of individuals with different characteristics as it may lead to incorrect conclusions.

The characteristic which is the most frequently discussed in the literature is sex, since women are supposed to have higher laxity compared to men. Some studies do not confirm this observation, reporting differences of less than 0.3 mm (Sharma et al. 1999, Scerpella et al. 2005), while others do, but based on differences of less than 1.5 mm (Rozzi et al. 1999, Uhorchak et al. 2003, Zyroul et al. 2014). Only one group of researchers reported a difference between males and females superior to 2.5 mm (Shultz et al. 2007b). Since the precision of arthrometers is rarely reported, the question remains open. On the other hand, sex differences regarding rotational laxity is less controversial (Hsu et al. 2006, Park et al. 2008, Branch et al. 2010a, Almquist et al. 2013). It has been shown that women have up to 40% higher knee rotation compared to men (Park et al. 2008), which could represent a risk factor for the higher ACL injury incidence in women.

Other parameters have been shown to influence physiological knee laxity. Body mass seems to have a considerable impact on rotational laxity (Shultz et al. 2012). Increased anterior knee laxity in the paediatric population is generally well accepted (Baxter 1988, Flynn et al. 2000, Hinton et al. 2008). Similar observations have been made regarding rotational laxity (Baxter 1988). Knee laxity then develops during knee maturation and stabilises around 14 years for girls and around 16 years for boys (Baxter 1988, Flynn et al. 2000, Hinton et al. 2008). Unlike adults, no difference has been observed in anterior knee laxity in the paediatric population between boys and girls (Baxter 1988, Flynn et al. 2000). As regards to changes in knee laxity at adult age, only few and contradictory data exist in the literature (Shultz et al. 2012, Almquist et al. 2013, Zyroul et al. 2014). Shultz et al. reported that older subjects had lower laxities. However, the authors did not include in their study a large range of age: males were 22 ± 3 years old and females were 21 ± 3 years old (Shultz et al. 2012). In a study including 521 healthy subjects aged from 15 to 74 years old, Zyroul et al. reported no effect of age on anterior knee laxity (Zyroul et al. 2014). A similar pattern was observed for rotational knee laxity where no significant influence of age has been observed in adulthood (Almquist et al. 2013).

Another factor, which could have an influence on the physiological knee laxity, is the menstrual cycle (Shultz et al. 2004, Shultz et al. 2010). A systematic review of the literature however revealed that: 6 out of 9 studies found no significant variation of anterior knee laxity throughout the menstrual cycle, 2 out of 9 studies reported a significant variation of knee laxity during the menstrual cycle of about 0.5 mm and the last study of 1.5 mm (Zazulak et al. 2006). The variations observed in anterior knee laxity across the cycle are thus minor and the ability of existing devices to detect such little differences can be questioned. As for rotational knee laxity, no variation amongst the menstrual cycle could be observed (Shultz et al. 2011).

An association may also exists between lower extremity alignment and anterior knee laxity. In a first study, Shultz et al (Shultz et al. 2009a) demonstrated that a greater genu recurvartum and a greater navicular drop were the strongest predictors of a greater anterior knee laxity. In a second study, the authors performed cluster analyses to determine the different knee laxity profiles observed in healthy subjects considering anterior, rotational and varus-valgus knee laxity as well as genu recurvatum (Shultz et al. 2012). The subjects in the cluster where all laxities were increased compared to subjects with decreased laxities had greater navicular drop (increased: 7.1 ± 5.0 mm, decreased: 5.2 ± 3.1 mm), lower body mass index (BMI) (increased: 21.3 ± 2.5 kg/cm^2, decreased: 26.3 ± 3.8 kg/cm^2), lower Q-angle (increased: 12.9 ± 3.9°, decreased: 11.6 ± 4.7°), lower tibial torsion (increased: 14.8 ± 7.3°, decreased: 18.6 ± 5.2°), lower quadriceps peak torque (increased: 2.3 ± 0.4 Nm/kg, decreased: 2.5 ± 0.4 Nm/kg) and shorter femur length (increased: 41.3 ± 2.6 cm, decreased: 44.5 ± 2.5 cm). Some differences are however minor and their clinical meaning is not yet established.

It remains unclear which individual parameter truly influence knee laxity measurements. Furthermore, the different laxity types (sagittal and rotational) have recently been shown to be only weakly correlated (Shultz et al. 2007b). A multiplanar approach may thus be preferable to describe how knee laxity is associated with ACL injuries especially as rotational knee laxity is recognized to be under the influence of the ACL (Wang et al. 1974, Shoemaker et al. 1985) and is part of the ACL injury mechanism (Olsen et al. 2006). The consideration of both laxities may provide with complementary information and should allow to establish more detailed individual knee laxity profiles. ***Chapters 4 and 5*** of the present thesis will help to clarify this situation to be able to establish individualised normative references.

4. Knee laxity in the injured knee: diagnosis of ACL injuries with arthrometers

4.1 Diagnostic performance of static non-invasive devices

Final diagnosis is often the sum of several individual clinical signs (Fowler et al. 1989). As manual tests may only be adequate when performed by experienced surgeons, laxity measurements could be used as a complement in the diagnosis of ACL injuries. In theory, the use of an arthrometer is indeed preferable to clinical examination as it should overcome their drawbacks such as the examiner-dependency. However, as for the clinical examination, an incorrect execution of laxity tests can lead to an erroneous interpretation of the diagnosis. For example, knee laxity measurement in the acute phase of the injury where the knee can be swollen and painful is less reliable and should be interpreted with caution.

The diagnosis of ACL injuries with arthrometers is based on the SSD between the injured and the healthy knee. The IKDC objective score currently represents the “gold standard” to describe the objective function of the knee. It allows for a classification of laxity in 4 grades: A, B, C and D. A SSD in anterior laxity inferior to 3 mm is classified as normal (grade A), between 3 and 5 mm as nearly normal (grade B), between 6 and 10 mm as abnormal (grade C) and superior to 10 mm as severely abnormal (grade D). Since its last update, this classification has never been questioned and it is generally accepted that a SSD greater than 3 mm relate to an ACL injury regardless of the device used to measure anterior knee laxity.

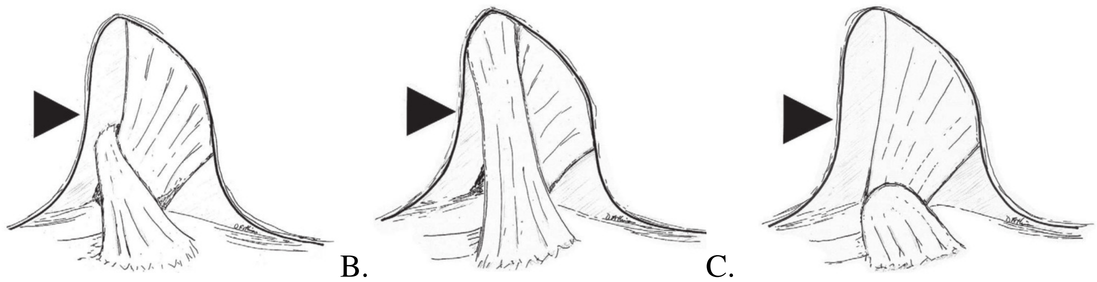
With this threshold of 3 mm, a meta-analysis reported the sensitivity and specificity of the KT-1000®, the Stryker Knee Laxity Device and the Genucom to detect complete ACL tears (van Eck et al. 2013a). The greatest sensitivity and specificity (93%) was reached with the KT-1000® at a maximal manual force (van Eck et al. 2013a). The Stryker Knee Laxity Device had a lower sensitivity of 82% and a lower specificity of 90% while the Genucom had a sensitivity of 74% and a specificity of 82% (van Eck et al. 2013a). As for the Rolimeter, its sensitivity of 89% and specificity of 95% are similar to the KT-1000® in chronic isolated ACL injuries (Ganko et al. 2000). Finally, the sensitivity and specificity of the GNRB® to detect non-isolated ACL tears is of 70 and 99%, respectively, for a SSD of 3 mm (Robert et al. 2009). For a SSD of 1.5 mm, sensitivity and specificity to detect anteromedial bundle rupture reached 80 and 87% at 134N respectively (Robert et al. 2009).

The diagnosis of ACL injuries currently mainly focuses on anterior laxity measurements. Concomitant measure of additional laxities such as rotational knee laxity to refine the diagnosis has been proposed (Di Iorio et al. 2014) as the ACL plays a role in knee internal rotation (Nielsen et al. 1984, Lane et al. 1994). However, this approach has never been reported and no real consensus exists on the minimal SSD to reach in IR to diagnose an ACL injury. Cadaveric studies revealed that the section of the ACL led to 2.4 to 4° increase in rotation in knee flexion angles below 30° (Nielsen et al. 1984, Lane et al. 1994). Above this degree, the increase in rotation induced by the lesion was not detectable anymore (Zarins et al. 1983, Shoemaker et al. 1985, Andersen et al. 1997). First in vivo studies could demonstrate a similar increase of rotation in the injured knee by 10% (3°) compared to the healthy knee (Markolf et al. 1984). These first results thus suggest that ACL injuries induce only small increase in rotation which highlights the need of precise arthrometers to diagnose ACL injuries. The ability of rotational knee laxity measurements to detect an ACL injury will thus be studied in ***Chapter 7***.

Furthermore, the different characteristics of the force-displacement curve (i.e. slope, representative of knee stiffness) have not been deeply explored yet in the context of ACL injuries although it was described in the 80's (Markolf et al. 1984, Shino et al. 1987, Steiner et al. 1990). With the commercialization of the GNRB®, few teams have started again to study the slope of the force-displacement curve (Robert et al. 2009, Lefevre et al. 2014), an aspect that will also be investigated in ***Chapter 7***.

4.2 Complexity of ACL injuries and influence on diagnosis

Studies, which have investigated the diagnostic performance of arthrometers, have often included patients with complete ACL lesions and excluded patients with a specific condition (*i.e.* non-complete ACL tears and/or associated lesions). This approach may have the consequence to inflate the accuracy of the diagnosis, by selecting the easiest cases to detect, and may prevent the physician from a correct conclusion. Associated injuries to menisci, cartilage and/or other knee ligaments are reported in 60% of ACL ruptures (Granan et al. 2009) of which some may influence knee laxity measurements (Musahl et al. 2010b).



A. B. C.

Figure 1.19: Subtypes of ACL tears . A.ACL healing to the posterior cruciate ligament B. ACL healing to the intercondylar notch C. ACL total resorbed (Crain et al. 2005)

Several subtypes of ACL lesions have been described in the literature. Based on arthroscopic classification, it is possible to distinguish lesions of a single bundle (the antero-medial bundle being more often concerned than the postero-lateral one) with or without a functional remnant, complete lesions with total resorption of the ligament or with a healed remnant on the notch or the PCL (Figure 1.19) (Crain et al. 2005). These different types of lesion can influence the SSD observed in anterior and rotational knee laxity measurements (Crain et al. 2005, Panisset et al. 2008, Beldame et al. 2012, Nakase et al. 2013, Lefevre et al. 2014). Complete lesions where the ligament has totally disappeared are the easiest to diagnose: they are frequently observed in patients with a chronic lesion, are more often associated with meniscal lesions and present greater SSD (Panisset et al. 2008). Patients with a ligament remnant healed on the PCL have a similar SSD in anterior laxity than the one with complete ruptures (Beldame et al. 2012). Lesions with conservation of the anteromedial bundle are more stable anteriorly (Beldame et al. 2012). This is in accordance with the fact that the antero-medial bundle restraints chiefly anterior translation at 30° of knee flexion (Gabriel et al. 2004). Finally, lesions with a healing on the notch pattern are the most stable ones in anterior knee laxity (Beldame et al. 2012). Despite differences observed in the SSD between the different ACL subtypes, a clear threshold has never been established to be able to differentiate between them at the time of the diagnosis. Regarding rotational knee laxity, no study report whether the subtype of ACL lesion influence the SSD. These aspects will thus be investigated in ***Chapter 7***.

5. Aims of the thesis

The general purpose of this thesis is to increase the knowledge of ACL-injured patients as well as on knee laxity measurements on an individual basis mainly through the implementation of individualized knee laxity profiles considering both anterior and rotational knee laxity measurements.

First, ***Chapter 2*** aims to present data from an intra-hospital registry which was set up during the present thesis. Its aim is to identify subtypes of ACL-injured patients and to understand how gender, age, sport activity and previous ACL injuries have an influence on the decision to operate a patient or not.

The next chapters will study anterior and rotational knee laxity. Available data on static rotational knee laxity are sparse and widely variable due to device discrepancies. ***Chapter 3*** therefore aims to review these data to understand how device discrepancies can affect rotational knee laxity variability and how to overcome this drawback.

Normative references for physiological laxity in healthy subjects have never been reported although they are crucial to fully understand pathologies and treatment outcomes. ***Chapter 4*** will analyse which individual characteristics amongst gender, age, height and weight, influence static rotational knee laxity and ***Chapter 5*** will propose a methodological approach to create individualized knee laxity scores and profiles combining both anterior and rotational knee laxity. Simultaneously, the precision of the GNRB® and the Rotameter will be reported.

Static anterior knee laxity has been reported to be higher in the contralateral knee of patients compared to healthy controls. The ***Chapter 6*** will thus determine whether the contralateral knees of ACL injured patients have different knee laxity profiles (combination of anterior and rotational knee laxity) than healthy control knees and establish thresholds to discriminate physiological laxity between both groups.

Finally, the diagnosis of ACL injuries with arthrometers has typically been reported with the SSD in ATD. The purpose of ***Chapter 7*** is to determine whether taking into consideration rotational knee laxity as well as the slope of the force-displacement curve improves sensitivity and specificity of the diagnosis of ACL injuries. It will furthermore investigate the influence the ACL subtype of tear on the sensitivity the diagnosis of ACL injuries and investigate whether it is possible to establish thresholds to differentiate between them at the time of the diagnosis.

Finally, ***Chapter 8*** consists of a general discussion, which critically reviews the results from the current thesis and includes recommendations and future perspectives regarding the use of knee laxity measurements.

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Chapter 2
There is no such thing like a single ACL injury: profiles of ACL-injured patients

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Abstract:

Background: Current ACL registries rarely include nonoperatively treated patients thus delivering an incomplete picture of the ACL-injured population. The aim of this study was to get an image of the population and treatment decision of an intrahospital registry. Our hypotheses were that patient-specific subtypes can be identified and that the percentage of operated patients differs between them.

Material and methods: 346 operated and nonoperated patients were included from March 2011 to December 2013. Standardized questionnaires allowed for data collection on gender, age, sports practice and previous ACL injuries. Chi-square tests allowed to compare these parameters between genders and age groups. A cluster analysis was computed to determine profiles of patients with similar characteristics.

Results: Three age groups were considered (I: ≤20; II: 21-35; III: ≥36 years). For males, the highest frequency of injuries was noted in group II with a greater proportion of injuries compared to females. In group III, more females were injured than males. Before injury, 54% patients were involved in competitive sports. Males were more likely to be injured in pivoting/contact sports before 35 and females during recreational skiing after 35. 21% of the patients had had a previous ACL injury. The percentage of surgical treatment was superior to 80% in patients under 35 years involved in competitive sports, of 60-80% for those not involved in competitive sports and inferior to 60% for patients above 35 years.

Discussion: Systematic data collection allowed to identify specific subtypes of ACL-injured patient according to gender, age, previous ACL injury and preinjury level of practice. The decision-making process for or against ACL reconstructions at time of presentation depended on these characteristics. Consideration of these parameters will serve as a basis for an individualised treatment approach and a better understanding of patients at risk for ACL injuries.

Level of evidence: III

Keywords: Anterior cruciate ligament, surgery, epidemiology

1. Introduction

ACL injuries caused 41937 reconstruction procedures in France in 2013 ((http://www.atih.sante.fr/statistiques-par-ghm-0) , with a tendency on the rise (Beaufils et al. 2009). This is similar to many other countries where national or healthcare-system specific ACL registries have been successfully developed (Csintalan et al. 2008, Granan et al. 2008, Granan et al. 2009, Lind et al. 2009, O'Leary 2013, Boyer et al. 2014). Such registries provide feedback to the physicians in order to improve treatment outcomes, to detect unreliable procedures and devices, and to identify outcome-associated prognostic factors (Engebretsen et al. 2009). However, they rarely include nonoperatively treated ACL-injured patients and thus deliver an incomplete picture of the ACL-injured population.

Although not all patients with an ACL injury need to undergo surgery, the line of distinction between surgical and nonsurgical treatment has not clearly been drawn yet (Daniel et al. 1994, Fithian et al. 2005, Fithian 2014, Grindem et al. 2014). The current treatment decision is based on recommendations of good clinical practice which were developed through the accumulation of surgical expertise (Beaufils et al. 2009). Little is however known about how such guidelines are put into practice because of a lack of detailed descriptive data.

A systematic, nationwide recording of ACL-injured patients may be difficult to establish in some countries because of the particular characteristics of different healthcare systems. Therefore, the creation of center- or community-based registries and clinical pathways within treating institutions may be an additional strategy to provide (1) an overview of the encountered spectrum of ACL-injured patients (Maletis et al. 2013), (2) an overview of the medical practice as well as of the compliance with recommendation guidelines.

The purpose of the present investigation was to characterize a prospective cohort generated from an in-house registry of ACL-injured patients seen in a single institution between March 2011 and December 2013. The analyses aim to get an image of the involved patients and the associated treatment decision. Our primary hypothesis was that patient specific subtypes could be identified. The secondary hypothesis was that the percentage of surgical treatment differs between these subtypes.

2. Material and methods

2.1 Participants

All patients with an ACL injury visiting our setting were proposed to enter a systematic and standardized follow-up regardless of the treatment decision (operative or nonoperative). The inclusion criterion was an ACL tear, which was diagnosed clinically and documented on magnetic resonance imaging (MRI). Between March 2011 and December 2013, 423 patients visited our institution of which 346 (82%) agreed to participate to the study and signed a consent agreement according to the National Ethics Committee for Research which approved the study protocol (N°201101/05 version 1.0). Data acquisition was notified to the National Data Protection Committee.

2.2 Data collection

Data were collected prospectively by surgeons, physiotherapists, study nurses and researchers and were saved in a secure database. At their first visit, patients were asked to fill in a standardized questionnaire indicating their personal data, their involvement in a sport before the injury, their previous lower leg injuries and the circumstances of their ACL injury. The preinjury level of practice was classified according to the categories: competitive sport, recreational sport or no regular sport (less than once a week). Four grades were used to classify the level of sport inducing the injury: level-I sports (handball, soccer, basketball), level-II sports (volleyball, gymnastics, tennis, alpine skiing), level-III sports (running, cycling, swimming) (Grindem et al. 2014) and non sport-related injury.

2.3 Treatment decision

The involved orthopaedic surgeons were fellowship-trained with a clinical experience of more than 10 years after national board certification. The medical visit included anamnestic data, which evaluated patient expectations, symptoms of functional instability and pain, clinical examination as well as imaging procedures including standard radiographs and MRI. The decision regarding surgical or non-surgical treatment was oriented according to commonly accepted guidelines of good clinical practice (Haute Autorité de Santé 2008, Beaufils et al. 2009): functional instability, age, professional and sports exposure, time from injury, laxity, associated meniscus and/or cartilage lesions, and social and occupational expectations.

2.4 Patient characterization

Three groups of patients were defined according to age: under 21 years (group I), between 21 and 35 years (group II) and over 35 years (group III). The rationale behind group I was the increasing evidence both of a gender-specific injury profile with particularly elevated injury rates in young females and an increased risk for recurrent injuries in this post-adolescent or young adult population (Lind et al. 2012, Nordenvall et al. 2012). Group II corresponds to a population which is generally highly active in organized sports and particularly in pivoting (level-I) sports. In group III, individuals usually refrain from level-I and / or organized sports and reorient their physical activity to more leisure-time activities.

2.5 Statistical analysis

Statistics were performed using version 20.0 of the SPSS software. Chi-square tests were used to analyse the distribution of genders and age groups in (1) preinjury level of practice, (2) level of sport inducing the injury, (3) previous ACL injuries and (4) treatment decision. A two-step cluster analysis was computed to determine the main subtypes of patients represented in the studied population considering age, gender, previous ACL injuries and activity. Activity is here defined either by the preinjury level of practice or by the level of sport inducing the injury. As there was no *a priori* on which of these parameters was the most efficient to determine patient subtypes, 2 different cluster analyses were computed. The model leading to the highest silhouette coefficient, which indicates the quality of clusters regarding both their cohesion and separation, was considered as the best one. The percentage of operated patients was calculated in each identified subtype and compared between groups with the use of a chi-square test. Significance was set at $p<0.05$ for all analyses.

3. Results

3.1 Age at ACL injury and gender distribution

Among the 365 patients who gave their consent, data were available for 346 patients (359 injuries). The cohort consisted of 222 males (64%; body mass index: 25.2±3.6 kg/cm^2) and 124 females (36%; body mass index: 24.3+4.6 kg/cm^2). The average age at injury was 30±11 (men: 28±10; women: 32±12, p<0.01) (Figure 2.1, Table 2.1).

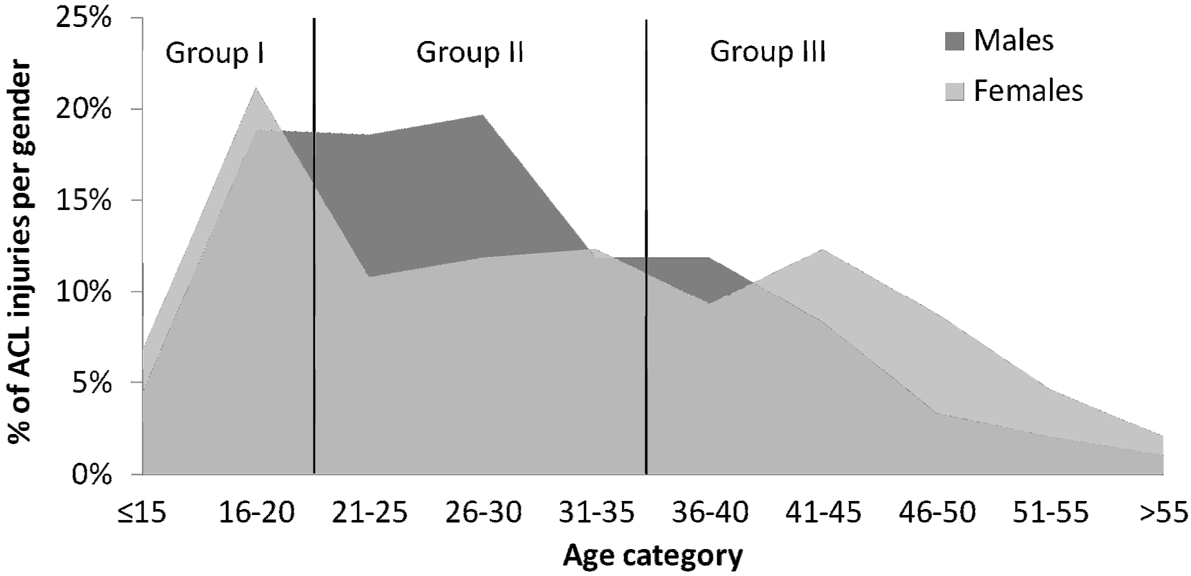

Figure 2.1: Distribution of ACL injuries per age category and gender. Age at injury and not age at surgery was considered. 3 groups of patients were defined: group I (≤ 20 years); group II (21-35 years); group III (≥ 36 years).

Table 2.1: Distribution of ACL injuries per identified age groups and gender . [a] proportion of females significantly different than proportion of males for this age group; p<0.01

	Age group		
	I ≤ 20 years	II 21-35 years	III ≥ 36 years
Males	51 (23%)	112 (50%)	59 (27%)
Females	35 (28%)	43 (35%)[a]	46 (37%)[a]

3.2 Pre-injury level of practice

Prior to injury, the majority of patients were involved in regular physical activity: 188 (54%) practiced competitive sports, 124 (36%) practiced recreational sports and 34 (10%) did not practice physical activity on a regular basis. The distribution of the preinjury level of practice was age and gender-dependent (Figure 2.2; $p<0.01$). Only 29% of the males aged over 35 were engaged in competitive sports (males younger than 35 years: 73%; $p<0.01$). Only 29% of females aged over 21 were engaged in competitive sports (females younger than 21 years: 68%; $p<0.01$).

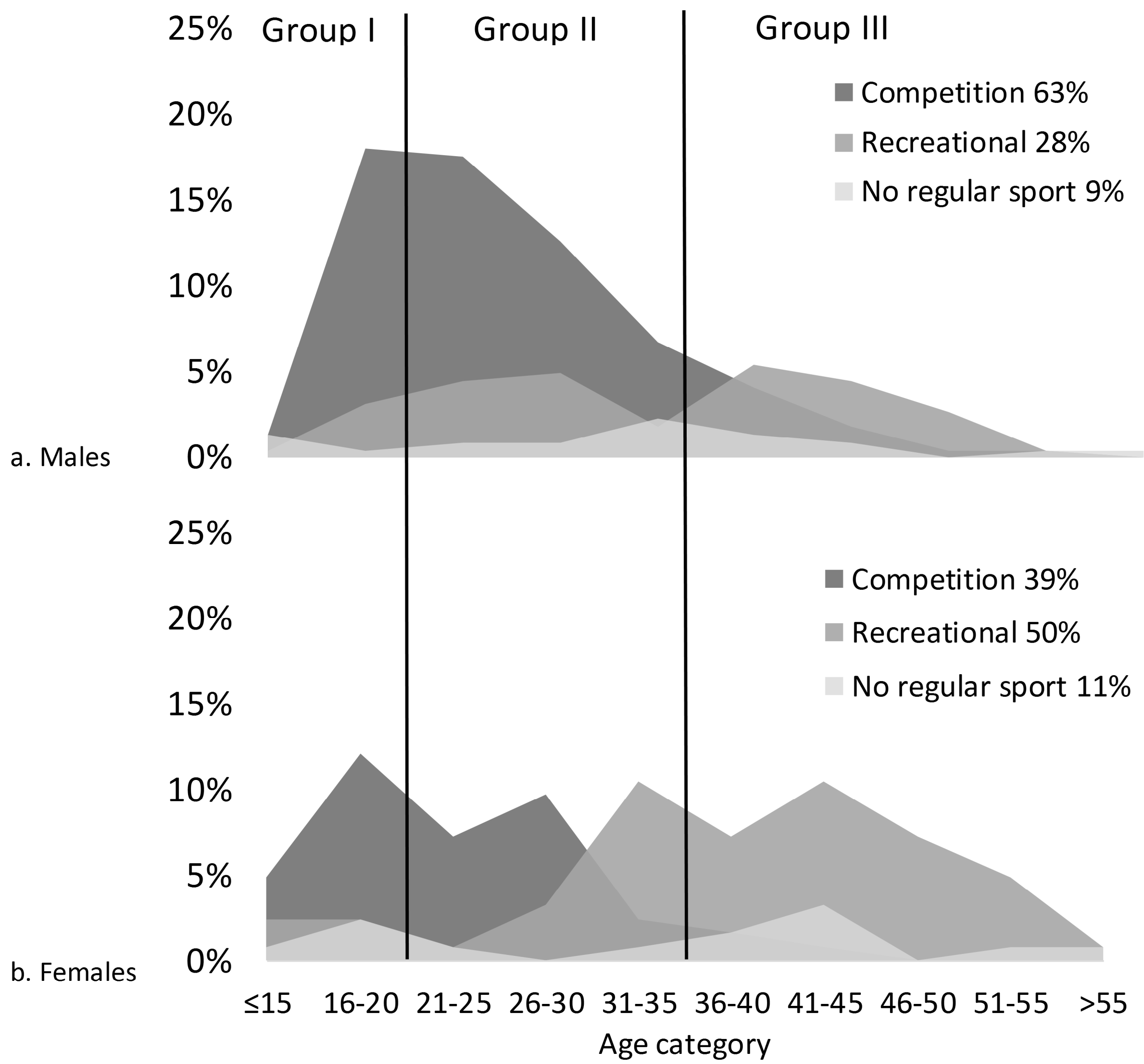

Figure 2.2: Distribution of the pre-injury level of practice per age category and gender.

3.3 Mechanism and level of sport associated with the injury

Non-contact injuries represented the majority of injuries observed (n=264, 74%). ACL injuries mainly occurred during a sporting activity (n=312, 87%): 122 (34%) during football, 80 (22%) during skiing, 29 (8%) during basketball, 28 (8%) during handball and 53 (15%) during other sports. The distribution of sport levels at injury was age- and gender-dependent (p<0.01; Figure 2.3). Males were more likely to be injured in level-I sports than females (67% versus 27%, p<0.01). More specifically, males were more likely to be injured in level-I sports before 35 (77% in age group I+II vs 31.5% in group III; p<0.01) and females were more likely to be injured in level-II sports after 35 (38.5% in group I+II vs 68% in group III; p<0.01).

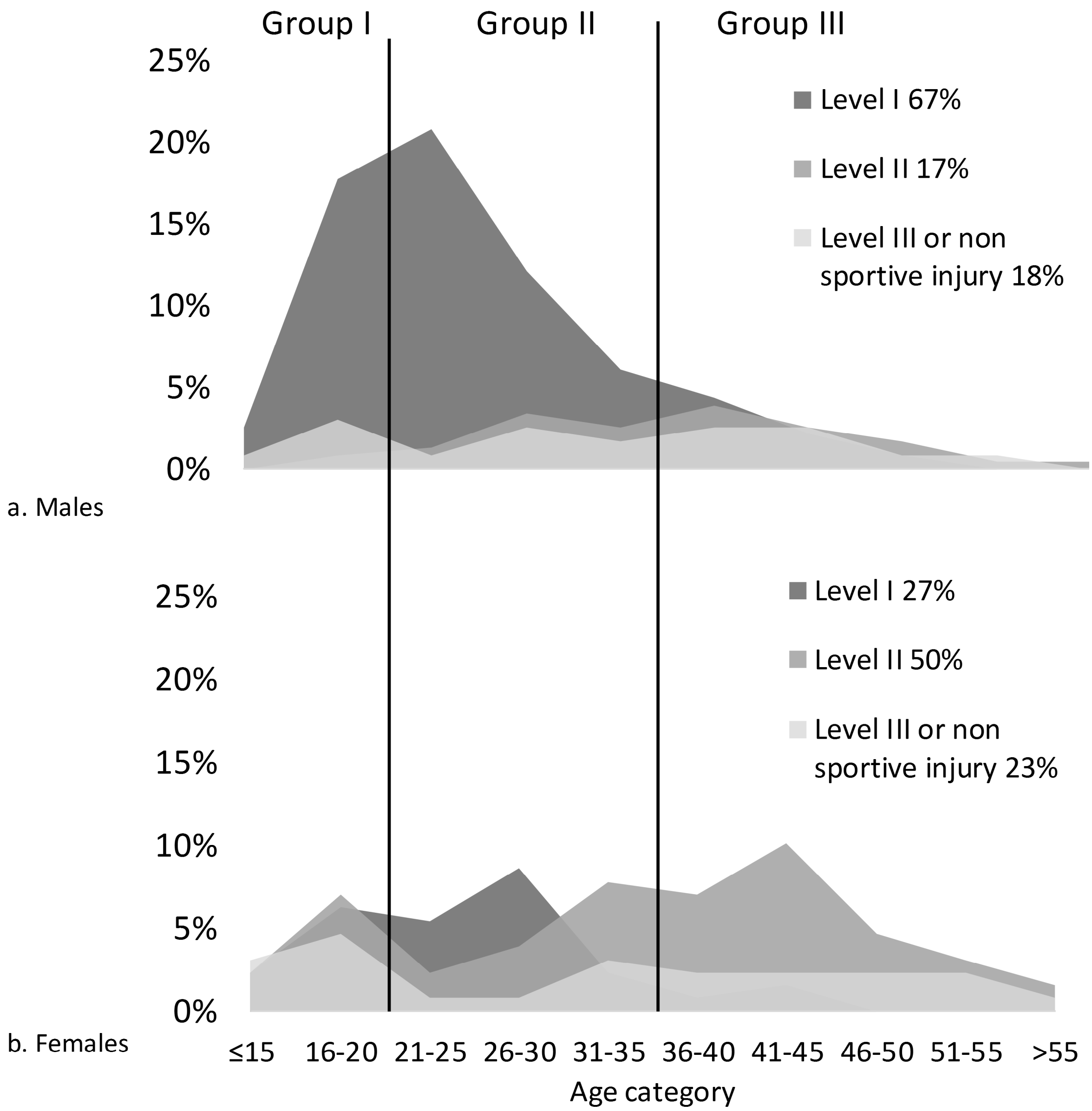

Figure 2.3: Distribution of the level of sport inducing the ACL injury per age category and gender.

3.4 Previous (recurrent/contralateral) ACL injuries

Overall, 72 patients (44 males / 28 females) out of 346 (20.8%) had a previous ACL injury: 32 patients had one recurrent tear (9.2%), 30 had one contralateral ACL injury (8.7%), 10 had more than one previous ACL injury or sprain (2.9%). The distribution of total previous ACL injuries, recurrent ruptures and contralateral ACL injuries did not differ between age groups and gender (Table 2.2).

Table 2.2: Distribution of previous ACL injuries per age group and gender.

		Age group			
		I ≤ 20 years	II 21-35 years	III ≥ 36 years	Total
		n (%)	n (%)	n (%)	n (%)
Males	Previous ACL injury (total)	10 (18%)	25 (21%)	9 (18%)	44 (20%)
	- *Ipsilateral*	*6 (11%)*	*14 (12%)*	*3 (6%)*	*23 (11%)*
	- *Contralateral*	*4 (7%)*	*9 (8%)*	*5 (10%)*	*18 (8%)*
	- *Both knees*	*0 (0%)*	*2 (2%)*	*1 (2%)*	*3 (1%)*
Females	Previous ACL injury (total)	9 (29%)	10 (23%)	9 (18%)	28 (23%)
	- *Ipsilateral*	*6 (19.5%)*	*2 (4.5%)*	*4 (8%)*	*12 (10%)*
	- *Contralateral*	*2 (6.5%)*	*6 (13.5%)*	*5 (10%)*	*13 (10.5%)*
	- *Both knees*	*1 (3%)*	*2 (4.5%)*	*0 (0%)*	*3 (2.5%)*

3.5 Treatment indication

Overall, 267 ACL reconstructions (74%) were performed, 87 patients were treated nonoperatively and 5 were lost to follow-up after their first visit. The distribution of treatment is presented in Figure 2.4 according to gender and age. Males had more operative treatments than females (81% vs 66%; p<0.01) and young individuals were also more likely to undergo surgery (Age group I: 89%, II: 81%, III: 54%; p<0.01). Patients were more likely to be operated if they practiced a competitive sport (87% *vs.* 61.5% for recreational sports; p<0.01). The treatment was also sport dependent (level-I sports: 87% of operative treatment, level-II sports: 70.5%, level-III sports or no sport: 59%; p<0.01).

The cluster analysis with the highest silhouette coefficient identified 8 profiles of similar patients (Table 2.3) according to gender, age category, preinjury level of practice and previous ACL injuries. Each profile represents 9 to 18% of the population studied. The distribution of operated patients was different amongst identified groups (p<0.01). The first 3 profiles (41%

of the population studied) included patients from age groups I and II practicing a competitive sport. The percentage of operated patients was superior to 80%. This percentage decreased to 60-80% in profiles 4 to 6 which mainly included patients younger than 35 years old not involved in competitive sports. Finally, in profile 7 and 8 mainly composed of patients above 35 years, the percentage of operated patients was inferior to 60%.

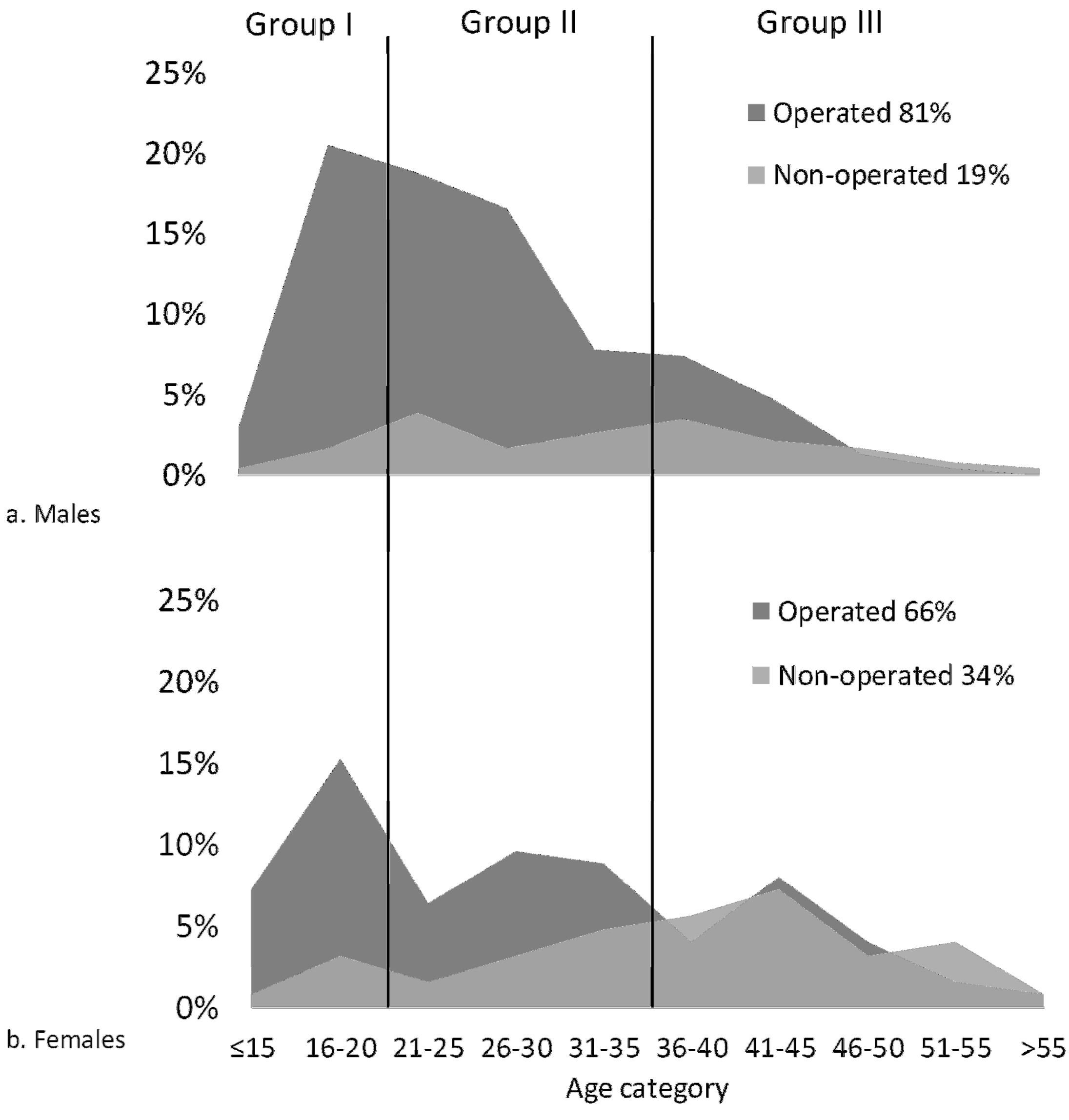

Figure 2.4: Distribution of treatment decision per age category (5 drop out out of 359 injuries). The percentage indicated represent the percentages of males (M) and females (F) concerned by operative treatment in each age category.

Table 2.3: Identification of subtypes of patients and percentage of patients receiving surgery according to gender, age category, pre-injury level of activity and previous ACL injuries.

Subtype	Group characteristics	% of population		% of patients receiving surgery
1	Males Competitive sport Age group I No previous ACL injury		10%	94%
2	Males Competitive sport Age group II No previous ACL injury	41 %	18%	89%
3	Females Competitive sport Age group I and II With or no previous ACL injury		13%	86%
4	Males Competitive sport All age groups With previous ACL injuries		9%	79%
5	Males and females Recreational sport or no regular sport for age group I Recreational sport for age group II No previous ACL injuries	33%	15%	75%
6	Males and females Recreational sport or no regular sport All age groups With previous ACL injuries		9%	69%
7	Males and females No regular sport for age group II Competitive sport or no regular sport for age group III No previous ACL injuries	26%	10%	59%
8	Males and females Recreational sport Age group III No previous ACL injury		16%	49%

4. Discussion

The concomitant analysis of gender, age, preinjury level of practice and previous ACL injuries allowed to establish an image of ACL-injured patients seen in our institution through the identification of patient specific subtypes. The percentage of operated patients varied significantly between these subtypes. The percentage of surgical treatment was superior to 80% in patients under 35 years of age involved in a competitive sport. This percentage decreased to 60-80% in patients younger than 35 years, but not involved in a competitive sport and with previous ACL injuries, and to less than 60% for patients above 35 years. The typical profiles of patients may serve in the future as a basis to improve our line of distinction between surgical and nonsurgical treatment through an individualised approach.

Our cohort showed strong similarities with previously published epidemiological data from ACL-reconstruction registries (Csintalan et al. 2008, Granan et al. 2008, Granan et al. 2009, Lind et al. 2009, Magnussen et al. 2010, Maletis et al. 2011, Janssen et al. 2012). A similar amount of injuries related to sport (74%) was observed compared to previous reports (72-88%) as well as a peak of injuries in females under the age of 21 and in males under 30. However, the inclusion of nonoperatively treated patients allowed to observe a second peak of injuries in females over 35 (age group III). They represent females, with no regular sports participation or involved in recreational sporting activities with a low demand for the knee such as level-III sports (swimming, running, cycling…), for whom the majority of ACL injuries originated from recreational alpine skiing. So far, a similar peak could only be identified in the Danish Ligament Reconstruction Registry in females (Lind et al. 2009) which may be the consequence of a higher rate of reconstructions for this specific population in Denmark. The reason for such injuries has not been clearly investigated, but they may have been caused, among other factors, by lack of physical fitness (Ruedl et al. 2011). As such, a significant amount of these skiing injuries may have been preventable. In this patient subtype, the difficult decision-making process has been previously reported (Hetsroni et al. 2013). These patients were mainly represented in subtype 7 and 8 and half of these patients were recommended for a nonoperative treatment despite their frequent desire to continue recreational alpine skiing. The primary nonoperative strategy in group III was based on the fact that modifications of the activity level towards avoidance of activities with high demands on the knee may facilitate to cope with an ACL-injured knee (Kostogiannis et al. 2007). For older patients with a lower activity, nonoperative treatment has indeed proven to be efficient (Buss et al. 1995).

The observed overall ratio of 74/26 operated vs. nonoperated patients is similar to some previous publications. In his early study, Noyes et al. introduced the “rule of thirds” concept, meaning that only one third of patients are able to compensate adequately without any surgery, one third will compensate but will have to give up significant activities, and one third will perform poorly and require future surgery (Noyes et al. 1983). This is in line with later studies published by Frobell (Frobell et al. 2010) and Grindem (Grindem et al. 2014). They reported a percentage of nonoperatively treated patients of 30% in their prospective studies addressing the decision-making process after ACL injury. In Fithian's study (Fithian et al. 2005), the percentage of nonoperated patients was higher with 54 %. In a more recent publication, Collins et al. reported a percentage of nonoperated patients of 77% the 3 first years after an ACL injury which may be explained by a high average age of the cohort (mean age: 47 years) (Collins et al. 2013). Currently, no evidence-based arguments exist to recommend a systematic surgical reconstruction to every patient with an ACL injury (Delince et al. 2012, 2013, Smith et al. 2014, Eggerding et al. 2015). As such, our percentage of operated patients may seem high, but is similar to some studies. Furthermore, the analysis of the individual patient profiles shows that they are well aligned with the current best practice guidelines for surgical treatment (Haute Autorité de Santé 2008, Beaufils et al. 2009).

Both gender and age were previously reported as influencing the decision for surgery (Collins et al. 2013). In our institution, the frequency of operated patients depended on gender with more males being operated altogether. The percentage of surgical treatment also revealed significant age-related differences: 89% of ACL injuries were surgically treated in age group I vs. only 54% in group III. This is in line with the variations of patients' activity profile with the practice of less strenuous sports with increasing age. Age group III was indeed composed of a majority of patients not involved in contact and pivoting sports. Overall, with 10% of patients claiming to have limited physical activity and 36% participating in recreational sports, one can assume that 46% of patients corresponded to the low and moderate sports exposure categories of Daniel's and Fithian's surgical risk factor criteria (Daniel et al. 1994, Fithian et al. 2005). This activity profile explains to a large extent the documented differences in the therapeutic decision-making process and is in accordance with previously published criteria of good clinical practice (Beaufils et al. 2009).

The individual patient profiles which were identified in this study underline the diversity of patients seen with an ACL injury. Extrapolating this diversity to outcome evaluations for instance after ACL reconstruction without taking into consideration the patients' varying profiles may thus provide a nonrealistic view of the ACL injury problem. A systematic identification of patient subtypes would allow for a more individualized approach and for an efficient and easy comparison between studies. Future outcome data should not only be presented according to gender as previously suggested (Ageberg et al. 2010) but also according to age, preinjury level of practice as well as previous ACL injuries. The latter have been observed in one patient out of 5 in our institution. A trend towards a higher number of recurrent injuries could be identified in young female patients of group I. Although our data did not reach clinical significance, this trend is in accordance with previous reports of retear rates of up to 25% in young patients corresponding to the demographic profile of age group I (Myklebust et al. 1997, Lind et al. 2012). Future studies should consider representing their retear rates according to age and gender.

The present study is not without limitations. Eighteen per cent of patients were not included in the study as we did not receive their consent at the time of the analysis. As such, our data are not exhaustive. In future studies, the influence of objective laxity measurements as well as the existence of associated lesions on the decision-making process should also be investigated. Future investigations from our clinical pathway of ACL-injured patients should also include follow-up data. Patients are naturally followed according to the clinical evolution of their injury and the clinical pathway was still ongoing at the time of analysis. To better address the line of distinction between patients who will benefit from surgery and those who will not, randomized studies and clinical follow-up studies are necessary.

To conclude, patient profiles could be identified according to gender, age, preinjury level of practice and previous ACL injuries. The percentage of operated patients varied significantly according to these parameters. In their clinical day-to-day management, surgeons thus oriented their treatment strategy based on current guidelines (Beaufils et al. 2009). The identified groups within the present study did not only appear to be age and gender-specific, but further specificities appeared regarding the preinjury level of sports practice. Similar to current trends in the approach of ACL reconstructions (Araujo et al. 2014, Hofbauer et al. 2014), our findings reflected an individualized approach for ACL-injured patients. In the future, consideration of gender, age, preinjury level of practice as well as previous ACL injuries could represent an additional help to find the most adapted individual management by allowing for a better dedifferentiation between patients who will benefit from surgery and those who will not.

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Chapter 3
Static rotational knee laxity in anterior cruciate ligament injuries

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Abstract

Purpose: The purpose was to provide an overview of the non-invasive devices measuring static rotational knee laxity in order to formulate recommendations for the future.

Results: Early cadaver studies provided evidence that sectioning the anterior cruciate ligament (ACL) led to an increase of static rotational knee laxity of approximately 10-20% between full extension and 30° of knee flexion. Sections of the menisci or of the peripheral structures induced a much higher increase of rotation. This supported the hypothesis that static rotation measurements might be useful for the diagnosis of ACL or associated injuries. In vivo evaluations with measurement devices are relatively new. Several articles were published during the last decade with many different devices and important differences were seen in absolute rotational knee laxity between them. This was due to the varying precision of the devices, the variability in patient positioning, the different methods of measurement, examination protocols and data analysis. As a consequence, comparison of the available results should be performed with caution. Nevertheless it has been established that rotational knee laxity was greater in females as compared to males and that the inter-subject variability was high. For this reason it will probably be difficult to categorise injured patients preoperatively and the interpretation of the results should probably be limited to side-to-side differences.

Conclusion: Future studies will show whether rotational laxity measurements alone will be sufficient to provide clinically relevant data or if they should be combined to static sagittal laxity measurements.

Keywords: Knee joint, measuring device, instrumented, laxity, tibiofemoral rotation, anterior cruciate ligament

1. Introduction

Along with growing expertise in knee ligament surgery, more key information on clinical outcome has recently become available in the scientific literature. As such it has become apparent that anterior cruciate ligament (ACL) reconstruction techniques were often unable to prevent knee osteoarthritis in the long term (Myklebust et al. 2005, van der Hart et al. 2008). Furthermore, the ongoing debate on the efficacy of ACL reconstruction techniques to restore normal knee kinematics (Bull et al. 2002, Favre et al. 2006, Georgoulis et al. 2007, Isberg et al. 2011) provides evidence for the need of validated methods for the measurement of knee laxity. In the past, many methods and devices have been developed to measure anterior knee laxity (Daniel et al. 1985, Robert et al. 2009, Branch et al. 2010b). Among them the KT1000 has been the most widely used (Daniel et al. 1985). Over the last decade increased attention has been paid towards a more anatomic ACL reconstruction and an improved control of rotational knee laxity. Clinically, rotational knee laxity has been evaluated by subjective manual tests like the pivot shift or the dial test (Jakob et al. 1987). However, these examinations are not standardised enough to allow for a good reproducibility and a precise quantification (Lubowitz et al. 2008), since they are highly biased by the examiners' skills and experience. The pivot-shift test which induces a complex movement of the knee might even be more difficult to standardise with a device. Increased attention has thus been paid over the last decade to instruments measuring static rotational knee laxity.

The aim of this review is to present the current status of knowledge about static rotational knee laxity measurements in the context of ACL injuries. Specific focus will be set on non-invasive devices measuring knee rotation angle *versus* torque applied during a simple movement of knee rotation in humans. Studies and instruments assessing complex knee movements like the pivot-shift test or the rotation associated with anterior or valgus movement of the knee will not be presented. The first part of the review provides an overview of cadaver studies analysing static axial rotation and defining the role of the ACL as a knee stabiliser. The second part will describe the first investigations into *in vivo* rotational knee laxity measurements. In the third part, the instruments presented in the literature over the past decade, their specific features and the study contexts in which they have been applied will be portrayed. To improve evaluation of rotational knee laxity and associated pathologies *in vivo*, the discussion will highlight their respective advantages and disadvantages to formulate recommendations for the future research and clinical applications.

2. Role of the ACL in static rotational knee laxity

The ACL acts as a primary stabiliser for anterior knee laxity (Butler et al. 1980, Fukubayashi et al. 1982). This is different for rotational laxity, where it plays only a secondary role (Wang et al. 1974, Shoemaker et al. 1985). Therefore, isolating the effect of the ACL is much more challenging for rotational laxity measurements than during anterior strain.

The first quantitative measurements of knee rotation were performed by Wang and Walker (Wang et al. 1974) on cadaver specimens. Using a cycling loading machine, they investigated internal (IR) and external rotation (ER) angles resulting from applied torques up to 5 Nm. Their results obtained on separate specimens before and after removal of knee soft tissues showed that double meniscectomies, removal of both cruciate ligaments and removal of both collateral ligaments induced increases in knee rotation (Wang et al. 1974). The collateral ligaments had a greater effect on knee laxity than the cruciate ligaments. A study by Shoemaker and Markolf (Shoemaker et al. 1985) confirmed that isolated primary section of the ACL showed less increase in knee rotation than primary medial collateral ligament section, suggesting that the ACL was not the primary restraint of tibial rotation. Hsieh and Walker (Hsieh et al. 1976) evaluated the increase of knee rotation after cutting both cruciate ligaments at 17% when applying a torque of 5 Nm. Andersen and Dyhre-Poulsen (Andersen et al. 1997) reported that the increase in total range (TR) of tibial rotation after cutting the ACL averaged 2.7° (+10%) at 10° of knee flexion for a torque of 8 Nm. The findings of Lipke et al. (Lipke et al. 1981) suggest that sectioning the ACL specifically increases the IR of the knee. In the study of McQuade et al. (McQuade et al. 1989), at 20° of knee flexion and a torque of 8.1 Nm, the increase in IR was 3° after cutting the ACL (from 20° to 23°; + 15%), while the ER decreased by 3°. Applying a 5 Nm torque, Lane et al. (Lane et al. 1994) found an increase in IR of 4° with the knee extended and of 3° at 60° of knee flexion. This represented an increase of 20% and 9% of the TR at 0° and 60° of knee flexion, respectively. Nielsen et al. (Nielsen et al. 1984) specified that sectioning the ACL leads to an increase in IR at 3 Nm of about 2.4° (baseline value not provided) at small knee flexion angles (from 0 to 30°). Sectioning specifically the anteromedial bundle led to a slight increase of 1.6° in IR at small knee flexion angles, an observation not made when sectioning the posterolateral bundle of the ACL first (Nielsen et al. 1984). Collectively, these results provide evidence that isolated ACL tears could be detected with rotational knee laxity measurements, provided that these measurements are performed at small flexion angles (below 30°). Given the rather limited amount of additional rotation induced by cutting the ACL, the challenge with non-invasive measurements is to reach a high enough degree of precision to detect changes smaller than 10 to 20% of the total rotational knee laxity (*cf.* below).

3. First attempts at *in vivo* measurements

The first in vivo measurements were performed in the early 1980s (Shoemaker et al. 1982) and involved complex set-ups with various instruments. These early results highlight some of the main issues to be considered when dealing with rotational knee laxity. Shoemaker and Markolf (Shoemaker et al. 1982) found that tibiofemoral rotation was greater at 90° compared to 20° of knee flexion. Hip flexion also influenced tibiofemoral rotation, with greater values observed near hip extension compared to hip flexion 90° (knee flexed at 20°). This result was attributed to the increased tension in the hamstring muscles. Another critical aspect when measuring rotational knee laxity was the amount of rotation occurring in the ankle joint when the torque was applied at the foot. For a 10 Nm torque, Shoemaker and Markolf (Shoemaker et al. 1982) estimated that foot rotation represented twice the tibiofemoral rotation, *i.e.* two thirds of the measured angle. Subject positioning, hip and knee flexion angles, as well as leg fixation are thus critical factors that deserve particular consideration when analysing rotational knee laxity. The first tests on chronic ACL deficient patients (Markolf et al. 1984) showed a 10% (about 3°) increase in total knee rotation in the injured knee compared with the contralateral knee. It should be stated, however, that not all patients of this study had isolated ACL injuries, which may have influenced the results. Nevertheless, these early findings suggested low side-to-side differences and the high inter-subject variability in rotational knee laxity, aspects which were confirmed in later studies. Considering IR and ER separately, Zarins et al. (Zarins et al. 1983) found a significant increase of IR at 15° of knee flexion and of both IR and ER at 5° of knee flexion between the injured and contralateral knee of ACL-injured patients. The results from the patients' injured knees were also significantly greater than those from a comparable control group. (Unfortunately, the authors did not specify the statistical test applied and presented their results only in graphical form). In that study (Zarins et al. 1983), patient positioning was complex, the participants lying on their side with their foot fixed in a boot fastened to an isokinetic dynamometer. As a consequence, only the amount of rotation could be measured without knowing the exact torque applied to the leg. This method had poor reproducibility for IR ($r = 0.34 – 0.8$) but not for ER ($r = 0.84 – 1.00$). TR was highly reproducible ($r = 0.92$ –

0.96), which suggest that the examiners may have had difficulties in determining a reproducible starting position for isolated IR and ER measurements.

This series of early studies demonstrates the challenge that *in vivo* rotational knee laxity measurements represent. Critical aspects include patient positioning, reproducibility and precise measurement of applied torque. These aspects are especially important due to the high inter-subject variability found *in vivo*. The definition of the starting position of the test seems to be essential, especially regarding the reproducibility of separate measurements in IR and ER. These features will be highlighted in the following paragraphs which describe the more recent devices that have been presented in the literature.

4. Current non-invasive devices measuring rotational knee laxity

The present section will depict currently used, non-invasive devices specifically designed to measure static rotational knee laxity *in vivo*. While torque is always applied at the foot, rotational knee laxity is measured either at the foot or the tibia, which will influence the absolute values obtained. A summary description of the properties of the different instruments, patient positioning and testing protocols are presented in Table 3.1. If the device was improved or the testing protocol changed throughout publications, the last publication to date was considered. Table 3.2 and Table 3.3 summarise the main results obtained from healthy subjects and ACL-injured patients, respectively. To permit fluent reading the results will not be repeated in the text, unless specific aspects were analysed or data pooled. Because of the diverse objectives of the different studies, the choice was made to present them hereafter in chronological order of appearance in the scientific literature.

About a decade ago, Almquist et al. (Almquist et al. 2002), presented the Rottometer. Their patients were seated on a modified chair with the thigh fixed by a dual clamp positioned on each side of the analysed knee. The foot was secured to the frame of the foot plate using soft-nosed screws. An adjustable spanner was used to apply torque and a stick following the foot plate indicated the resulting degree of rotation. A comparison study between the Rottometer results and roentgen stereophotogrammetic analyses (RSA) was performed on 5 male subjects with tantalum markers implanted during an ACL reconstruction. The results showed an overestimation of the rotational knee laxity when assessed with the Rottometer. With increasing torque, differences between the two techniques increased (12°, 20° and 35° in TR; 5°, 8° and 18° in IR; 7°, 12° and 18° in ER, respectively at 3, 6 and 9 Nm) (Almquist et al. 2002). However, correlation coefficients remained high for TR at all tested knee flexion angles and torques ($r > 0.87$) but tended to show large variations for IR and ER (respective range: 0.48-0.87 and 0.47-0.77). No references for healthy subjects were provided for the Rottometer.

Musahl et al. (Musahl et al. 2007) described a portable device consisting of a handle bar attached to an Aircast boot via a 6-degress of freedom universal force/moment sensor. Magnetic sensors were positioned on the boot at the medial surface of the proximal tibia and the anterior surface of the thigh to measure the relative rotation angle of the tibia with respect to the femur. As the instrument only consisted of a boot and a handle bar, no support was provided for the leg except for the examiner holding the leg. As a consequence, knee flexion angles were less well controlled during the tests. In their in vivo study (Tsai et al. 2008), 3 aspects of reproducibility were assessed using intraclass correlation coefficients (ICC). The intra-tester ICC was lowest (0.77), the within session ICC was greatest (0.95), and the inter-tester ICC had intermediate results (0.81). A possible explanation for these findings might be that the test subjects were not de- and reinstalled for the two latter test situations.

Table 3.1: Measuring methods, patient positioning, testing protocols, data and validations of non-invasive devices for static rotational knee laxity measurements . IR internal rotation, ER external rotation, NR not reported.

Author	Device				Patient installation		
	Torque applied		Rotation angle measurement		Position	Knee flexion	Hip flexion
	Measurement	Application	Location	Type of sensor			
Almquist	Spanner (precision ±3%)	Manual	Foot	Measuring stick on the foot plate	Seated	0–90	Probably 90° as seating
Musahl-Tsai	Moment sensor	Manual	Tibia	Electromagnetic	Supine	Variable	Variable
Shultz	Force transducer	Manual	Tibia	Electromagnetic	Supine	20	10
Park	Servomotor + torque sensor	Motorised	Tibia	LED markers	Seated	60	85
Lorbach	Strain gauge (precision ±3%, resolution 0.001 Nm)	Manual	Foot	Electronic (resolution 0.01°)	Prone	30	0
Branch	Servomotor	Motorised	Foot	Inclinometer (accuracy 0.2°)	Supine	25	NR

Author	Patient installation		Protocol				Data analysis	Validation/reproducibility
	Thigh fixation	Ankle fixation	Amount of maximal torque applied (Nm)	Starting–Calibration position	Number of trials	Order of trial		
Almquist	Dual locking clamp	2 soft nosed screws for calcaneus, 4 for medial and lateral malleolus	9	Spontaneous resting positions	3	NR	Rotation angle at 3, 6 and 9 Nm	Comparison with RSA techniques: better correlation for total range ($r > 0.87$)
Musahl-Tsai	None	Boot with inflated air cells	6	Bubble level on the handle bar to align load cell to the ground	5	Cycle IR–ER	Relative rotation angle of the tibia with regards to the femur at 6 Nm	In cadavers: intra and inter-rater ICC > 0.94; In vivo: within session, intra-tester and inter-tester ICC > 0.95, 0.77 and 0.81 respectively
Shultz	Fixed proximal to the femoral epycondyles	Brace	5	Second metatarsal aligned in the frontal plane with the knee	3 + 3	Cycle IR–ER	Rotation angle at 5 Nm; stiffness	Intra-tester ICC > 0.86 for IR, ER and TR
Park	Femur fixed with a clamp	Foot fixed in a splint	7	Second toe directed forward	6	Cycle IR–ER	Rotation angle at 7 Nm; stifness; energy loss from 0 to 6 Nm	NR
Lorbach	Modified splint	Custom-made boot	15	Boot perpendicular to the ground	3	IR and ER	Rotation angle at 5, 10 and 15 Nm	Intra ICC: 0.67–0.94. Inter ICC: 0.88–0.98. Validation with knee navigation system: mean overestimation of 5°, 15° and 25° at 5,10 and 15 Nm
Branch	Femur and patella stabilisers	Fixed in dorsiflexion and pronation	5.65	Second toe directed forward	3 + 3	Cycle ER-IR	Rotation angle at 5.65 Nm; Stiffness from 0 to 1 Nm, Terminal stiffness from 4.65 to 5.65 Nm	Validation with electromagnetic sensors: tibial rotation$n$ = 48.7% total rotation measured at the foot; ICC (1 examiner each day for 4 days) = 0.97

Table 3.2: In vivo results of static rotational knee laxity in healthy subjects . IR internal rotation, ER external rotation, TR total range, NR not reported

Author	Tested leg	Hip flexion angle (°)	Knee flexion angle (°)	Subjects	*N*	Torque (Nm)	IR (°)	ER (°)	TR (°)	Location of angle measurement	Correction factor
Lorbach	Right	0	30	Mixed	30	5	22.0 ± 1.1	39.1 ± 2.2	61.1 ± 2.8	Foot	None
						10	36.2 ± 1.0	58.8 ± 2.0	95.0 ± 3.5		
						15	46.8 ± 0.7	71.0 ± 11.0	115.6 ± 4.5		
	Left					5	22.5 ± 1.5	41.4 ± 1.8	63.9 ± 3.1		
						10	39.0 ± 1.2	59.7 ± 1.7	98.7 ± 3.7		
						15	50.4 ± 1	72.3 ± 1.3	120.8 ± 4.8		
Mouton	Average left and right	0	30	Male	35	5	16.8 ± 3.7	25.0 ± 5.9	41.8 ± 8.9	Foot	None
						10	31.2 ± 4.8	40.0 ± 7.8	71.2 ± 11.5		
				Female	25	5	23.2 ± 5.0	35.6 ± 4.5	58.8 ± 8.8		
						10	39.4 ± 6.3	53.0 ± 6.3	92.5 ± 11.8		
Branch	Pooled left and right	NR	25	Mixed	14	5.65	11.4 ± 6.2	26.6 ± 4.9	38.1 ± 8.4	Foot	48.7% of measured angle
Shoemaker	Right	10	20	Mixed	20	10	NR	NR	40.6 ± 9.7	Foot	33% of measured angle
	Left						NR	NR	40.5 ± 12.1		
Shultz	Pooled left and right	10	20	Male	10	5	8.9 ± 2.5	11.3 ± 3.5	20.2 ± 4.1	Tibia	None
				Female	10		11.8 ± 4.8	15.7 ± 3.3	27.5 ± 7.5		
				Mixed	20		10.3 ± 4.0	13.5 ± 4.0	NR		
Shultz	Dominant leg	10	20	Male	43	5	8.9 ± 4.1	12.4 ± 3.6	21.2 ± 6.9	Tibia	None
				Female	64		10.6 ± 4.7	15.5 ± 4.5	26.0 ± 6.9		
Tsai	Pooled left and right	NR	30	Male	11	6	NR	NR	25.8 ± 5.9	Tibia	None
			90				NR	NR	18.5 ± 4.7		
Park	NR	85	60	Male	10	7	16.4 ± 2.6	19.3 ± 3.7	NR	Tibia	None
				Female	10		17.6 ± 3.9	25.3 ± 6.4	NR		

Table 3.3: In vivo results of static rotational knee laxity in injured and ACL-reconstructed subjects . ACLR, ACL-reconstructed knees, Contralateral, contralateral knee of ACL-injured patients, NR not reported, NA non-applicable, IR internal rotation, ER external rotation, TR total range. [a] Results represent 48.7% of the measured values.

Author	ACL status	Leg	Hip flexion angle (°)	Knee flexion angle (°)	Gender	N	Torque (Nm)	IR (°)	ER (°)	TR (°)	Side-to-side difference (°)
Markolf	ACL rupture (some associated injuries)	Injured	30	20	Mixed	35	10	NR	NR	32.8 ± 8	3.0 ± 6.6
		Contralateral						NR	NR	29.9 ± 8	
Almquist	ACLR	Reconstructed	90° as seated	60	Male	5	3	11 ± 5	16 ± 6	26 ± 7	NA
				90				11 ± 4	17 ± 6	29 ± 8	
				60			6	15 ± 9	25 ± 5	NR	
				90				21 ± 6	27 ± 6	NR	
				60			9	31 ± 3	34 ± 5	65 ± 7	
				90				30 ± 9	36 ± 7	66 ± 15	
Lorbach	ACLR	Reconstructed	0	30	Mixed	52	5	16.6 ± 8.9	33.2 ± 9.5	50 ± 12.1	NR
							8	26.4 ± 10.1	45 ± 10.5	71.4 ± 13.7	
							10	32.2 ± 10.9	51.9 ± 11.4	84 ± 15.9	
		Contralateral					5	18.2 ± 9.3	31.5 ± 9.4	49.8 ± 11.1	
							8	28.4 ± 10.6	43.9 ± 9.6	72.4 ± 13.7	
							10	34.5 ± 11.9	50.9 ± 10.2	84.7 ± 15.9	
Mouton	ACL tear regardless of treatment	Contralateral	0	30	Male	19	5	18.4 ± 8.4	23.9 ± 6.0	42.3 ± 12.2	NA
							10	32.4 ± 6.3	38.6 ± 7.6	70.8 ± 13.7	
					Female	4	5	23.3 ± 4.7	34.3 ± 6.4	58.5 ± 8.9	NA
							10	41.6 ± 3.4	52.5 ± 7.4	91.1 ± 10.5	
Branch[a]	ACLR	Contralateral	NR	25	Mixed	79	5.65	20.6 ± 5.7	16.7 ± 3.1	37.3 ± 7.5	NA

The Vermont Knee Laxity Device was first presented as a tool for antero-posterior knee laxity measurements (Uh et al. 2001). A few years later the same group reported on rotational knee laxity and investigated several interesting aspects. They reported intra-tester ICC values greater than 0,86 for IR, ER and TR (Shultz et al. 2007a). The apparatus presented absolute measurement errors (calculated as 95% confidence interval of the standard deviation of the difference between 2 tests) of 5° to 7° for both IR and ER (Shultz et al. 2007a). IR and ER for females were not significantly different compared with males, but TR showed a significant increase, with values of 27.5° ± 7.5° for females and 20.2° ± 4.1° for males (Shultz et al. 2007b, Shultz et al. 2011). Incremental stiffness (change in applied torque divided by the change in displacement, in Nm/°) assessed every 1 Nm was lower in females at low magnitudes of applied torque (from 0 to 1 Nm) but augmented with increasing torque (from 3 to 5 Nm). For males, incremental stiffness remained unchanged in IR and ER (Schmitz et al. 2008). Reproducibility for each increment was nevertheless highly variable, with day-to-day ICCs ranging from -0.28 to 0.92. Lower values were found for higher torques (Schmitz et al. 2008), which could partly be explained by a lack of consistency of the movement velocity, previously shown to influence anterior knee joint stiffness (Gross et al. 2004). Shultz et al. (Shultz et al. 2011) tested 64 women and 43 men using the Vermont Knee Laxity Device to analyse the influence of the menstrual cycle on rotational knee laxity in female participants. Although no such relationship could be established, females experienced significant cyclic variations in anterior knee laxity, genu recurvatum and general joint laxity compared with males. Additionally, they had greater TR, varus-valgus and general joint laxity. Overall, anterior laxity was a strong predictor of rotational laxity (Shultz et al. 2007b, Shultz et al. 2011) explaining between 30 and 42% of IR, ER and TR in the left knee. However, prediction was poor in the right knee (10% of the variance explained) (Shultz et al. 2007b), a finding that the authors could not explain. Varus-valgus laxity was an even better predictor of knee rotational laxity in both knees explaining 46 to 76% of the variance in ER and TR, but only 18% in IR (Shultz et al. 2007b).

Park et al. (Park et al. 2008) presented a motorised device to measure knee rotational laxity. Three LED markers were positioned on the anteromedial surface of the tibia to measure the angle of rotation. Unfortunately, the model used for the motion analysis was not described The authors declared that the “resting position” in females was more externally directed compared with males (1.4±1.2°; -0.1±1.0° respectively) (Park et al. 2008). Although significant, it is not clear in how far these differences lie outside the measurement error range and thus represent clinically meaningful differences. Females also presented greater ER angles and lower ER stiffness, while IR angles and stiffness were not different from males (Park et al. 2008).

The Rotameter (Lorbach et al. 2009a) is an instrument to apply torques to the lower leg via a custom-made boot attached to a handle bar. The device is equipped with an electronic torque sensor and an inclinometer and is attached to the frame of a small platform installed underneath the leg of the test subject who is installed in a prone position. Intra-rater ICCs ranged from 0.67 to 0.93 in IR and ER and 0.84 to 0.94 in TR for the different torques applied (5-15 Nm) (Lorbach et al. 2009b). Inter-rater ICCs ranged between 0.94 and 0.98 in IR and ER and 0.88 to 0.97 in TR (Lorbach et al. 2009b). Greater inter-tester ICCs compared with intra-tester ICCs suggests that, again, the participant was not reinstalled between the measurements undertaken by the two examiners. A validation study on cadaver specimen using a knee navigation system (Lorbach et al. 2009a) showed high correlations between the two techniques (Pearson $r > 0.85$), but the Rotameter systematically overestimated TR by 5°, 15° and 25° at 5Nm, 10Nm and 15Nm of applied torque, respectively. A later cadaver study confirmed these results (Lorbach et al. 2010). However, the overestimation increased to, respectively, 10°, 20° and 30° after ACL resection (Lorbach et al. 2010). The major finding of the Rotameter studies so far was that a posterolateral ACL bundle resection led to a significant increase of rotational knee laxity (Lorbach et al. 2010). A subsequent resection of the AM bundle did not lead to a further increase in knee rotational laxity for most variables analysed. When comparing the ACL-reconstructed knee and the contralateral leg in patients 2 to 3 years after ACL surgery, no significant differences were observed (Lorbach et al. 2012). These studies demonstrate that static rotational laxity measurements have the potential to detect complete as well as partial ACL tears. Further prospective studies are needed to confirm these data *in vivo*. Mouton et al. (Mouton et al. 2012) described the second version of the Rotameter prototype and presented normative reference data based on 60 healthy participants. Gender and body mass influenced rotational knee laxity measurements, with females having higher results and a greater body mass being associated with lower laxity. The contralateral, healthy knees of ACL-injured patients tended to have increased primary compliance (slope of the angle-torque curve between 2 and 5 Nm) in IR, which could sanction increased knee laxity in IR as a risk factor for non-contact ACL injuries. However, the authors stated that their results are preliminary and require confirmation.

Branch et al. (Branch et al. 2010a) developed a custom robotic knee system which is adjustable to the patient’s natural lower limb alignment, so as to avoid potential error sources through pretension in the knee ligaments. The femur, the patella and the ankle were fixed with stabilisers. The foot was positioned in dorsiflexion and pronation to obtain maximal ankle stabilisation. The device permitted to assess both knees simultaneously by applying torques to the foot via a computer-controlled motor. Electromagnetic sensors placed on the proximal tibia showed that tibial rotation represented an average 48.7% of the total rotation measured at the foot (Branch et al. 2010a). Therefore, the authors applied this value as a correction factor to all their acquired measurements. The instrument has shown a high reliability (ICC=0.97 for TR and stiffness) based on 10 subjects tested on 4 consecutive days by four different examiners (Branch et al. 2010a). However, no ICCs were provided for IR and ER separately. In a multicenter study, IR in the contralateral knee of ACL reconstructed patients was found to be higher compared with the control group, while ER was lower (Branch et al. 2010a). The authors concluded that an increased IR could be a risk factor for ACL injuries. However, TR was similar in the two groups, a finding that could point to a systematic difference in the starting position. In the same study (Branch et al. 2010a), the influence of gender was also investigated. Females demonstrated greater laxity than men for IR (20.9° ± 6.9° vs 16.8° ± 6.8°), ER (21.1° ± 7.0° vs 18.4° ± 4.9°) and TR (42.0° ± 7.1° vs 35.2° ± 7.0°) (Branch et al. 2010a). It must be highlighted, however, that these values stem from both patients and control subjects, the pooling was justified by the authors due to the small number of females in the control group (n=4). A matched-pairs analysis to compare patients with either double bundle or single bundle ACL reconstruction showed that on average side-to-side differences in IR were similar between the two techniques (1.3 and 1.1 ° respectively) (Branch et al. 2011).

5. Discussion

Six different measurement devices to assess static rotational knee laxity identified in the recent literature to assess static rotational knee laxity (Almquist et al. 2002, Musahl et al. 2007, Shultz et al. 2007a, Park et al. 2008, Lorbach et al. 2009a, Branch et al. 2010a). The most important finding of the present review was that, testing procedures and *in vivo* measurement conditions were highly variable, yielding results with up to 3-fold differences. Therefore, comparisons of results obtained from different instruments must be performed with caution and require a thorough understanding the testing methodology involved. The following paragraphs present relevant parameters that need to be considered in this respect, should be standardised and be systematically reported in scientific publications.

Three different patient positions were used, including the supine (Musahl et al. 2007, Shultz et al. 2007a, Branch et al. 2010a), seated (Almquist et al. 2002, Park et al. 2008) and prone (Lorbach et al. 2009a) position (*cf.*Table 3.1). These positions have their respective advantages regarding knee and hip flexion. It has been shown that the latter 2 factors have an influence on axial knee rotation (Shoemaker et al. 1982). The prone position reproduces the conditions of the dial test which has been described initially to diagnose injuries of the posterolateral corner of the knee (Cooper 1991). Results obtained in this position have demonstrated that the detection of rotational changes in relation with ACL injuries is possible (Lorbach et al. 2010). This position allows easy adaptations of the knee flexion angle and good control of hip extension angle, with an appropriate fixation of the thigh to limit hip rotation. Testing in the supine position may be easier with respect to patient positioning and comfort, but minimising hip rotation might be more difficult. Installation comfort could be optimised with the seated position, potentially enhancing patient relaxation and limiting artefacts, provided that the thigh can be securely fixed.

With 4 out of 6 devices, the knee angle of the test participant was fixed at 20-30° or 60° (*cf.*Table 3.1) (Shultz et al. 2007a, Park et al. 2008, Lorbach et al. 2009a, Branch et al. 2010a). The other 2 allowed for measurements at different knee flexion angles (Almquist et al. 2002, Musahl et al. 2007). Tsai et al. (Tsai et al. 2008) investigated the influence of knee flexion in healthy subjects (Table 3.2) and found a TR of 25.8° ± 5.9° at 30° of knee flexion and a decrease to 18.5° ± 4.7° at 90° of knee flexion. Cadaver studies showed that the amount of axial rotation related to an ACL deficiency was apparent mainly between 0 and 30° of knee flexion and disappeared with further knee flexion (Zarins et al. 1983, Nielsen et al. 1984, Andersen et al. 1997). Taken together, these results suggest that knee flexion should be standardised and that ACL-injured patients should be assessed at a maximal angle of 30°. Considering the influence of patient positioning on rotational knee laxity, it is recommended that patient installation, as well as knee and hip flexion angles should be explicitly reported in future publications.

With all of the aforementioned instruments, torque is applied at the foot and not directly at the tibia. This is probably the best solution given the anatomy of the lower leg. A disadvantage of this approach is that the torque is partially absorbed by the fixation device and other anatomical structures of the leg than the knee joint. Since it is difficult to evaluate the amount of torque effectively applied to the tibia, a direct comparison of the results from different instruments is of little value, since they are related to the efficacy of foot immobilisation and measurement site (foot or tibia). Similarly, thigh fixation is supposed to limit absorption of the torque by other structures in the leg than the knee, but again different positions and fixation methods will influence the results. To our knowledge, no study has investigated the effectiveness of thigh immobilisation to minimise of hip rotation.

As already mentioned above, some devices measured knee rotation at the foot (Almquist et al. 2002, Lorbach et al. 2009a, Branch et al. 2010a), others directly at the tibia using electromagnetic sensors or (Musahl et al. 2007, Shultz et al. 2007a) LED markers (Park et al. 2008) (Table 3.1). Using skin sensors, Branch et al. (Branch et al. 2010a) estimated the amount of real tibiofemoral rotation at 48.7% of TR measured at the foot and corrected all measured angles by this amount in later studies. Nevertheless, this approach may introduce some error, since the correction factor represents an average measurement (IC95%: 45.3-52.1%) and does not necessarily apply for each individual and condition. Although the use of positioning sensors is more time-consuming, it might be advantageous to use this technique systematically to obtain measurements that represent tibiofemoral rotation more closely (Alam et al. 2011).

Another aspect that differentiates the methodologies and deserves attention is the application of torque manually (Almquist et al. 2002, Musahl et al. 2007, Shultz et al. 2007a, Lorbach et al. 2009a) or using a motor (Park et al. 2008, Branch et al. 2010a). The rate of force application has been shown to influence stiffness results for anterior knee laxity (Gross et al. 2004). It is likely that a similar effect can be found for rotational knee laxity. Therefore, manual torque application requires some experience from the operator and should preferably be feedback-controlled. Using a motor to apply torque offers the possibility to control the rate of torque development, thus standardising better the measurement conditions. As to the amount of torque applied, it usually varies between 5 and 15 Nm, most groups having used a maximum value of 10 Nm (*cf.*Table 3.1). An important issue concerning applied torque is patient comfort and the integrity of knee structures. Based on our own experience, patient discomfort usually occurs with torques greater than 15 Nm and in isolated cases before reaching that level. We have now adopted a maximal torque applied of 10 Nm to standardise our testing procedures (applied post-surgery after 3 months at the earliest). Based on *in vitro* failure experiments, Shoemaker and Markolf showed that the structural integrity of the knee ligaments is compromised with a torque of 35 Nm directly applied to the tibia (Shoemaker et al. 1982). What these limits are in case of an ACL graft *in vivo* remains unknown. The best rule for now is to take into account the patient's comfort during the test and avoid any pain in the knee joint.

To allow for precise measurements of rotational knee laxity, adjusting the zero of the device is a crucial step. There is also some degree of confusion between the mechanical zero used with some devices and the subject's resting position. The first should be calibrated before each test, while the second should be controlled to enhance reproducibility of the measurements. Indeed, some authors found that their method of measurement had better reliability for TR than for IR and ER separately (Zarins et al. 1983, Almquist et al. 2002). Branch et al. (Branch et al. 2010a) observed an increased IR and decreased ER in the contralateral knees of patients compared with a healthy control group. The TR was however not significantly different between both groups.

These findings suggest a lack of reproducibility of the starting position of the test, an aspect related to patient installation and that should be carefully monitored.
Another confounding effect comes with the hysteresis phenomenon when the tests encompass full cycles in IR and ER. Unpublished data from our group have shown that the results are influenced when preceded by a manoeuvre in the opposite direction. Therefore, our current test procedure foresees separate measurements of IR and ER and includes 2 "preconditioning trials" (Branch et al. 2011, Shultz et al. 2011) to minimise movement artefacts (Mouton et al. 2012). This approach is likely to increase reliability of IR and ER measurements and of within-patient side-to-side comparisons.
The validity of the non-invasive instruments presented here has not always been fully established. Accuracy is usually established through comparison of non-invasive measurements to those obtained with a "gold standard" method (*e.g.* a knee navigation system used with cadaver specimen). Accuracy has not been tested with all devices. The presented reliability studies are often limited to computations of ICCs, and statistical tests examining systematic error are seldom applied. Often different versions of the ICC metric are used, and interpretations of the results are more or less "generous". However, ICCs strongly depend on data dispersion, do not always accurately reflect trial-to-trial consistency and do not evaluate if a recorded difference or change in the measurement is clinically meaningful (Weir 2005). A better approach here is the use of the minimum detectable change (MDC) (Weir 2005). This statistic determines the precision of a device, *i.e.* the minimal difference required with a given instrument in a given setting to be confident that a true change has indeed occurred. The determination of MDC is in fact incontrovertible to draw meaningful conclusions from any comparison study, as it accounts for the measurement error (systematic and random) associated with any device in a certain context. MDC should be assessed for all outcome variables computed, and the precision of the device should be checked to ensure that it is high enough to detect differences of rotational laxity of less than 20% of the measurement (*cf.* above).
From the previous investigations, a series of conclusions can be drawn regarding general results pertaining to rotational knee laxity. Regardless of the health status of the participants (healthy or injured), ER was always greater than IR (*cf.* Table 3.2 and Table 3.3), except in the study of Branch et al. (Branch et al. 2010a). Several investigations suggest that females have greater rotational knee laxity than males (Hsu et al. 2006, Shultz et al. 2007b, Park et al. 2008, Mouton et al. 2012). Therefore, future studies dealing with axial rotation measurements should provide a gender-specific analysis. Physiologic side-to-side differences for TR have been quantified by Tsai et al. (Tsai et al. 2008) at an average of 3.5°, whereas Branch et al. (Branch et al. 2010a)

evaluated them at 1.53°. Unfortunately, no standard deviations, confidence intervals or statistical analyses were provided in these studies. Future perspectives with non-invasive rotational knee laxity measurements are broad. Little information has been provided so far with respect to *in vivo* measurements in ACL-injured and ACL-reconstructed patients, especially in women. No systematic analyses have been performed on the side-to-side differences caused by isolated ACL injuries, associated meniscal tears or even the gender-specific changes on axial rotation after injury. No threshold has been determined to distinguish normality from pathology, and the potential to diagnose ACL injuries has not yet been tested.

This study is not a systematic review. Due to the small amount of devices measuring *in vivo* rotational knee laxity with several devices being only at their experimental phase, the authors did not consider that a systematic review would have added significant findings to this paper. Moreover, too little data have been presented in the literature on rotational knee laxity in healthy, injured and reconstructed knees.

Nevertheless, the clinical relevance of this review is that the discrepancies between procedures and devices must not be neglected when comparing results. Gender specific differences as well as side-to-side comparisons should also be systematically considered.

Considering the current state of the art, we recommend a 5-step systematic approach to establish qualitatively high research programmes on *in vivo* rotational laxity evaluations: (1) evaluate accuracy, reliability and precision (MDC) of the instrument for the given setting, (2) establish normative references based on a healthy population, (3) evaluate diagnostic and (4) prognostic potential of these measurements through systematic data acquisitions from injured and reconstructed knees at different time points of patient follow-up, taking into account ACL status and associated injuries, and (5) assess the influence of surgical techniques on static rotational knee laxity.

6. Conclusion

Significant knowledge has been gained from early studies on cadaveric knees about the role of the soft tissue envelope on static rotational knee laxity. These investigations demonstrated that the ACL is a secondary stabiliser of axial rotation and, more precisely, of internal rotation for knee angles of 0° to 30° flexion. These data present the basis for the development of current devices to measure static rotational knee laxity *in vivo*. Six devices have been presented in the scientific literature so far. Most of them yielded reproducible measurements, although some limitations have to be acknowledged. The technical and procedural discrepancies are such that a direct comparison of their respective results appears difficult or even impossible. Despite these differences most studies agreed on a high inter-individual variability, the fact that healthy females have a higher rotational knee laxity than males and that the clinical use of rotational laxity measurements may be more promising with side-to-side comparisons. Few publications have reported on pathologic changes in relation to ACL injuries, be it through cadaver studies or after ACL reconstructions. The existing set of results is encouraging to investigate further static rotational laxity in healthy and ACL-injured persons, as well as the implications of associated injuries. To allow for a more systematic method of development of these instruments and research topics, we recommend a 5-step methodological approach which will define the clinical value of rotational laxity measurements for our therapeutic approach of ACL injured patients.

7. References

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Chapter 4
Influence of individual characteristics on static rotational knee laxity using the Rotameter

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Abstract

Purpose: The purpose of this study was to evaluate the influence of individual characteristics on rotational knee laxity in healthy participants. Our second aim was to verify if the contralateral knee of patients with a non-contact ACL injury presents greater rotational knee laxity than a healthy control group.

Methods: Sixty healthy participants and 23 patients having sustained a non-contact ACL injury were tested with a new Rotameter prototype applying torques up to 10 Nm. Multiple linear regressions were performed to investigate the influence of gender, age, height and body mass on rotational knee laxity and to establish normative references for a set of variables related to rotational knee laxity. Multiple analyses of covariance were performed to compare the contralateral knee of ACL-injured patients and healthy participants.

Results: Being a female was associated with a significantly ($p<0.05$) higher rotational knee laxity, and increased body mass was related to lower laxity results. In the multiple analyses of covariance, gender and body mass were also frequently associated with rotational knee laxity. When controlling for these variables, there were no differences in measurements between the contralateral leg of patients and healthy participants.

Conclusion: In the present setting, gender and body mass significantly influenced rotational knee laxity. Furthermore, based on these preliminary results, patients with non-contact ACL injuries do not seem to have excessive rotational knee laxity.

Level of evidence: III (Retrospective comparative study)

Keywords: Rotameter, knee laxity, tibial rotation, anterior cruciate ligament, risk factor

1. Introduction

Over the past years the evaluation of rotational knee laxity has received increased attention from the medical and scientific community. Its main interests lie with the examination of the anterior cruciate ligament (ACL) after serious knee injury and the follow-up of patients after ACL reconstruction. The pivot-shift test is currently the best approach to diagnose an ACL tear (Benjaminse et al. 2006). However, it is highly subjective and does not allow for precise quantification of knee laxity (Noyes et al. 1991). Therefore, several devices have been designed to measure static rotational knee laxity non-invasively under controlled conditions (Almquist et al. 2002, Musahl et al. 2007, Shultz et al. 2007a, Park et al. 2008, Lorbach et al. 2009a, Branch et al. 2010). Normative references for the different instruments are often lacking, which makes it currently difficult to distinguish pathological cases from normality. Several studies have found that females tend to have greater rotational knee laxity than males (Hsu et al. 2006, Shultz et al. 2007b, Park et al. 2008). Except for gender, no individual characteristics have so far been investigated. Additional factors such as age, height and body mass could potentially influence rotational knee laxity measurements and could thus have relevance when comparing patients with uninjured controls.

Some investigations put forward that anterior knee laxity and generalized joint laxity might be risk factors for ACL injury (Woodford-Rogers et al. 1994, Uhorchak et al. 2003, Griffin et al. 2006). Rotational knee laxity has been little investigated, but it has been suggested that increased external tibial rotation could be a risk factor (Alentorn-Geli et al. 2009), despite the fact that internally directed torques generate greater strain on the ACL (Markolf et al. 1990). If increased rotational knee laxity is indeed a risk factor for non-contact ACL injuries, then patients having sustained such an injury should have greater results compared with a control group. The assessment of the uninjured, controlateral knee could serve as a proxy measurement for rotational knee laxity of the involved knee before the injury.

The main purpose of the present study was to analyze if individual characteristics influence rotational knee laxity of healthy control subjects with no previous knee injuries, evaluated with the second Rotameter prototype (P2). We hypothesized that rotational knee laxity is influenced by gender, age, height and body mass. A secondary aim was to investigate the rotational knee laxity of the contralateral knee of patients who sustained a non-contact ACL injury. Our hypothesis was that these patients have a greater rotational knee laxity compared with a healthy control group, which would suggest that increased rotational knee laxity is a risk factor for sustaining a non-contact ACL injury. This question was addressed based on preliminary patient data from an ongoing clinical research project.

2. Material and methods

Healthy participants were recruited based on the following selection criteria: aged between 18 and 60 years, no previous knee injury, no lower limb injury during the 6 months preceding the test, no disease influencing joint mobility or restricting activities of daily living and ability to take part in high demanding sports activities, such as basketball, football or handball. Patients with ACL injuries were recruited from an ongoing clinical research project at our institution. Only patients with non-contact ACL injuries were included. The knee laxity results of the contralateral knee were considered regardless of the treatment of the involved knee (surgical or conservative), associated injuries or treatment phase. Patients were excluded if they had had previous knee injuries on their contralateral leg. Pregnancy was an exclusion criterion for female participants in both the control and injured group. Sixty healthy participants and 23 patients were recruited for this study according to their respective inclusion criteria. All participants received a full account of the study objectives and procedures in oral and written form and signed a consent agreement. The study protocol had previously been approved by the National Ethics Committee for Research.

2.1 New Rotameter prototype (P2)

Rotational knee laxity was assessed using the second version of the Rotameter prototype (P2) and a similar testing procedure as previously described (Lorbach et al. 2009b). Briefly, the patient was positioned on an examination table in the prone position with his/her thighs secured into 2 half cone-shaped leg supports using Velcro straps. The tested leg was tightly immobilized in a ski boot of appropriate size, which was itself fixed to the rotational handle bar and frame of the Rotameter. The device was fixed to the examination table at an angle so as to induce a knee flexion of 30° and a hip flexion of 0°, given the patient position. Different torques can be applied to the examined lower limb in internal and external rotation via the handle bar. The applied torque was measured using a custom-made, previously calibrated electronic torque sensor (strain gauge, resolution 0.001 Nm) integrated into the handle bar. Rotation angle was measured using an inclinometer (NG4U, SEIKA Mikrosystemtechnik GmbH, Germany, resolution 0.01°) fitted to the rotational part of the device. During the test, applied torque and resulting rotation angle were amplified, sampled at 60 Hz by a 24-bit A/D converter (USB NI 9219DS, National Instruments, Texas, USA) and stored on a PC. Custom-made software was used to handle all data and to provide real time feedback to the operator.

2.2 Testing procedures and calculations

Once the patient was installed, the zero angle of the system was defined with the rotational handle bar placed horizontally and the position of the patient's foot perpendicular to the ground. Following the calibration, the handle bar was released so that the leg returned to its natural resting position (offset) which was used as the starting position for the test. Four trials were subsequently performed with applied torques of up to 10 Nm, first in internal rotation (IR), then in external rotation (ER). Separating evaluations of knee laxity for IR and ER was preferred compared to applying entire cycles in both directions (Park et al. 2008, Tsai et al. 2008, Ahrens et al. 2011, Branch et al. 2011, Shultz et al. 2011). Based on previous pilot testing (data not shown), this procedure was found to allow for optimal foot positioning within the boot during "preconditioning" trials and thus decrease the influence of movement artefacts during subsequent trials. The same procedure was applied on both limbs. The order of testing was randomized for the control group while in patients the tests were first performed on the uninvolved leg.

Acquired data were smoothed using a 10-point moving average. Subsequently, offset due to the natural resting position of the leg was set to zero. Instead of limiting the analysis of rotational knee laxity to the mere angle reached for a given torque applied in internal or external rotation (Almquist et al. 2002, Musahl et al. 2007, Lorbach et al. 2009a), we wanted to draw a more complete picture of rotational knee laxity by measuring additional variables (Park et al. 2008, Schmitz et al. 2008, Branch et al. 2010). Therefore, the following 10 variables were calculated on the ascending limb of the curve (Figure 4.1): rotation angle at 5 and 10 Nm, primary compliance (PC) calculated as the slope of the curve between 2 and 5 Nm, and secondary compliance (SC) computed as the slope of the curve between 5 and 10 Nm. All variables were determined separately for IR and ER. Finally, total range (TR) was taken as the sum of angles obtained with applied torques of 5 and 10 Nm for IR and ER. The first 2 preconditioning trials were used to optimize foot positioning within the boot and were therefore discarded; data are reported as average values of trials 3 and 4. With this measurement procedure, the precision of the device was determined by the minimum detectable change (MDC) according to Weir (Weir 2005). MDC calculation was based on a repeated measures analysis of variance performed on the results of 50 healthy participants tested on 2 different occasions by 2 different examiners. The MDC was comprised between 3 and 5° for IR and ER at 5 and 10 Nm; MDC was 6 and 7° for TR at 5 and 10 Nm, respectively; MDC was between 0.3 and 0.8°/Nm for PC and SC.

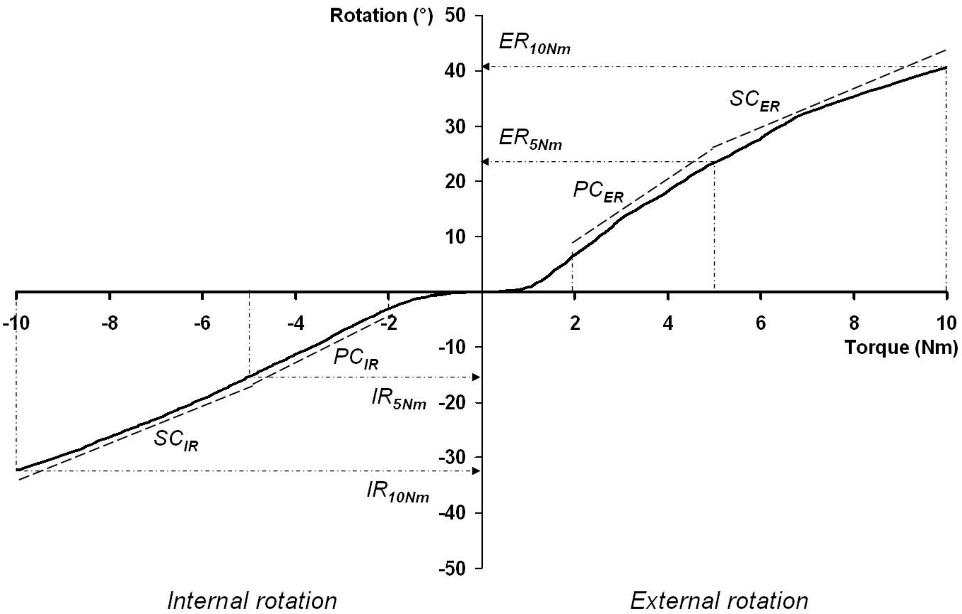

Figure 4.1: Outcome variables for rotational knee laxity measured with the second Rotameter prototype (P2). IR_{5Nm} internal rotation angle at a torque of 5 Nm; ER_{5Nm} external rotation angle at a torque of 5 Nm; IR_{10Nm} internal rotation angle at a torque of 10 Nm; ER_{10Nm} external rotation angle at a torque of 10 Nm; PC_{IR} primary compliance in internal rotation; PC_{ER} primary compliance in external rotation; SC_{IR} secondary compliance in internal rotation; SC_{ER} secondary compliance in external rotation.

2.3 Data analysis

All statistics were performed using version 19.0 of the SPSS software. Differences between the left and right knee of healthy participants were evaluated using independent Student t-tests. To analyze the influence of individual characteristics on the different variables representing rotational knee laxity, multiple linear regressions (descending method) were performed including gender, age, height and body mass as independent variables. Final models were analysed using the independent variables that were most frequently significant. All variables were reviewed for normality and heteroscedasticity using normal P-P plots and residuals plots, respectively. Multicollinearity was considered if the variation inflation factor was superior to 10 and the condition index superior to 30.

To compare the rotational knee laxity of the contralateral knee of patients with that of the healthy participants, multiple analyses of covariance (MANCOVA) were performed. The models included health status (control vs patients) and those variables which were previously found to have an influence on rotational knee laxity. Significance was set at $p<0.05$.

3. Results

Table 4.1 provides an overview of the basic demographics of the healthy participants and the patients recruited for the present study.

Table 4.1: Demographic data of the study participants.

	Healthy participants		Patients	
	Women (n = 25)	Men (n = 35)	Women (n = 4)	Men (n = 19)
Age	38 ± 12	40 ± 11	38 ± 15	30 ± 10
Height (cm)	167 ± 6	179 ± 7	165 ± 7	179 ± 7
Body mass (kg)	60 ± 6	76 ± 10	71 ± 13	85 ± 14

3.1 Influence of individual characteristics on rotational knee laxity

No significant differences were found between the left and the right knee of healthy subjects. Therefore, the results from the left and right side of each subject were averaged to represent the values for the healthy participants. Stepwise linear regressions revealed that gender had a significant influence on 8 out of 10 variables of rotational knee laxity. Body mass was found to be significant for 7 out of 10 variables ($p<0.05$). No systematic influence was found for the other factors analysed. Considering these results, only gender and body mass were entered into the final regression models. Unstandardized coefficients, their 95% confidence intervals, associated p-values and R square values of the final models are provided in Table 4.2. Being a female was associated with a significantly higher rotational knee laxity for 7 out of 10 variables ($p<0.05$). Increased body mass was related to lower laxity results for 6 out of 10 variables ($p<0.05$). The model including gender and body mass explained between 22 and 57% of the variance of rotational laxity variables.

*Table 4.2: Unstandardized coefficients, 95% confidence intervals, associated p-values and R square values of the final regression models. * p<0.05; gender coded as 0 for men and 1 for women; IR_{5Nm} internal rotation angle at a torque of 5 Nm; ER_{5Nm} external rotation angle at a torque of 5 Nm; TR_{5Nm} total range of rotation at a torque of 5 Nm; IR_{10Nm} internal rotation angle at a torque of 10 Nm; ER_{10Nm} external rotation angle at a torque of 10 Nm; TR_{10Nm} total range of rotation at a torque of 10 Nm; PC_{IR} primary compliance in internal rotation; PC_{ER} primary compliance in external rotation; SC_{IR} secondary compliance in internal rotation; SC_{ER} secondary compliance in external rotation.*

Dependent variable	Independent variable	Unstandardized coefficient (*B*)	Confidence interval for (*B*)		*R* square
			Lower bound	Upper bound	
IR_{5Nm} (°)	Gender	4.29*	1.16	7.41	0.40
	Body mass	−0.12	−0.25	0.01	
ER_{5Nm} (°)	Gender	6.24*	2.51	9.97	0.57
	Body mass	−0.26*	−0.41	−0.10	
TR_{5Nm} (°)	Gender	10.52*	4.34	16.70	0.55
	Body mass	−0.38*	−0.64	−0.12	
IR_{10Nm} (°)	Gender	5.23*	1.28	9.18	0.41
	Body mass	−0.18*	0.34	−0.01	
ER_{10Nm} (°)	Gender	7.41*	2.39	12.42	0.53
	Body mass	−0.33*	−0.54	−0.12	
TR_{10Nm} (°)	Gender	12.64*	4.52	20.76	0.53
	Body mass	−0.51*	−0.85	−0.17	
PC_{IR} (°/Nm)	Gender	0.82*	0.29	1.35	0.43
	Body mass	−0.02	−0.04	0.00	
PC_{ER} (°/Nm)	Gender	0.63	−0.09	1.34	0.38
	Body mass	−0.04*	−0.07	−0.01	
SC_{IR} (°/Nm)	Gender	0.18	−0.10	0.46	0.22
	Body mass	−0.01	−0.02	0.00	
SC_{ER} (°/Nm)	Gender	0.23	−0.14	0.60	0.24
	Body mass	−0.01	−0.03	0.00	

3.2 Comparison of contralateral and healthy knees

Differences between the laxity measurements of our healthy participants and the contralateral knee of patients were tested using status (control subject or patient) as the dependent variable, and including gender and body mass as independent variables in the MANCOVA model. None yielded a significant result for an interaction term of the tested variables, such that the simpler model with no interaction was eventually preferred. Table 4.3 shows descriptive data and the results from the MANCOVA. As for the multiple linear regressions, gender and body mass were frequently associated with rotational knee laxity. However, there were no differences in rotational knee laxity measurements between the contralateral leg of patients and our healthy participants. Statistical power for status determined *post hoc* was generally low, with a maximal value of 0.50 for PC_{IR}.

*Table 4.3: Rotational knee laxity of the healthy participants and patients (contralateral leg) and results of the MANCOVA. * $p<0.05$; IR_{5Nm} internal rotation angle at a torque of 5 Nm; ER_{5Nm} external rotation angle at a torque of 5 Nm; TR_{5Nm} total range of rotation at a torque of 5 Nm; IR_{10Nm} internal rotation angle at a torque of 10 Nm; ER_{10Nm} external rotation angle at a torque of 10 Nm; TR_{10Nm} total range of rotation at a torque of 10 Nm; PC_{IR} primary compliance in internal rotation; PC_{ER} primary compliance in external rotation; SC_{IR} secondary compliance in internal rotation; SC_{ER} secondary compliance in external rotation.*

	Healthy subjects		Contralateral leg of patients		Status (healthy vs. contralateral leg)	Gender	Body mass
	Men ($n = 35$)	Women ($n = 25$)	Men ($n = 19$)	Women ($n = 4$)	F-value	F-value	F-value
IR_{5Nm} (°)	16.8 ± 3.7	23.2 ± 5.0	18.4 ± 8.4	23.3 ± 4.7	1.94	10.64*	1.09
ER_{5Nm} (°)	25.0 ± 5.9	35.6 ± 4.5	23.9 ± 6.0	34.3 ± 6.4	0.08	23.12*	10.48*
TR_{5Nm} (°)	41.8 ± 8.9	58.8 ± 8.8	42.3 ± 12.2	58.5 ± 8.9	0.93	21.06*	5.86*
IR_{10Nm} (°)	31.2 ± 4.8	39.4 ± 6.3	32.4 ± 6.3	41.6 ± 3.4	2.05	12.14*	3.44
ER_{10Nm} (°)	40.0 ± 7.8	53.0 ± 6.3	38.6 ± 7.6	52.5 ± 7.4	0.37	18.99*	13.05*
TR_{10Nm} (°)	71.2 ± 11.5	92.5 ± 11.8	70.8 ± 13.7	91.1 ± 10.5	1.29	20.10*	9.97*
PC_{IR} (°/Nm)	3.8 ± 0.7	4.9 ± 0.8	4.1 ± 1.5	5.5 ± 0.9	3.92	13.26*	1.56
PC_{ER} (°/Nm)	5.3 ± 1.1	6.6 ± 0.9	5.1 ± 1.2	6.9 ± 0.8	1.00	7.51*	11.58*
SC_{IR} (°/Nm)	2.9 ± 0.4	3.2 ± 0.4	2.8 ± 0.5	3.5 ± 0.5	0.52	3.24	8.17*
SC_{ER} (°/Nm)	3.0 ± 0.5	3.4 ± 0.5	2.9 ± 0.5	3.6 ± 0.4	1.07	3.07	9.79*

4. Discussion

The present study revealed two key findings. First, gender and body mass influenced rotational knee laxity in the present setting with the second Rotameter prototype, thus partly confirming our first hypothesis. Second, our preliminary results suggest that the rotational laxity of the contralateral knee of patients suffering a non-contact ACL injury is not significantly greater than the one from healthy controls. However, these results must be viewed as preliminary considering the limited number of patients tested and the low statistical power.

The gender effect on rotational knee laxity has been previously investigated by Shultz et al. (Shultz et al. 2007b). They found that females (n=10) showed significantly greater TR_{5Nm} than males (n=10). Their difference of 35% fits well with the difference of 40% found in the current investigation. However, in the study of Shultz et al. (Shultz et al. 2007b), IR_{5Nm} and ER_{5Nm} were not significantly different between genders. Park et al. (Park et al. 2008) found a significant difference between females (n=10) and males (n=10) with an applied torque of 7 Nm, but only in external rotation. Unfortunately they did not investigate total range and did not provide quantitative data for internal and external rotations (except for graphical representation). The present study revealed differences between females (n=25) and males (n=35) for a greater number of variables related to knee joint laxity. The reason for these slight discrepancies with the two prior investigations might result from a greater sample size studied here, as well as differences in subject positioning and measuring methods. Shultz et al. (Shultz et al. 2007b) studied their participants in a supine position, with a hip flexion of 10° and a knee flexion of 20° and measured tibio-femoral rotation with electromagnetic sensors on the thigh and the tibia. On the other hand, Park et al. (Park et al. 2008) had their subjects seated with the hip flexed at 85° and the knee flexed at 60°, using a kinematical approach to measure knee rotation. In spite of these methodological differences, collectively their results plus our own findings suggest that females have a higher rotational knee laxity compared with males.

When considering compliance data, females either tended to have (PC_{ER}, +25%) or did have (PC_{IR}, +29%) significantly greater values compared with males for torques between 2 and 5 Nm. These findings suggest that the gender difference in knee laxity could mainly be related to differences in the first degrees of knee rotation under low torques. A similar conclusion was reached by Schmitz et al. (Schmitz et al. 2008) who found a lower stiffness (*i.e.* greater compliance) in females but only for torques up to 1 Nm. For greater torques (up to 5 Nm), stiffness was either similar (external rotation) or greater (internal rotation) than in males. Well in line with the current results, the cadaver study of Hsu et al. (Hsu et al. 2006) revealed that stiffness between 2.5 and 5 Nm was 25% lower in female specimens.

The higher primary compliance and greater rotational knee laxity observed in females could be a risk factor for non-contact ACL injuries. Indeed, in a sport context, female athletes were shown to have a significantly greater ACL injury incidence than males (0.43 injuries/1000 athlete's exposure vs 0.09 injuries/1000 athlete's exposure) (Hewett et al. 1999). Amongst other determinants (anatomic, genetic, neuromuscular or hormonal), anterior knee laxity has been identified as a risk factor for non-contact ACL injuries, but only for females (Uhorchak et al. 2003). In a similar way, increased rotational knee laxity could represent a higher injury risk.

To the authors' knowledge the present study is the first to investigate other individual characteristics than gender. Body mass was found to negatively influence rotational knee laxity. The explanation for this effect is not straightforward. It could be that people with a greater body mass have an increased amount of leg soft tissue, leading to a greater stiffness of the leg and lower measured rotational knee laxity. Another explanation could be linked to the testing procedure and patient installation used here, with a greater leg mass and volume causing a firmer immobilisation of the thigh, thus controlling better for hip rotation during the test. The influence of body mass and other personal characteristics should be further investigated with other rotational knee laxity measurement devices.

Regarding rotational knee laxity, the contralateral knees of patients suffering a non-contact ACL injury had similar responses compared with our healthy control group. These preliminary findings do not support our second hypothesis. However, it should be noted that the study was clearly underpowered, which calls for attention when interpreting these negative results. Still, there was a tendency for PC_{IR} to be increased in our patients ($p = 0.051$). Although speculative, it is possible that testing a greater sample of patients could have revealed significant differences for variables related to internal rotational knee laxity. The study of Branch et al. (Branch et al. 2010) found increased IR at 5.65 Nm in the contralateral knees of ACL-injured patients compared with uninjured controls. They suggested that increased IR may place a subject at greater risk of sustaining an ACL injury. The mechanism of non-contact ACL injuries provides further support that excessive rotational knee laxity could be a risk factor. Investigating the phenomenon in real sport situations, Koga et al (Koga et al. 2010) found that during the first 40 milliseconds after initial contact, the knee rotated internally by approximately 8° and then externally by 17° (Koga et al. 2010). The external rotation might occur after the ACL is already torn. It should be noted, however, that ACL injuries are generally caused by complex movements occurring in multiplanar directions (Quatman et al. 2010) including knee valgus and/or excessive anterior tibial displacement (Krosshaug et al. 2007, Alentorn-Geli et al. 2009, Hewett et al. 2009, Quatman et al. 2010). It has been suggested that only combined movements produce a sufficiently high strain on the ACL and that mere internal or external rotations might not suffice to tear an ACL (Berns et al. 1992). Future research is warranted to draw final conclusions on whether increased knee laxity in internal rotation is a risk factor. In that context it should be acknowledged that static rotational knee laxity measurements do not reflect functional knee movements.

The second prototype of the Rotameter used in the present study yielded lower rotational knee laxity results than the previous one (Lorbach et al. 2009b). Lorbach et al. (Lorbach et al. 2009b) found a TR of about 97° at 10 Nm in a mixed healthy population (15 men and 15 women), which is higher than the TR which was measured here, both in males (71.2°±11.5°) and females (92.5°±11.8°). The second prototype of the Rotameter provides a better ankle immobilization via the ski boot, limits thigh movements and has an enhanced overall rigidity. Despite these improvements, TR_{5Nm} measured here (42° and 59° for males and females, respectively) was approximately twice the values reported by Shultz et al. (Shultz et al. 2007a, b, Shultz et al. 2011) in a control population (20° and 27° for males and females, respectively). This difference could be largely explained by the measuring method used, Shultz et al. (Shultz et al. 2007a, b, Shultz et al. 2011) analysing the tibio-femoral rotation directly at the knee via electromagnetic sensors positioned on the thigh and the tibia. Rotational knee laxity at 10 Nm measured here (on average around 80° here) also represent twice the results of Shoemaker et al (Shoemaker et al. 1982). They described a TR_{10Nm} of some 40° for a mixed population, as they also measured the rotation angle directly at the tibia. Based on results from a sub-group of their study participants, Branch et al. (Branch et al. 2010) calculated that tibio-femoral rotation represented 49% of the total leg rotation using tibial electromagnetic sensors. The authors therefore corrected all their presented results by this factor, a procedure which would have yielded similar results in the current investigation compared with the previously cited studies.

From the preceding discussion, it appears that absolute measurements of rotational knee laxity performed at the foot are overestimated with regard to true tibial rotation (Alam et al.). This shortcoming also concerns the present device and represents a limitation that should be taken into account when interpreting absolute results. However, this does not disqualify the approach for repeated measurements during patient follow-up or within patient side-to-side comparisons, given the satisfactory precision of the measurements. Another drawback of this investigation is the lack of patients included in the second part of the study. A greater and more balanced patient group might have yielded significant results and confirmed our hypothesis of increased knee laxity in the contralateral leg of individuals with non-contact ACL injuries. Thus, further study is warranted to elucidate this question.

5. Conclusion

Age and height do not seem to influence rotational knee laxity. However, being a female lead to greater values of rotational knee laxity and increased body mass to lower values. The clinical relevance of these findings is that individual characteristics can have a significant influence on rotational knee laxity and should be more systematically investigated. These factors should be taken into account when different groups are being compared, using appropriate statistical models. When controlling for gender and body mass, the contralateral leg of patients having sustained a non-contact ACL injury did not exhibit excessive rotation compared to a healthy control group. However, this negative finding could be due to a small sample size tested and should be further investigated.

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Chapter 5
Combined anterior and rotational laxity measurements allow characterizing personal knee laxity profiles in healthy individuals

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Abstract

Purpose: The aim of this study is to quantify sagittal and rotational knee laxity profiles taking into account individual influencing factors.

Methods: Linear regression models were used to determine which individual characteristics (age, height, body mass and sex) influenced the outcome in a group of 104 healthy subjects. The standardized residuals were used as individualized (corrected) laxity scores and were combined to determine knee laxity profiles.

Results: Anterior knee laxity was not influenced by individual characteristics. Rotational knee laxity was higher in females and inversely related to body mass. The correlation between anterior laxity and internal rotation scores was weak ($r=0.24$, $p=0.02$). The proportion of knees concerned by increased laxity scores (scores >1) was similar for anterior displacement, internal and external rotation (15%). Only 32% of the tested subjects showed a normal profile (score >-1 and <1) for all 3 directions, 33% were concerned by hyperlaxity, 40% by hypolaxity and 5% by both. **Conclusions:** The diversity of laxity profiles found here highlight that the interpretation of multidirectional knee laxity is complex and suggests the necessity for individualized care of knee diseases and injuries. These results contribute to the understanding of knee laxity and throw the basis for prevention strategies and improvement of treatment outcomes in injuries and diseases. **Level of evidence:** Level IV, Case series with no comparison groups.

Keywords: anterior knee laxity, rotational knee laxity, knee laxity profiles

1. Introduction

Defining physiological knee laxity, i.e. the natural knee laxity of non-symptomatic and non-traumatic individuals, is a complex issue because of the wide variety of individual anatomical properties of each knee joint. Laxity has been considered to play a role in the development of knee osteoarthritis (OA) (Wada et al. 1996) and the occurrence of primary non-contact anterior cruciate ligament (ACL) injuries (Uhorchak et al. 2003), secondary knee injuries (Neuman et al. 2012) as well as worse ACL reconstruction outcomes (Branch et al. 2011, Kim et al. 2011). It has been shown that patients with hyperextension displayed better stability with a B graft compared to a hamstrings tendon graft (Kim et al. 2010). However, no data is available on physiological knee laxity. Therefore, establishing individual knee laxity profiles may be helpful to improve the prognostic and therapeutic criteria for primary and recurrent knee injuries and diseases.

Sagittal knee laxity measurements are widely used in the context of ACL injuries diagnosis (van Eck et al. 2013) and reconstructions (Meredick et al. 2008). The interest to measure rotational laxities is relatively new and arose as a consequence of the discussion on the lack of rotational control provided by the technique of ACL reconstructions which were performed a decade ago (Branch et al. 2011, Lorbach et al. 2012). Data documenting normative references for physiological laxity or combined anterior and static rotational knee laxities are however sparse. Furthermore, interpreting static knee laxity is a complex matter. It is not only influenced by the precision of measurement devices, but also by individual variables such as gender, BMI and other anatomical factors (Shultz et al. 2007, Mouton et al. 2012a, Shultz et al. 2012). Therefore, the practice of comparing laxity results between groups of individuals may be improved by using standardized laxity scores taking into account those individual variables (Mouton et al. 2012a).

The main purpose of the present study was to explore anterior and rotational knee laxity in a group of healthy participants and: (1) to determine which individual characteristics influence static anterior and rotational knee measurements, (2) to establish individualized laxity scores for anterior and rotational knee laxity separately and determine their distribution, and (3) to describe the different physiological laxity profiles by combining both laxity measurements. The hypothesis of the present study was that anterior and rotational knee laxity are influenced by gender, height, body mass and age and are poorly correlated to each other. These results are expected to improve the understanding of physiological and pathological knee laxity.

2. Materials and methods

One hundred and four healthy participants (45 females, 33±14 years, 168±7 cm, 58±7 kg; 59 males, 35±12 years, 179±8 cm, 76±11 kg) were included in the study. They reported no history of knee injury or surgery, no other lower limb injury in the 6 months preceding the tests and, for women, no pregnancy. All participants had both knees tested for anterior and rotational joint laxity by a first experienced examiner. The first leg tested was randomized. The precision of the devices was established based on an inter-examiner test-retest design. A second experienced examiner therefore retested 61 participants for anterior laxity and 65 for static rotational knee laxity following the test by the first examiner. All participants signed a consent agreement. The study protocol had previously been approved by the National Ethics Committee for Research.

Anterior knee laxity was measured with the GNRB® with an accuracy of 0.1 mm (Figure 5.1) (Robert et al. 2009), a motorized laximeter that mimics the anterior drawer test. The participant was evaluated in a supine position with the knee at 20° flexion. The joint line was placed at the edge of the thigh support. The foot was firmly fixed in neutral rotation using an ankle shell. The tested knee was then fixed with a patella shell carefully positioned so as to keep its center aligned with the tibial axis. The fixation force applied to the knee was monitored by way of a force sensor placed under the thigh: a minimum pressure of 100 N was applied via the patella shell at the beginning of the test. Finally, the tibia displacement sensor was placed perpendicularly to the tibia on the tibial tubercle. Three separate trials were subsequently performed applying a standard anterior tibial force up to 200N. The test was considered valid if the sensor placed under the thigh indicated a patellar fixation force above 90 N for the different trials. To permit valid side-to-side comparisons, care was taken to use a similar fixation force for both knees (≤10N difference).

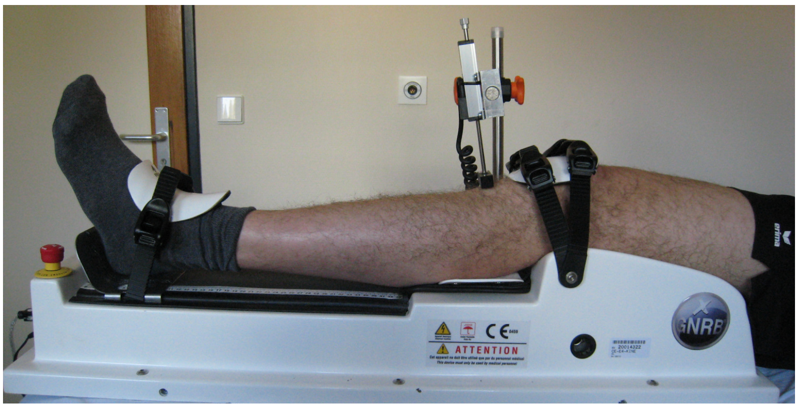

Figure 5.1: Device used for the static anterior knee laxity measurements (GNRB®)

Static rotational knee laxity was measured with a previously described device with an accuracy of 0.01° (Figure 5.2) (Mouton et al. 2012a, Tardy et al. 2013). The foot was tightly immobilized in a ski boot of appropriate size. The subject lay prone with thighs secured in half-cone supports using Velcro straps. The ski boot was attached to the frame of the device where torques can be applied manually by the examiner through a handle bar. Progressive torques up to 5 Nm were applied for both internal rotation (IR) and external rotation (ER) tests. The starting position (set to 0° angle) of each test was taken as the natural resting position of the tested leg. Four trials were sequentially performed, first in IR then in ER. Between each trial, the handle bar was released to allow the leg to return to its resting position.

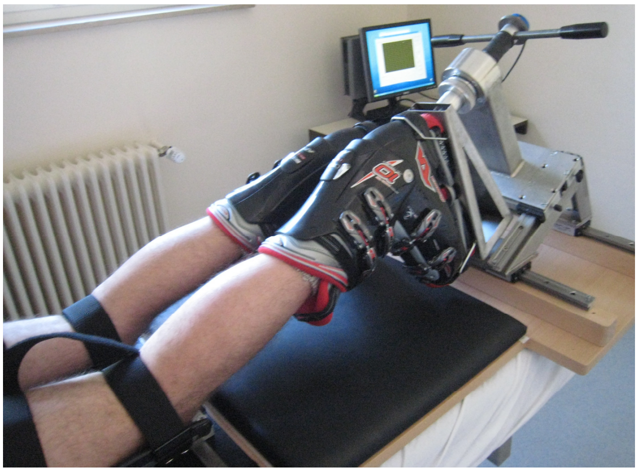

Figure 5.2: Device used for the static rotational knee laxity measurements

Statistical analysis

The average of the two last trials was considered for the different variables studied: anterior tibial displacement at 134 (ATD_{134}) and 200 N (ATD_{200}) as well as internal rotation (IR_5) and external rotation (ER_5) at 5 Nm. The total range of rotation at 5 Nm (TR_5) was obtained by adding IR_5 and ER_5. To calculate the side-to-side difference (SSD = displacement of one knee - displacement of reference knee), one knee was randomly chosen as the reference knee for each subject.

Statistics were performed using version 20.0 of the SPSS software. The reproducibility and precision of the device were determined by the Minimum Detectable Change (MDC) (Weir 2005). It represents the minimum change in a measurement that can be considered a true change. The MDC was established both for absolute and SSD values for all previously described variables. It was calculated as follow: MDC = SEM * 1.96 * $\sqrt{2}$ with the standard error of measurements (SEM) being the square root of mean square error term obtained from a repeated measures analysis of variance. To test if age, height, body mass and sex (coded males: 0, females: 1) influence knee laxity measurements, a multiple linear regression analysis (backward method) was performed. Interactions between sex and the other variables were considered. Assumptions for linear regressions were checked. Linear relationship was confirmed with the lack of fit test of a general linear model. Normality of errors was checked with the Kolmogorov-Smirnov test. Homoscesdasticity was confirmed by visual inspection of the graph representing standardized residuals versus standardized predicted values, and independence of error was assumed with the Durbin Watson test. Finally, multicollinearity was considered acceptable if the variation inflation factor was lower than 10 (Myers 1990) and a value was considered as an influential outlier if its Cook's distance was above 1 (Cook 1982). If no individual characteristics were found to be significant, the average and standard deviation values were used to calculate a z-score: (observed value – average value) / standard deviation. If one or several characteristics influenced the laxity measurements, the standardized residuals of the final model were used as the laxity score. Standardized residuals indicate by how many standard deviations a value is located from the predicted value given by the model. These are computed as: (Observed value- Predicted value given by the model) / standard deviation of residuals (given by SPSS software). Based on a threshold of 1 (Uhorchak et al. 2003), knees were categorized as being hypo- (score <-1), normo- ($-1<$ score <1) or hyperlax (score >1). Pearson correlations were calculated to determine the correlation between anterior and rotational laxity scores. Significance was set at $P<0.05$ for all analyses.

3. Results

The average, standard deviation and MDC for absolute and SSD measurements are presented in Table 5.1 for both anterior and static rotational knee laxity. MDC for SSD was 1.5mm for ATD_{200}, 4.4° in IR_5, 6.4° in ER_5 and 8.2° for TR_5.

Potential predictors for knee laxity results included sex (45 females, 59 males), age (range 11-59), body mass (42-106 kg) and height (150-198 cm). Absolute anterior knee laxity was not significantly influenced by any of the considered individual characteristics. Average anterior displacement was 3.3±0.7mm at 134N and 4.7±0.7mm at 200N. Regarding rotational laxity measurements, females had significantly greater laxity than males, and body mass was negatively associated with IR_5, ER_5 and TR_5. Assumptions of linear regression were confirmed, neither a collinearity problem nor influential outliers could be identified. In addition, no interaction between the significant predictors could be identified. Adjusted R square, unstandardized coefficients and standard deviations of residuals are presented in Table 5.2. SSD results were not influenced by any considered individual characteristic, neither for anterior nor rotational knee laxity. Average SSD was 0.0±0.7mm for ATD_{134}, 0.0±0.8mm for ATD_{200}, -0.2±2.2° for IR_5, -0.7±3.7° for ER_5 and -0.9±4.8° for TR_5.

Table 5.1: Absolute and side-to-side differences (SSD) measured by the two examiners and minimum detectable changes (MDC) in anterior and static rotational knee laxities

	Examiner 1		Examiner 2		MDC	
	Absolute value	SSD	Absolute value	SSD	Absolute value	SSD
Anterior knee laxity (mm), $n = 61$						
ATD134	3.2 ± 0.6	0.1 ± 0.5	3.6 ± 0.6	0.0 ± 0.6	1.1	1.3
ATD200	4.5 ± 0.7	0.1 ± 0.6	4.9 ± 0.7	0.0 ± 0.8	1.2	1.5
Rotational knee laxity (°), $n = 65$						
IR5	20.6 ± 6.1	−0.1 ± 2.7	20.0 ± 6.3	−0.3 ± 2.7	4.2	4.4
ER5	30.0 ± 9.5	−0.0 ± 4.0	27.3 ± 9.2	−0.3 ± 3.9	5.9	6.4
TR5	50.7 ± 14.8	−0.1 ± 5.4	47.3 ± 14.7	−0.6 ± 5.2	8.2	8.2

*Table 5.2: Regression model summary for laxity in 104 healthy knees . An individual score can be calculated according to the formula: Score = [Measured value – (Constant + βSex*Sex + βbodymass*bodymass)] / Standard deviation of residuals. Sex is coded as 0 for males and 1 for females, body mass is expressed in kg.*

Dependent variable	Adjusted R square	Unstandardized coefficients β			Standard deviation of residuals
		Constant	Sex	Body mass	
Rotational knee laxity (°)					
IR5	0.46	32.7	3.7	−0.2	4.1
ER5	0.59	51.1	6.4	−0.3	5.5
TR5	0.60	83.8	10.0	−0.6	8.6

ATD_{134} and ATD_{200} laxity scores were highly correlated (r=0.98; p<0.01). The distribution of the laxity score is represented for ATD_{200} in Figure 5.3. 15% of knees were hyperlax (corrected score >1 corresponding to an anterior displacement > 5.4mm) and 16% were hypolax (corrected score < -1 corresponding to an anterior displacement < 3.9 mm). IR_5 and ER_5 laxity scores were moderately correlated (r=0.60; p<0.01). The distributions of the laxity score for IR_5 and for ER_5 are presented in Figure 5.4 and Figure 5.5, respectively. 15% of the tested knees were hyperlax (scores> 1) both for IR_5 and ER_5.The proportion of hypolax knees (scores < -1) was 19% for IR_5 and 14% for ER_5.

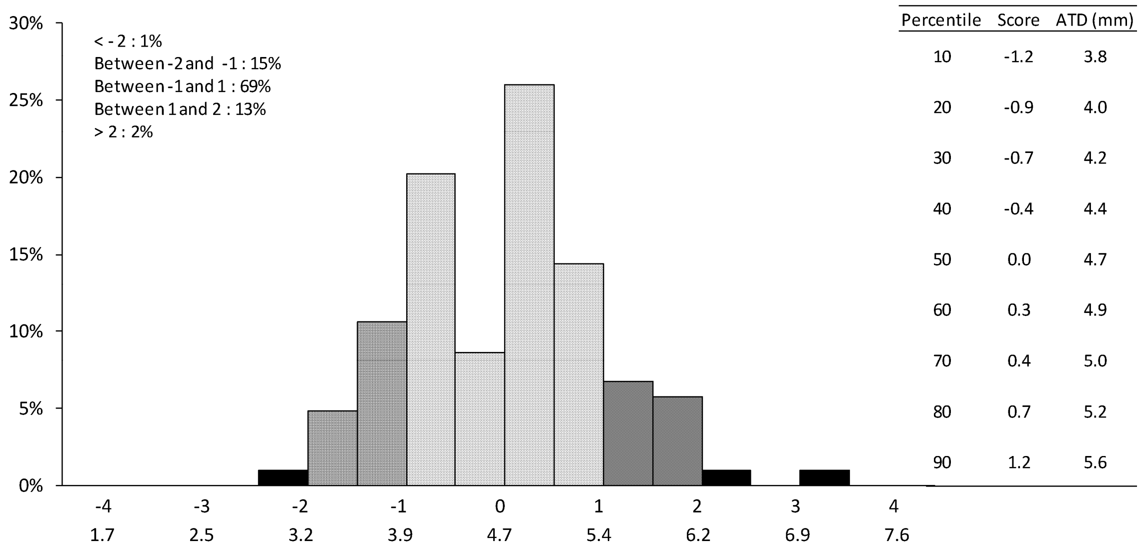

Figure 5.3: Distribution of the knee laxity score for anterior tibial displacement at 200 N

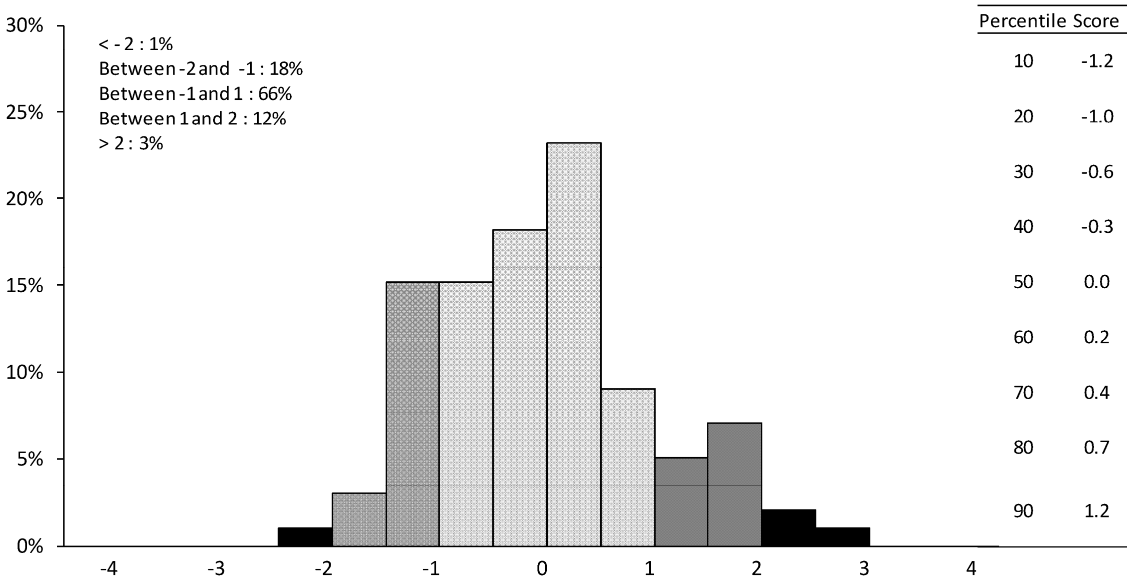

Figure 5.4: Distribution of the knee laxity score for internal rotation at 5 Nm corrected for sex and body mass

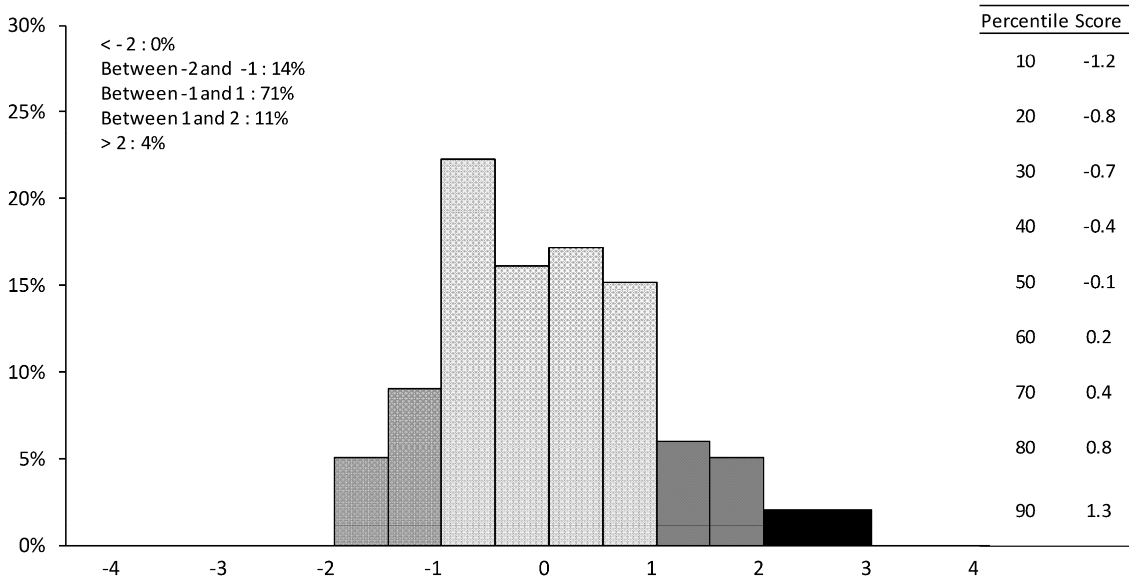

Figure 5.5: Distribution of the knee laxity score for external rotation at 5 Nm corrected for sex and body mass

Laxity scores between anterior and static rotational knee laxity were poorly correlated ($r<0.24$), although significant between anterior displacement and IR. Figure 5.6 indicates the distribution of laxity profiles in our healthy population considering IR_5, ER_5 and ATD_{200}.Only 32% of healthy knees with normal anterior laxity also demonstrated a normal rotational laxity in both internal and external rotation (IR_5 and ER_5). Two per cent of the knees were hyperlax and 2% hypolax for all 3 measured parameters. Four percent of the knees displayed increased (score > 1) laxity scores in two (of the three studied) directions, and 5 % displayed 2 decreased (score < -1) laxity scores. 22% of the knees showed one increased laxity score and 28 % one decreased score (the two other scores being normal). Five percent of the knees demonstrated both increased and decreased laxity scores.

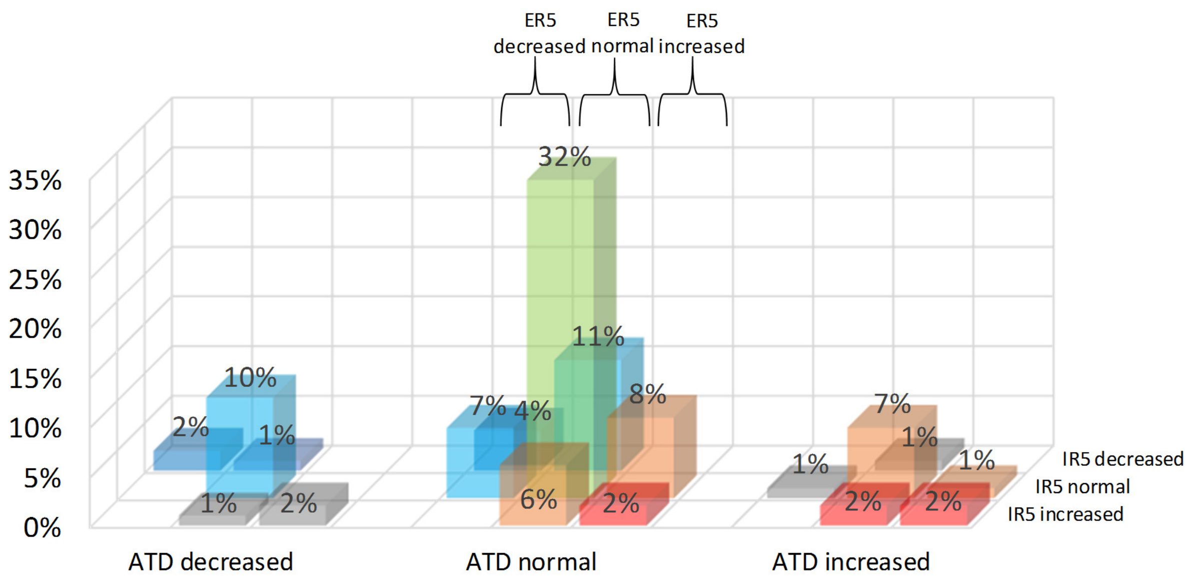

Figure 5.6: Distribution of laxity profiles expressed in percentage (%). Decreased: laxity score <−1, normal: laxity score between −1 and 1, increased: laxity score >1. ATD_{200}: anterior tibial displacement at 200 N, IR_5: internal rotation at 5 Nm, ER_5: external rotation at 5 Nm. Knee laxity profiles: green—normal for all three directions, light blue—decreased for one direction, dark blue—decreased for at least two directions, orange—increased for one direction, red—increased for at least two directions, grey—mixed profile, increased and decreased scores

4. Discussion

The main findings of this study were that rotational, but not anterior static laxity was related to individual characteristics like gender and body mass and that both laxities were poorly correlated. Insofar, our starting hypotheses were only partly confirmed. Furthermore, we observed a wide individual variety of laxity scores through the combination of the measured anterior and rotational laxity. According to our definitions, only 32% of healthy knees showed a normal laxity profile for all 3 measured laxity directions (anterior displacement, internal and external rotation). A high proportion of healthy knees (33 and 40 % respectively) were concerned by either hyper- or hypolaxity (stiffness), 5 % of them being affected by both.

The low correlation between anterior displacement and internal rotation (r<0.24) is in agreement with the current literature (Shultz et al. 2007). It suggests that both measurements yield complementary information which may play a role in the occurrence of knee injuries or diseases, like in the context of non-contact ACL injuries: both anterior and rotational knee laxity are influenced by the ACL which plays a role in constraining the knee both in the sagittal (Fukubayashi et al. 1982) and the transverse plane (Shoemaker et al. 1985). Combined measurements of anterior and rotational knee laxity might therefore also be useful in the prevention, diagnosis and follow-up of ACL ruptures and may provide new insight into the role of associated injuries on knee laxity. The existence of specific laxity profiles has been previously suggested (Shultz et al. 2012), but their distribution in a general population has not yet been reported. The proposed laxity score allowed for a precise categorization of knee laxity, independently of individual influencing parameters like body mass or gender. The normative data presented here may allow improving the comprehension of physiological and pathological laxity. Furthermore, they could represent a basis for further observations trying to identify which type of laxity profile might put a person at increased risk for knee injuries or degenerative diseases. Similar attempts have been made previously to define, for instance, the bony morphotypes of the lower extremities (Bellemans et al. 2012) and their relation with osteoarthritis.

Physiological knee laxity has received little attention in spite of indications that it influences knee diseases/injuries and their outcomes. Excessive laxity has been recognized as a risk factor for non-contact ACL injuries (Uhorchak et al. 2003) and more importantly for worse reconstruction outcomes (Branch et al. 2011, Kim et al. 2011). As a consequence, patients being identified with hyperlaxity (i.e. in the contralateral leg) at the diagnosis might require specific surgery and a close follow-up regarding laxity and OA symptoms throughout the years following surgery. This approach has already been applied to assess the influence of hypermobility on ACL reconstruction outcomes: patients with hyperextension displayed better stability with a patellar tendon graft compared to a hamstrings tendon graft (Kim et al. 2010). No data is available yet on physiological laxity; insofar the present results represent an interesting contribution to this field. Excessive knee laxity is also assumed to be a risk factor for knee OA in non-traumatic knees. Anterior laxity is indeed known to be increased in patient knees with a Kellgren/Lawrence score of I compared to healthy controls, and cross-sectional studies showed that anterior and rotational laxity decrease with severity of knee OA (Wada et al. 1996). These findings highlight the potential of knee laxity measurements to follow OA progression in a non-invasive manner, providing sufficiently precise evaluations to compare a particular patient to the healthy population. Hypolaxity has not been previously defined, and its potential influence on injuries or degenerative joint disease is unknown. Our findings may therefore stimulate the debate around the need for individualized care of knee injuries and disease. More work is needed to improve the comprehension of the role of individual knee function in the occurrence of degenerative knee diseases, knee injuries (e.g. non-contact ACL injuries) and poor treatment outcomes.

None of the considered individual characteristics was found to influence anterior knee laxity measurements. So far, there is no agreement in the literature regarding the relationship between anterior laxity and gender. Some studies showed greater anterior knee laxity in females (up to 2.5mm) compared to males (Uhorchak et al. 2003, Shultz et al. 2007) whereas others did not (<0.3mm) (Sharma et al. 1999).Unlike us, some authors also reported a significant effect of BMI, height, age, hip anteversion and navicular drop on anterior laxity (Shultz et al. 2012). As for rotational knee laxity, several studies recognized an increased rotational laxity in females as compared to males (Shultz et al. 2007, Mouton et al. 2012a, Almquist et al. 2013). According to our own experience (Mouton et al. 2012a, Tardy et al. 2013), interpretation of static rotational laxity measurements is very complex and requires further investigation. Some authors recently hypothesized that the increased laxity often observed in females may be explained by sex differences in body composition (Mouton et al. 2012a, Shultz et al. 2012) and lower limb alignment (Shultz et al. 2012). Its significance has not been completely elucidated yet, but it may be one of the multiple factors playing a role in the increased risk of non-contact ACL injuries or certain types of OA in females.

A critical appraisal of previously reported differences in laxity measurements is difficult, since the precision of the used devices has rarely been reported. A difference which is inferior to the precision of the device might reveal a measurement error rather than a real difference. A strength of this study is the test-retest design and the reporting of MDC values for both anterior and rotational knee laxity measurement devices. Measurement of anterior laxity has been shown to be more reproducible with the GNRB® than the KT-1000 regardless of the examiner's experience (Robert et al. 2009, Collette et al. 2012). Previous work evaluated intra-examiner reproducibility precision of the GNRB® at 2-4 mm depending on the installation procedures (Vauhnik et al. 2013).Here we found a considerably better inter-examiner precision of 1.2mm at 200N, probably related to our rigorous standardization of subject positioning, as previously recommended (Vauhnik et al. 2013). Considering the static rotational laxity measurement device (second version), this study reports for the first time its precision.

The present study has some limitations. Anatomical knee integrity was limited to the participants' self-report of previous knee injuries or surgery. Only anterior and rotational knee laxities were considered, although varus-valgus laxity and genu recurvatum assessment may also be interesting to describe individual knee laxity profiles. The use of other laxity devices, especially for rotational knee laxity measurement, might yield different laxity values due to the technical discrepancies (Mouton et al. 2012b). Measuring knee rotation at the foot has indeed been shown to be less accurate than directly on the overlying skin (Alam et al. 2011). The approach presented in this paper can however easily be adapted to any laxity measurement device. It allows for a convenient classification of knees as hypo-, normo- and hyper-lax for rotation and anterior tibial displacement. Moreover, through the standardization of the score, comparison of an individual person to a general population is now possible irrespective of individual differences in gender or BMI.

5. Conclusion

To conclude, the large variation of knee laxity profiles, the influence of gender and body mass on rotational knee laxity as well as the low correlation between static anterior and rotational knee laxities illustrate the high degree of complexity of knee function. This suggests that combined measurements of anterior and rotational static knee laxity might provide additional clinical information for the understanding of OA development and the diagnosis of knee soft-tissue injuries. These results contribute to the understanding of knee injuries and diseases and are the starting point for prevention strategies and improvement of treatment outcomes.

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Chapter 6
Non-injured knees of patients with non-contact ACL injuries display higher average anterior and internal rotational knee laxity than healthy knees of a non-injured population

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Abstract

Background: Excessive physiological anterior and rotational knee laxity is thought to be a risk factor for non-contact ACL injuries and inferior reconstruction outcomes but no thresholds have been established to identify subjects with increased laxity. Furthermore, mainly anterior knee laxity has been examined so far.

Purpose: (1) To determine if the healthy contralateral knees of ACL-injured patients have greater anterior and rotational knee laxity leading to different laxity profiles (combination of laxities) than healthy control knees. (2) To set a threshold to discriminate knee laxity between both groups.

Study design: Case-control study.

Methods: One hundred and seventy-one healthy contralateral knees of non-contact ACL-injured patients (ACL-H group) and 104 healthy knees of control participants (CTL group) were tested for anterior and rotational laxity. Laxity scores (measurements corrected for gender and body mass) were used to classify knees as hypolax (score <-1), normolax (between -1 and 1) or hyperlax (>1). Proportions of subjects in each group were compared using chi-square tests. ROC curves were computed to discriminate laxity between groups. Odds ratios were calculated to determine the probability of being in the ACL-H group.

Results: The ACL-H group displayed greater laxity scores for anterior displacement and internal rotation ($p<0.05$). Laxity profiles were different between groups for the following associations: normolaxity in anterior displacement / hypolaxity in internal rotation (ACL-H: 6%; CTL: 15%; $p=0.02$); hyperlaxity in anterior displacement / normolaxity in internal rotation (ACL-H: 27%; CTL: 10%; $p<0.01$). The laxity score thresholds were 0.75 for anterior laxity and -0.55 for internal rotation. With both scores above these thresholds, an individual was 3.18-fold more likely to be in the ACL-H group (95% CI: 1.74-5.83).

Conclusions: The healthy contralateral knees of patients with non-contact ACL injuries display different laxity values both for internal rotation and anterior displacement compared to healthy control knees.

Clinical relevance: Identification of knee laxity profiles may be of relevance for primary and secondary prevention programs of non-contact ACL injuries. A prospective study is needed to confirm that laxity profiles may predict the risk for non-contact ACL injuries.

Key Terms: anterior knee laxity; rotational knee laxity; knee laxity profiles; anterior cruciate ligament injury

1. Introduction

Excessive physiological anterior knee laxity is assumed to be a risk factor for non-contact anterior cruciate ligament (ACL) injuries (Uhorchak et al. 2003). However, no data exist on the influence of excessive static rotational knee laxity on the individual injury risk. Patients with a non-contact ACL injury appear to display more anterior (Daniel et al. 1985, Woodford-Rogers et al. 1994, Sernert et al. 2004) and rotational (Branch et al. 2010) knee laxity on their healthy contralateral knee compared to healthy knees from control subjects. In addition, during landing after a jump task, individuals with increased laxity are more likely to have abnormal motion patterns associated with non-contact ACL injuries (Shultz et al. 2009b) and are less sensitive to joint displacement due to delayed muscle contractions (Shultz et al. 2004). Therefore, it seems relevant to be able to identify those individuals with increased laxity through more systematic screening, because of the potentially higher associated ACL-injury risk. However, no laxity thresholds have ever been reported in the literature to identify them.

Correlation between static rotational and anterior laxities is low (Shultz et al. 2007, Mouton et al. 2014) suggesting that the two measurements provide complementary information. Combining both anterior and rotational laxity measurements might thus lead to a better description of the status of the knee envelope and function and would help to better identify individuals at risk for non-contact ACL injuries. The interpretation of physiological knee laxity measurements is however complex. Absolute values should be interpreted with caution as they are known to be influenced by individual characteristics such as gender and body mass (Mouton et al. 2012). The use of laxity scores which are corrected for individual characteristics might thus be preferred to allow comparisons between groups with different characteristics.

The aims of the present study were (1) to determine if the healthy contralateral knees of ACL-injured patients have greater anterior and rotational knee laxity, yielding different knee laxity profiles as measured by the combination of anterior and rotational knee laxity than healthy control knees; (2) to determine a threshold to discriminate physiological knee laxity between both groups. The underlying hypotheses were that (1) the ACL-injured patients would be more likely to have profiles of greater knee laxity in their contralateral knees than healthy control knees and that (2) it is possible to optimise laxity thresholds to discriminate non-injured knees of healthy individuals and ACL-injured patients for future prospective screening purposes.

2. Materials and methods

One hundred and seventy one ACL-injured patients (62 females, 32±12 years, 167±6 cm, 66±11 kg; 109 males, 29±10 years, 179±7 cm, 81±12 kg) were included in the study and were tested for anterior and static rotational joint laxity of their contralateral healthy knee (ACL-H group). They all had a primary non-contact ACL injury and reported no prior history of injury or symptoms in their contralateral knee. Physical examination by experienced orthopedic surgeons and MRI confirmed the anamnestic data. Pregnancy was an exclusion criterion for women. . A previously described group of 104 healthy individuals (45 females, 33±14 years, 168±7 cm, 58±7 kg; 59 males, 35±12 years, 179±8 cm, 76±11 kg) (Mouton et al. 2014) was used as a control group (CTL group). They reported no lower limb injury in the 12 months preceding the test and no previous knee injury. All were tested with the same protocol for anterior and rotational knee laxity. The first knee tested was randomly chosen.
All study participants gave their written informed consent. The study protocol had previously been approved by the National Ethics Committee for Research.

2.1 Procedures

All tests were performed by 3 experienced examiners. All had at least 3 years of experience to perform the anterior and rotational knee laxity measurements. They were not blinded to the participant's status (healthy or injured). To avoid measurement bias and limit inter-examiner variability, the following standard opertaing procedures were followed: (i) test execution in accordance with a detailed written description of the measurement protocols , (ii) extensive prior training of the examiners by a single experienced researcher and (iii) regular verification (at least twice a year) of compliance with testing protocols.
Anterior knee laxity was measured using the GNRB® (Robert et al. 2009) arthrometer as previously described (Mouton et al. 2014) (Figure 6.1). The knee was tested at 20° of flexion. The foot was firmly fixed in neutral rotation, and the femur was immobilized via a knee cap shell inducing a minimal compression force of 100 N, as determined by a force sensor located under the thigh. A progressive, motor-generated anterior force up to 200 N was then applied to the tibia while measuring the displacement (mm) by a sensor applied perpendicularly to the tibial crest. Although the maximal force was greater than the one usually applied with the more classical KT-1000 arthrometer, it did not induce any discomfort and was well tolerated by all participants. Three successive trials were performed, since preliminary tests within our setting

had shown that anterior laxity measurements were stable after the second trial. The displacement sensor of the GNRB has an accuracy of 0.1 mm (Robert et al. 2009) and the measurements have a reproducibility (as calculated by the Minimum Detectable Change) of 1.2 mm at 200 N (Mouton et al. 2014).

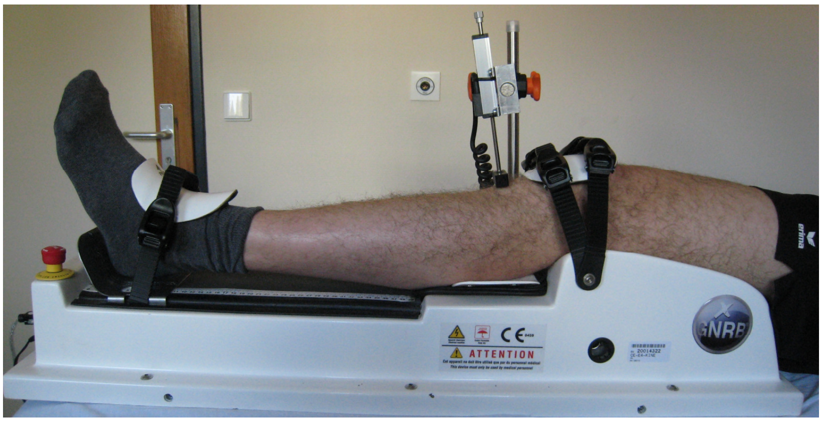

Figure 6.1: Measurement of anterior knee laxity with the GNRB® arthrometer. The patient's ankle and knee are secured with shells, and the motorized platform underneath the shank allows the application of a calibrated anterior force. The variable of interest is anterior tibial displacement for a given force.

Static rotational knee laxity was measured with a static rotational laxity measurement device as previously described (Mouton et al. 2012, Tardy et al. 2013, Mouton et al. 2014) (Figure 6.2). The subject lay prone with thighs secured in supports and the foot immobilized in a ski boot attached to the frame of the device. The natural resting position after installation of the participant was used as the starting position (0° rotation) for each trial. Subsequently, the examiner manually applied a progressive torque on the lower limb up to 5 Nm via the handle bar. A torque of 5 Nm found to be comfortable and easily tolerated by all participants (Mouton et al. 2012). The angle of rotation (°) was continuously measured and recorded during the maneuver. Four successive trials were performed, first in internal rotation (IR) then in external rotation (ER), since preliminary tests had shown that the rotational laxity measurements became stable after the third trial. The sensor of the Rotameter has an accuracy of 0.01° and the measurements have a reproducibility (as calculated by the Minimum Detectable Change) of 4.2° for internal rotation at 5 Nm (Mouton et al. 2014).

Figure 6.2: Measurement of static rotational knee laxity with the Rotameter. The patient's thigh is secured in half-cone supports, the boot is attached to the frame of the arthrometer and the examiner uses the handle bar to apply a torque in internal or external rotation. The variable of interest is the rotation angle for a given torque.

2.2 Data analysis

The average of the two last trials was considered for anterior tibial displacement at 200 N (ATD_{200}) and for internal rotation (IR_5) and external rotation (ER_5) at 5 Nm. The total range of rotation (TR_5) at 5 Nm was obtained by adding the results for IR_5 and ER_5. Laxity scores were calculated by using the previously established formulas based on the CTL group (Mouton et al. 2014). The score for anterior displacement at 200N ($zATD_{200}$) was calculated as follows: (Observed value – 4.7) / 0.7, 4.7 mm being the average displacement at 200N observed in the CTL group and 0.7 mm its standard deviation (SD). To calculate zIR_5, zER_5 and zTR_5, the following formula was applied: (Observed value – Theoretical value) / SD. Rotational knee laxity in healthy knees is influenced by gender and body mass (Mouton et al. 2012, Mouton et al. 2014). The theoretical value is thus calculated as 32.722 + 3.658*Sex -0.205*Body mass for IR_5, 51.062 + 6.380*Sex – 0.346*Body mass for ER_5 and 83.772 + 10.032*Sex – 0.551*Body mass for TR_5 (Mouton et al. 2014). Sex is coded as 0 for males and 1 for females; body mass is expressed in kg. The SD is 4.140 for IR_5, 5.499 for ER_5 and 8.644 for TR_5. For each subtype of laxity, the score represents the distance of one individual to the average of the CTL group with the units being the standard deviation of the CTL group. As a consequence, average scores for CTL group are always 0 with a SD of 1.

2.3 Statistical analysis

Statistics were performed using version 20.0 of the SPSS software. For the CTL group, one knee was randomly chosen for the analysis. First, an independent t-test allowed for comparison of laxity scores between the 2 groups. Participants were then separated into 3 categories of laxity (hypolax: score ≤-1; normolax: score between >-1 and <1, hyperlax: score ≥1) for each laxity score. Chi-square tests allowed to compare the distribution of laxity scores between the 2 groups, first for each laxity separately and second for combined laxity. To be able to discriminate knee laxity between both groups, ROC curves were computed. The Youden index (Youden 1950), which is used to establish optimal thresholds, was calculated as follows: sensitivity + specificity − 1 for all laxity score thresholds. The greatest value of the Youden index was considered as the optimal threshold. Logistic regressions were performed to determine the odds ratio of being in the ACL-H group when having increased laxity for both scores. Significance was set at $p<0.05$ for all analyses.

3. Results

Anterior tibial displacement at 200N reached 5.1 ± 1.0 mm in the ACL-H group. IR_5, ER_5 and TR_5 was 20 ± 6°, 30 ± 9° and 50 ± 14° respectively. Laxity was significantly different between the ACL-H and the CTL group for normalized anterior laxity (zATD was 0.6 ± 1.3 for the ACL-H group, $p<0.01$: Figure 6.3) and normalized internal rotation scores (zIR_5 was 0.2 ± 0.9, $p=0.04$ for the ACL-H group: Figure 6.4). zER_5 and zTR_5 did not differ between the two groups.

The significantly different laxity scores, $zATD_{200}$ and zIR_5, were combined to determine individual knee laxity profiles (Figure 6.5). Overall, they differed significantly between both groups ($p<0.01$). More specifically, the ACL-H group displayed two different associations in their laxity profile compared to the healthy control knees. Fifteen per cent of the CTL group had a normolax knee in anterior displacement associated with hypolaxity in internal rotation versus only 6% of the ACL-H group ($p=0.02$). Ten per cent of the CTL group had a hyperlax knee in anterior displacement associated with normolaxity in internal rotation versus 27% of the ACL-H group ($p<0.01$).

For $zATD_{200}$, the Youden index was highest for a score threshold of 0.75. Twenty-one per cent of CTL group were above this threshold versus 44% of the ACL-H group. For zIR_5, the Youden index was highest for a score threshold of -0.55. Sixty-seven per cent of CTL group were above this threshold versus 83% of the ACL-H group. When combining both laxity scores, 17% of the CTL group had the two laxity scores above the thresholds versus 40% of the ACL-H group ($p<0.01$). For $zATD_{200}$, zIR_5 and combined laxity, an individual had a greater probability of being in the ACL-H group if the laxity score was above the previously established thresholds

($zATD_{200}$: OR = 2.97, 95% CI: 1.68-5.24; zIR_5: OR = 2.45, 95% CI: 1.37-4.36: combined: OR = 3.18, 95% CI: 1.74-5.83).

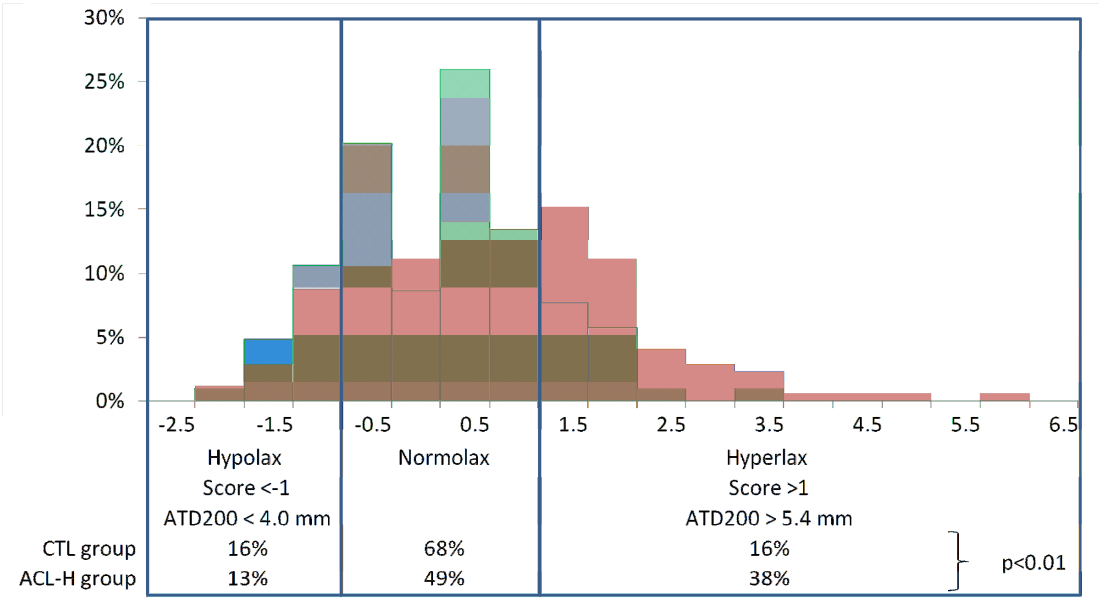

Figure 6.3: Distribution of anterior laxity score ($zATD_{200}$) in the healthy knees (CTL, green bars) and in the contralateral healthy knees of ACL-injured patients (ACL-H, red bars).

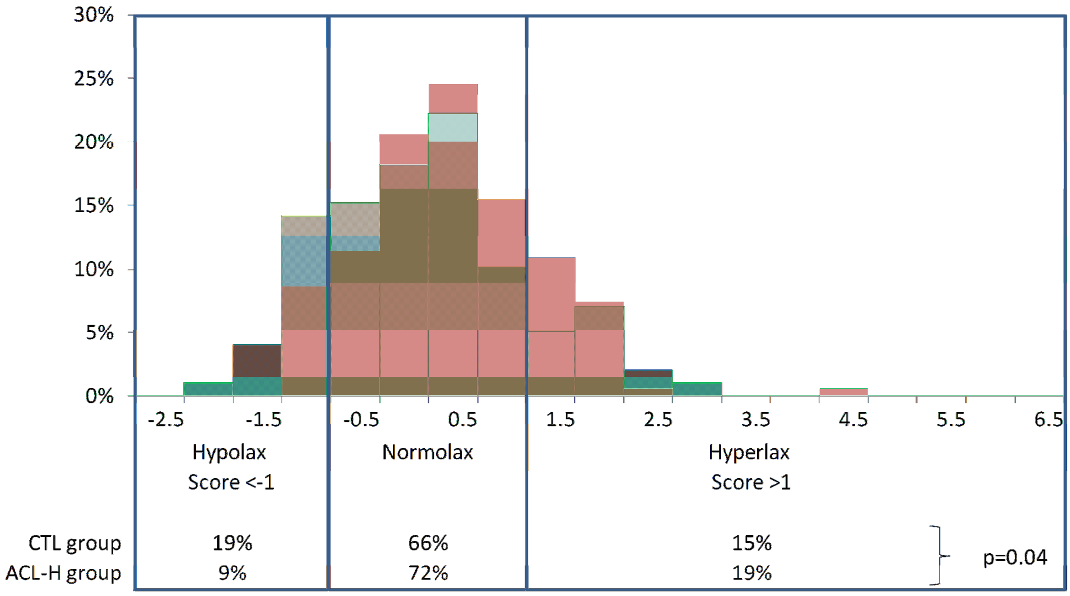

Figure 6.4: Distribution of internal rotation score (zIR_5) in the healthy knees (CTL, green bars) and in the contralateral healthy knees of ACL-injured patients (ACL-H, red bars).

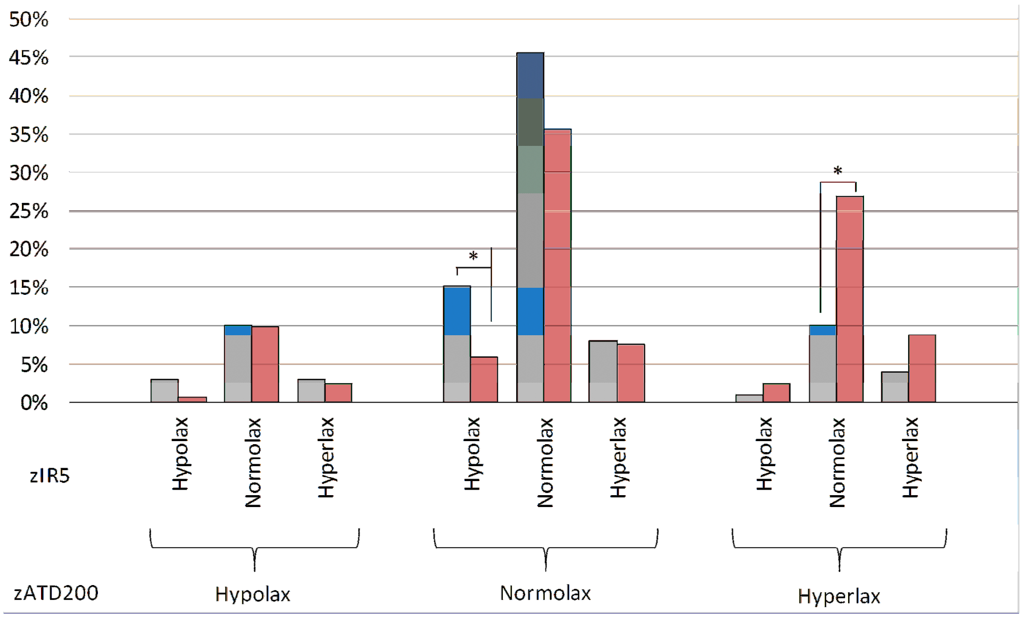

Figure 6.5: Distribution of knee laxity profiles ($zATD_{200}$ and zIR_5) between the healthy knees (CTL, green bars) and the contralateral healthy knees of ACL-injured patients (ACL-H, red bars). $zATD_{200}$: corrected score for anterior displacement at 200N, zIR_5: corrected score for internal rotation at 5 Nm, hypolax: score < -1, normolax: score between -1 and 1, hyperlax: score > 1.

4. Discussion

The main finding of this study is that 40% of the healthy contralateral knees of ACL-injured patients (ACL-H group) were identified as having both knee laxity scores above established thresholds, compared to only 17% of healthy control knees of a non-injured population (CTL group). An individual with both laxity scores above the defined thresholds was 3.18 times more likely to be in the ACL-H group. Furthermore, the group differences regarding knee laxity profiles suggest that prospective screening of healthy individuals regarding anterior and rotational knee laxity might be of interest, because of their potentially increased risk for non-contact ACL injury.

The question whether different knee laxity profiles are related to the risk of sustaining a non-contact ACL injury remains open. So far, laxity measurements of healthy knees were mainly performed in a single direction. Multidirectional laxity determinations are sparse (Shultz et al. 2012) as well as comparisons between healthy knees of injured and non-injured populations. In this study, 15% of the CTL group had a normolax knee in anterior displacement associated with hypolaxity in internal rotation versus only 6% of the ACL-H group (p=0.02). The CTL group combination may represent a protective effect against a non-contact ACL injury. On the opposite, 10% of the CTL group had a hyperlax knee in anterior displacement associated with normolaxity in internal rotation versus 27% of the ACL-H group ($p<0.01$), an association which may reflect an increased risk for non-contact ACL injuries. Future prospective studies are required to clarify whether a particular knee laxity profile represents an increased or decreased risk factor for non-contact ACL injuries. This would probably imply following large cohorts of participants for several years to reach sufficient events of interest and allow drawing solid conclusions.

In this study, the ACL-H group displayed greater anterior knee laxity than the CTL group. According to our definition, 38% of the ACL-H group had hyperlax knees in anterior laxity versus only 16% of the CTL group. Woodford-Rogers et al. (Woodford-Rogers et al. 1994) were the first to report this difference in 1994 in a case-control study. In a group of football players, anterior displacement as measured with the KT-1000 arthrometer reached 4.8 ± 2.2 mm (maximum manual force) for the non-injured group and 6.5 ± 3.3 mm for the healthy contralateral knee of ACL-injured patients ($p=0.02$). In a group of female athletes, anterior displacement reached 3.8 ± 1.5 mm for the non-injured group and 6.1 ± 2.7 mm for the healthy contralateral knee of ACL-injured patients ($p=0.02$). Surprisingly, anterior displacement was lower in females as compared to males, which is in contradiction to the current literature (Rozzi et al. 1999, Shultz et al. 2007). In a 4 year prospective cohort study involving 625 participants (Uhorchak et al. 2003), those who were going to have an ACL injury ($n=19$) displayed significantly greater anterior knee laxity (6.2 ± 2.4 mm, KT-1000 at 178 N) than those not being injured (5.0 ± 1.9 mm). Participants with an anterior laxity greater than one standard deviation above the average presented a relative risk of non-contact ACL injury 2.6 (95% CI not provided) times higher than individuals below that threshold (Uhorchak et al. 2003). Anterior knee laxity is therefore a potential risk factor for non-contact ACL injuries. Our results of anterior displacement are difficult to compare with previous studies using a different arthrometer (KT-1000 *versus* GNRB®) with differences in the final applied force (Uhorchak et al. 2003) and amounts of displacement (Collette et al. 2012). Nevertheless, 21% of the CTL group were identified with a score threshold superior to 0.75 versus 44% of the ACL-H group. The odds ratio of being in the ACL-H group if laxity score is above threshold was 2.97, which is in line with prior findings (OR=2.6) (Uhorchak et al. 2003). Our methods however proposed an optimized threshold. Future prospective studies are needed to determine if the 21% of the CTL group are more likely to get injured and if preventive measures like a more intensive neuromuscular training would be beneficial for them to compensate for their laxity-related injury risk.

Static rotational knee laxity in relation with ACL injuries is under discussion (Musahl et al. 2012). So far it has not been specifically reported as a risk factor for non-contact ACL injuries, although it is recognized to be influenced by the ACL (Wang et al. 1974, Shoemaker et al. 1985, Lorbach et al. 2010) and to be part of the injury mechanism (Olsen et al. 2004). One previous study reported that the contralateral knee of ACL-injured patients displayed, on average, greater internal rotation values than in healthy controls (Branch et al. 2010). However, the authors also reported a decreased external rotation in the same patients, so that no difference in the total range of rotation between both groups could be observed. The reason of this shift towards internal rotation is not clear. This was not the case in the present study where zER_5 was similar in both groups confirming increased zIR_5 being a potential risk factor for noncontact ACL injuries. In the present study, zIR_5 was higher in the ACL-H group compared to the CTL group. The increased internal rotation was especially marked by the fact that the ACL-H group is less likely to be hypolax than the CTL group as illustrated in Figure 6.4. Sixty-seven per cent of CTL group were above a score threshold of -0.55 versus 83% of the ACL-H group. A laxity score under -0.55 may thus represent a protective effect against a non-contact ACL injury. A subject above this threshold was however 2.45 times more likely to be in the ACL-H group.

In the current study a combination of anterior and rotational laxity measurements was chosen because the correlation between static rotational and anterior laxities was previously reported to be low (Shultz et al. 2007, Mouton et al. 2014). An individual with both laxity scores above the defined thresholds was 3.18 times more likely to be in the ACL-H group. This combination of laxities led to a higher odds ratio than anterior and rotational knee laxity considered separately. These thresholds as defined by the Youden index allow for an optimal distinction between both groups. Again, future prospective investigations are needed to analyze if a single laxity score is satisfactory to evaluate the risk of ACL injury or if a combination of several laxities is superior in characterizing an individual at risk.

The present study is not without limitation. Many factors such as generalized joint laxity, body weight, lower extremity alignment, biomechanical and neuromuscular factors are thought to influence the risk for a non-contact ACL injury (Woodford-Rogers et al. 1994, Uhorchak et al. 2003, Ramesh et al. 2005, Myer et al. 2008, Alentorn-Geli et al. 2009, Konopinski et al. 2012). Some of them (i.e. generalized joint laxity) are partly correlated with physiological knee laxity (Shultz et al. 2009a, Shultz et al. 2012). As subjects with generalized joint laxity (hypermobility) have an increased incidence of injury (Konopinski et al. 2012), it is thus expected that hyperlax subjects as defined in the present study are also more likely to get injured. We decided to focus on knee laxity as a primary and a secondary risk factor. Patients with increased physiological anterior or rotational knee laxity indeed have poorer functional outcome as assessed by the IKDC subjective form and poorer stability after ACL reconstruction (Branch et al. 2011, Kim et al. 2011, Kim et al. 2014). It was found that patients with genu recurvatum had better stability and function with patellar tendon grafts than with hamstrings grafts (Kim et al. 2010). Similarly, it is possible that patients with increased knee laxity profiles of the controlateral healthy knee may require a specific surgery to improve clinical outcome. Moreover, individuals with increased knee laxity may display abnormal motion patterns when landing from a jump task (Shultz et al. 2009b) or a delay in muscle activation (Shultz et al. 2004). Consequently, it is possible that these individuals will benefit from intensive neuromuscular training to compensate for their high laxity. Finally, the case-control design of this study does not allow to infer conclusions as to the causal relationship between knee laxity profile and ACL injury risk. However, this study is a smaller scale study that paves the way for a future larger scale prospective study of that sort.

To conclude, the non-injured knees of patients with non-contact ACL injuries display higher average static anterior and internal rotational knee laxity scores leading to different knee laxity profiles than healthy control knees. The combination of static anterior and rotational laxity measurements may provide a potential new insight in risk factor analysis for non-contact ACL injuries. Prospective follow-up studies are needed to investigate if particular knee laxity profiles place some individuals at a greater risk for non-contact ACL injuries and poor reconstruction outcomes.

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Chapter 7
Combined anterior and rotational knee laxity measurements improve the diagnosis of anterior cruciate ligament injuries

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Abstract

Purpose: This study analysed whether associating the side-to-side difference in displacement and the slope of the load-displacement curve of anterior and rotational knee laxity measurements would improve the instrumental diagnosis of anterior cruciate ligament (ACL) ruptures and help to detect different types of ACL tears.

Methods: Anterior and rotational knee laxity were measured in 128 patients with an arthroscopically confirmed ACL injury and 104 healthy controls. Side-to-side differences were determined for 3 variables in anterior laxity: anterior displacement at 200N (ATD_{200}), primary compliance from 30 to 50N (PC_A) and secondary compliance from 100 to 200N (SC_A). Furthermore, 4 variables in rotational laxity were considered: internal and external rotation at 5Nm (IR_5/ER_5) and compliance from 2 to 5Nm (C_{IR}/C_{ER}). Receiving Operating Characteristic (ROC) curves allowed to determine thresholds, specificities and sensitivities to detect ACL lesions, based on single variables considered and combinations thereof.

Results: Sensitivity and specificity reached respectively 75% and 95% for ATD_{200} (threshold: 1.2 mm) and 38% and 95% for IR_5 (threshold: 3.2°). If either 2 out of the 3 variables were positive for anterior laxity or both IR_5 and C_{IR} were positive, 81% of patients were identified without a false positive. All patients for whom ATD_{200} was >3.7mm, PC_A>48 µm/N or SC_A>17.5µm/N had ACL remnants that were either totally resorbed or healed on the posterior cruciate ligament.

Conclusions: Combined instrumented anterior and rotational knee laxity measurements have excellent diagnostic value for ACL injury, provided that several measurements be considered concomitantly.

Level of evidence: Level III, diagnostic study

Keywords: anterior knee laxity, rotational knee laxity, anterior cruciate ligament, injury diagnosis, combined laxity measurements

1. Introduction

The diagnosis of anterior cruciate ligament (ACL) injuries is usually established based on clinical examination and magnetic resonance imaging (MRI) techniques. However, manual clinical tests have the disadvantage to be highly subjective and examiner-dependent (Branch et al. 2010), and MRI is not completely reliable either, with a sensitivity of 81% and a specificity of 96% (Rayan et al. 2009).

Arthrometric measurements may offer an interesting alternative for the diagnosis and follow-up of ACL-injured patients. The KT-1000 (Daniel et al. 1985) is one of the most popular laxity devices in this respect. However, its reproducibility has been questioned, since several factors like the soft-tissue envelope (Jorn et al. 1998), examiner experience (Ballantyne et al. 1995) and hand dominance (Sernert et al. 2007) have been reported to influence knee laxity results. More recent motorised devices such as the GNRB® (Robert et al. 2009) apply a standardised force and display a better measurement reproducibility (Collette et al. 2012) which might even help to distinguish between ACL remnants. Moreover, this device offers the possibility to analyse the characteristics of the force-displacement curve, which has not been deeply explored yet in the context of ACL injuries.

So far, arthrometric measurements have been mainly limited to the anterior direction. Recently, the evaluation of rotational knee laxity in combination with anterior knee laxity has been introduced (Mouton et al. 2014), but this approach has received limited attention in the context of ACL injury diagnosis so far. Previous studies have demonstrated the role of the ACL in knee internal rotation (Nielsen et al. 1984, Lane et al. 1994). It is however not clear yet whether an ACL injury lead to both an increase in anterior and rotational laxity or whether some ACL injuries only lead to an increase in rotational knee laxity. As such, the additional analysis of rotational knee laxity may provide a more comprehensive evaluation in the context of ACL injuries by improving the sensitivity of their diagnosis.

The purpose of the present study was thus to determine whether a combination of variables derived from the load-displacement curves of anterior and rotational knee laxity measurements with the use of two specific devices, respectively the GNRB® and the Rotameter, would improve the instrumental diagnosis of ACL ruptures. Our underlying hypotheses were that (1) combining measurements of anterior and rotational knee laxity, as well as of the slope of the load-displacement curves would improve the ability to diagnose ACL ruptures as opposed to individual variables, and that (2) combined knee laxity measurements would provide sufficient precision to detect different types of ACL tears.

2. Materials and methods

2.1 Study participants

One hundred and twenty-eight patients (39 females, 27±11 years, 168±7 cm, 67±10 kg; 89 males, 28±9 years, 179±7 cm, 80±12 kg) with an arthroscopically confirmed ACL injury were prospectively included in the study and tested for knee laxity measurements prior to surgical treatment. None reported any previous knee injury to the contralateral knee.

A group of 104 healthy individuals was analysed and served as a control group (Mouton et al. 2014). They reported no lower limb injury in the 12 months preceding the recruitment and no previous knee injury. Pregnancy was an exclusion criterion for women in both groups. All patients and participants signed a written informed consent. The study protocol had previously been approved by the National Ethics Committee for Research.

2.2 Anterior and rotational knee laxity measurements

All measurements were performed by 3 experienced examiners who were not blinded to the participant's status (healthy or injured). However, to avoid measurement bias and limit inter-examiner variability, the following standard operating procedures were applied: (i) test execution in accordance with a detailed written description of the measurement protocols, (ii) extensive prior training of the examiners by a single experienced researcher and (iii) regular verification (at least twice a year) of operator compliance with the testing protocols.

Anterior knee laxity was measured with the GNRB® (Robert et al. 2009) at 20° of knee flexion following a previously described protocol (Mouton et al. 2014) (Figure 7.1.a). Three separate trials were performed applying a continuously increasing anterior force to the tibia up to 200 N. Static rotational knee laxity was measured with a static rotational laxity measurement device as previously described (Mouton et al. 2014) at 30° of knee flexion (Figure 7.1.b). Internal (IR) and external rotation (ER) of the tibia were induced by applying a progressive torque up to 5 Nm. Four trials were performed, first in IR then in ER. For each variable under study (cf. below), the measurement retained for the analyses was the average result obtained from the 2 last trials.

All patients and participants were tested on both knees for anterior and static rotational joint laxity. In patients, the non-injured knee was tested first, while the first knee tested in controls was randomly chosen. The measurements were performed a median of 10 days prior to reconstructive surgery in patients.

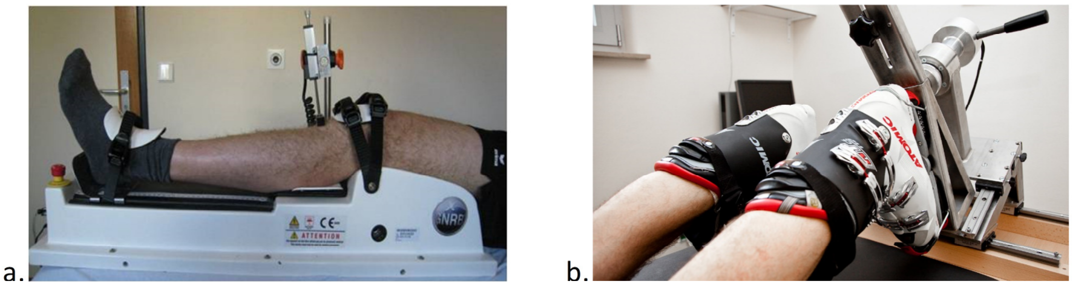


Figure 7.1: Anterior and rotational knee laxity measurement devices. A. The GNRB®. The ankle and patella of the tested leg are fixed and a motorised platform apply the anterior force from behind the shank. The sensor placed on the tibial tuberosity measures the anterior displacement B. The Rotameter. The subject is lying prone while wearing ski boots attached to the frame of the device. The handle bar allows the examiner to apply the torque both in internal and external rotation.

2.3 Data reduction and analyses

For patients, the side-to-side differences (SSD) for each variable were calculated as the average of the 2 last trials for the injured knee minus the average of the 2 last trials for the contralateral knee. For controls, the average of the 2 last trials for the contralateral knee minus the average of the 2 last trials for the reference knee (randomised) was considered. The SSD was determined for the following variables (Figure 7.2): anterior tibial displacement at 200N (ATD_{200}; mm), slope of the curve from 30 to 50N (primary compliance in anterior displacement: PC_A; um/N), slope of the curve from 100 to 200N (secondary compliance for anterior displacement: SC_A; um/N), internal rotation at 5 Nm (IR_5; °), slope of the curve from 2 to 5 Nm in internal rotation (compliance for internal rotation: C_{IR}; °/Nm), external rotation at 5Nm (ER_5) and slope of the curve from 2 to 5 Nm in external rotation (compliance for external rotation: C_{ER}). The slopes were determined based on least squares linear regression lines of the respective recorded data points.

Independent t-tests were used to compare the SSD between patients and controls. For each variable being significantly different between both groups, Receiver Operating Characteristic (ROC) curves were computed to determine the threshold and the associated specificity and sensitivity to detect an ACL rupture. The threshold was chosen to obtain a high specificity (>95%) to avoid false positives. Positive Predictive Value (PPV) was calculated as: Sensitivity / (Sensitivity + (1-Specificity)), and Negative Predictive Value (NPV) as: Specificity / (Specificity + (1- Sensitivity)). They respectively represent the proportions of positive and negative results that are truly positive and truly negative. Finally, the percentage of correctly classified subjects or accuracy of the test was computed as: (Number of truly negative controls + Number of truly positive patients) / Total number of tested subjects. The most discriminant variable for each test (anterior or rotational knee laxity test) was considered as the variable yielding the highest sensitivity.

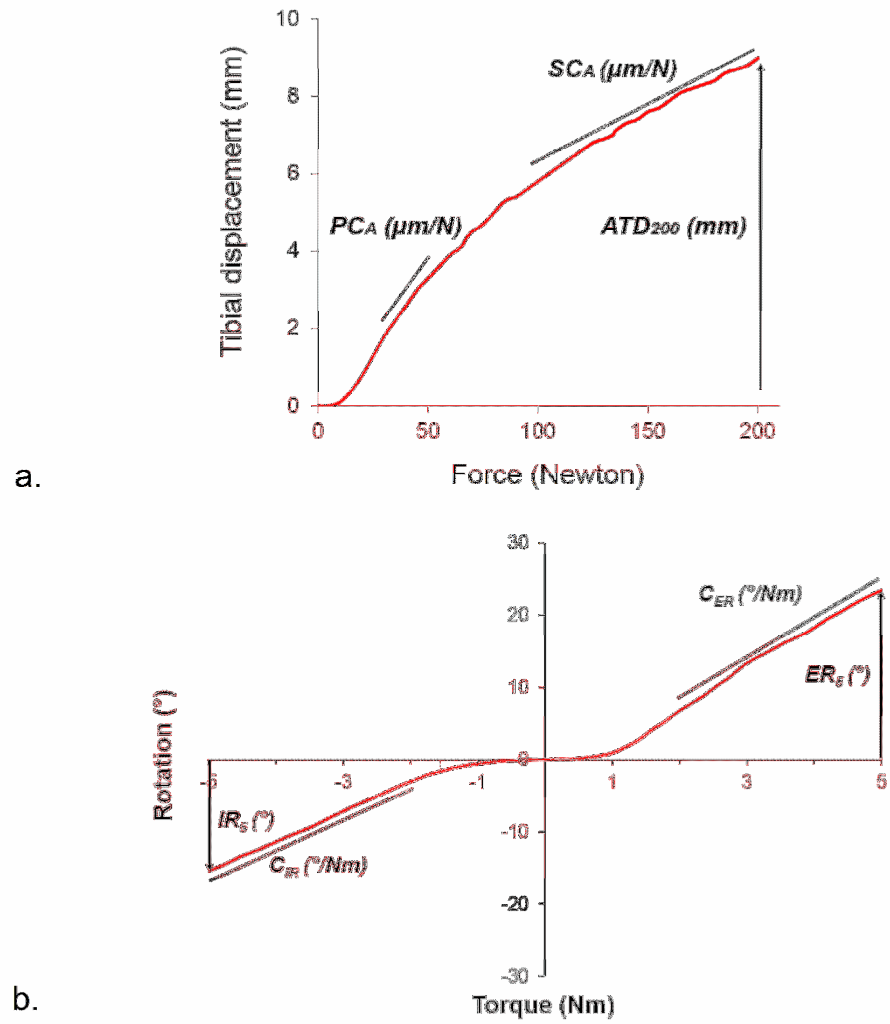


Figure 7.2: Variables of interest for the diagnosis of ACL injuries. A. Anterior knee laxity measurements with 3 variables computed: ATD_{200}, anterior displacement (mm) at 200N; PC_A, primary compliance (um/N) in anterior displacement represented by the slope of the curve from 30 to 50N; SC_A, secondary compliance for anterior displacement represented by the slope of the curve from 100 to 200N. B Rotational knee laxity measurements with 2 variables calculated: IR_5, internal rotation (°) at 5 Nm ; ER_5, external rotation at 5Nm; C_{IR}, compliance for internal rotation represented by the slope of the curve from 2 to 5 Nm in internal rotation; C_{ER}, compliance for external rotation represented by the slope of the curve from 2 to 5 Nm in external rotation.

Second, several variables of interest were associated to determine whether combining variables increases the diagnostic power for ACL injuries. Associations were first tested among variables from the anterior or the rotational knee laxity test separately. To determine the sensitivity and specificity of each association, a simple calculation was made to determine how many patients and participants were positive. A result was considered positive if the considered values were above the previously established threshold. Third, associations of variables from both tests were computed together. The association of ATD_{200} and IR_5 was tested first, then all variables of interest were taken into account and finally, the best association retained for each test at the previous step. The association of variables leading to the highest PPV was considered as the best association. If the PPV was equal for different associations, the combination with the highest percentage of correctly classified subjects was privileged.

All ACL injuries were classified *post hoc* under arthroscopy by 2 senior fellowship-trained orthopaedic surgeons into 1 of 4 categories (Crain et al. 2005, Panisset et al. 2008): 1. Complete ACL tears with total resorption of the torn ACL (no substantial ACL remnant), 2. ACL remnant healed on the posterior cruciate ligament (PCL), 3. ACL remnant healed on the intercondylar notch, 4. partial tear of the ACL (rupture of either the anteromedial or the posterolateral bundle with conservation of the other bundle).

2.4 Statistical analyses

The different injury categories were compared regarding the variables from the laxity tests using an analysis of variance (ANOVA). Significance was set at $p<0.05$ for all analyses.

3. Results

In the patient group, ACL reconstruction was performed a median of 5 months after the injury. Forty-eight patients (38%) had a complete ACL tear, 44 (34%) had an ACL remnant healed on the PCL, (19%) displayed a remnant which had healed on the intercondylar notch and 12 (9%) had a partial tear of the ACL (8 of the AM bundle and 4 of the PL bundle). Twenty-nine (23%) ACL injuries were isolated: 3 had an associated ligament injury (2%), 43 a cartilage damage (34%) and 85 a meniscal tear (28 medial meniscus tear: 22%, 42 lateral meniscus tear: 33%, 15 bimeniscal tear: 12%).

3.1 Overall sensitivity and specificity

The mean (±standard deviation) SSD results for each variable of interest are shown in Table 7.1 for both groups. The SSD in ER_5 and C_{ER} were not different between patients and controls and were thus not considered for the remaining analyses.

*Table 7.1: Average side-to-side differences and standard deviations for the healthy participants (control group) and patients with an ACL injury. ATD_{200}, anterior displacement at 200N; PC_A, primary compliance; SC_A, secondary compliance; IR_5, internal rotation at 5 Nm; ER_5, external rotation at 5Nm; C_{IR}, compliance in internal rotation; C_{ER}, compliance in external rotation. *, significantly different from the control group.*

	Control group	Patients
ATD_{200} (mm)	0.0 ± 0.7	2.5 ± 1.6*
PC_A (μm/N)	−0.3 ± 10.7	24.1 ± 22.1*
SC_A (μm/N)	0.2 ± 3.4	7.9 ± 6.7*
IR_5 (°)	−0.3 ± 2.2	2.1 ± 2.9*
C_{IR} (°/N m)	−0.1 ± 0.5	0.4 ± 0.7*
ER_5 (°)	−0.7 ± 3.7	−0.2 ± 3.7
C_{ER} (°/N m)	−0.1 ± 0.9	−0.1 ± 0.8

Thresholds, sensitivity, specificity, PPV and NPV are presented for the different variables and their combinations in Table 7.2. For anterior knee laxity, the most discriminant variable (with the highest sensitivity) was ATD_{200} (75%). An anterior knee laxity test with 2 positive variables out of 3 had a sensitivity of 71% with a PPV of 100% and correctly classified 84% of subjects. In other words, with 2 positive variables in the anterior knee laxity test, an ACL tear is guaranteed. Healthy knees never had more than 1 out of the 3 variables positive in the anterior knee laxity test. Rotational knee laxity measurements were less discriminant than anterior knee laxity, as the highest sensitivity reached 38% for IR_5. A rotational knee laxity test with the 2 variables tested positive correctly classified 58% of subjects and had a PPV of 100%. Combining IR_5 measurements to ATD_{200} (either ATD_{200} or IR_5 positive) increased the diagnostic sensitivity (from 75 to 84%) and the percentage of correctly classified subjects (from 84 to 87%) but yielded a lower specificity (from 95 to 90%) and PPV (from 94% to 90%). The latter percentage reached 98% when considering the test as positive if 2 or more variables of interest out of 5 were above their respective thresholds. The highest PPV (100%) was however found if either 2 out of 3 variables from anterior knee laxity measurements (best association for anterior knee laxity test) or both variables from rotational knee laxity measurements were positive (best association for rotational knee laxity test). The latter association led to a sensitivity of 81%.

Table 7.2: Thresholds for side-to-side differences and associated sensitivity, specificity and positive (PPV) and negative (NPV) predictive values to detect ACL tears based on anterior and rotational knee laxity measurements. Results presented in bold were considered as the best associations. ATD_{200}, anterior displacement at 200N; PC_A, primary compliance; SC_A, secondary compliance; IR_5, internal rotation at 5 Nm; C_{IR}, compliance in internal rotation.

		Threshold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	% of subjects correctly evaluated
Anterior knee laxity test	ATD_{200}	*≥1.2 mm*	*75*	*95*	*94*	*79*	*84*
	PC_A	≥18 μm/N	55	95	92	68	72
	SC_A	≥6.2 μm/N	58	96	93	69	74
	$ATD_{200} + PC_A + SC_A$	One or more variables above threshold	83	86	85	83	84
		Two or more variables above threshold	*71*	*100*	*100*	*78*	*84*
		Three variables above threshold	34	100	100	60	63
Rotational knee laxity test	IR_5	*≥3.2°*	*38*	*95*	*88*	*60*	*63*
	C_{IR}	≥0.6°/N m	31	95	86	58	59
	$IR_5 + C_{IR}$	One or more variables above threshold	44	90	81	62	64
		Two variables above threshold	*25*	*100*	*100*	*57*	*58*
Combined tests	$ATD_{200} + IR_5$	*At least one variable above threshold*	*84*	*90*	*89*	*85*	*87*
		Two variables above threshold	25	100	100	57	58
	$ATD_{200} + PC_A + SC_A + IR_5 + C_{IR}$	One or more variables above threshold	90	78	80	88	85
		Two or more variables above threshold	*83*	*98*	*98*	*85*	*89*
		Three or more variables above threshold	53	100	100	68	74
		Four or more variables above threshold	22	100	100	56	56
		Five variables above threshold	9	100	100	52	48
	Anterior knee laxity (≥2 variables positive) Rotational knee laxity (2 variables positive)	*One or both tests positive*	*81*	*100*	*100*	*84*	*89*

3.2 Detection of different categories of ACL injuries

Only the SSD for ATD_{200} and SC_A were significantly different between the different categories of ACL injury ($p<0.05$). For ATD_{200}, the average SSD reached 2.8 ± 1.6 mm for patients displaying a complete ACL tear, 2.8 ± 1.8 mm for ACL remnants healed on the PCL, 1.8 ± 1.2 mm for ACL remnants healed on the intercondylar notch and 1.5 ± 1.2 mm for partial tears. For SC_A, the average SSD reached 9.7 ± 6.4 µm/N for complete ACL tears, 8.6 ± 7.5 µm/N for ACL remnants healed on the PCL, 5.6 ± 5.1 µm/N for ACL remnants healed on the intercondylar notch and 2.8 ± 4.4 µm/N for partial tears.

Figure 7.3 represents the SSD categorised by ACL tear subtype for the 3 variables from the anterior knee laxity test. The three graphical illustrations of individual results show that it is possible to determine thresholds to distinguish between “no substantial ACL remnants” and “ACL remnants healed on the PCL” on the one hand, and “ACL remnants healed on the intercondylar notch” and “partial tears” on the other hand. None of the latter two categories had an SSD superior to 3.7 mm for ATD_{200} (Figure 7.3.a), 48 µm/N for PC_A (Figure 7.3.b) and/or 17.5 µm/N for SC_A (Figure 7.3.c). In total 35 out of 92 (38%) “no substantial ACL remnants” and “ACL remnants healed on the PCL” could be identified above these thresholds. Rotational knee laxity measurements were not conclusive to detect ACL tear subtypes (Figure 7.4).

4. Discussion

The main finding of the present study is that combined measurements of anterior and rotational knee laxity, in addition to a refined analysis of the load-displacement curve, yield a high potential of diagnosing ACL injuries. Compared to the common analysis of anterior displacement, further analysis of knee internal rotation increased the diagnostic sensitivity by 10%, whereas further analysis of the slope of the load-displacement curve enhanced the specificity to 100%. The simultaneous analysis of these parameters allowed to identify 81% of ACL-injured patients without a false positive, regardless of the ACL tear and associated injuries. The diagnostic performance thus reached a similar level to the one reported in the literature for the Lachman test (Benjaminse et al. 2006) and MRI (Rayan et al. 2009).

It has previously been proposed that the combination of anterior and rotational knee laxity measurements would refine the diagnosis of ACL injuries (Di Iorio et al. 2014). To the best of the authors’ knowledge, this is the first time that combined measurements are reported. Although the combination of anterior and rotational knee laxity measurements improved ACL diagnosis in the present study, it must be acknowledged that acquiring multiple laxity measurements with two separate arthrometers goes along with a greater time investment in the daily medical practice. Insofar, it would be advantageous if laxity measurements in both planes could be performed with a single instrument. On the other hand, arthrometric measurements have the advantage to be less error prone due to the examiner’s experience compared to manual tests, although standardised test execution is critical to ensure the proper use of the device and to increase reliability of the results.

Figure 7.3: Side-to-side differences in anterior knee laxity for each ACL tear subtype in a. Anterior displacement at 200 N (ATD_{200}), b. Primary compliance (PC_A) and c. Secondary compliance (SC_A). The black lines represent the average of each group. The dotted red lines represent the threshold of 1.2 mm, 18 µm/N and 6.2 µm/N determined for all categories of ACL injuries (see Table 7.2). The dotted blue lines represents the threshold to distinguish between "complete tears"/"ACL remnants healed on the PCL" and "partial tears"/"ACL remnants healed on the intercondylar notch".

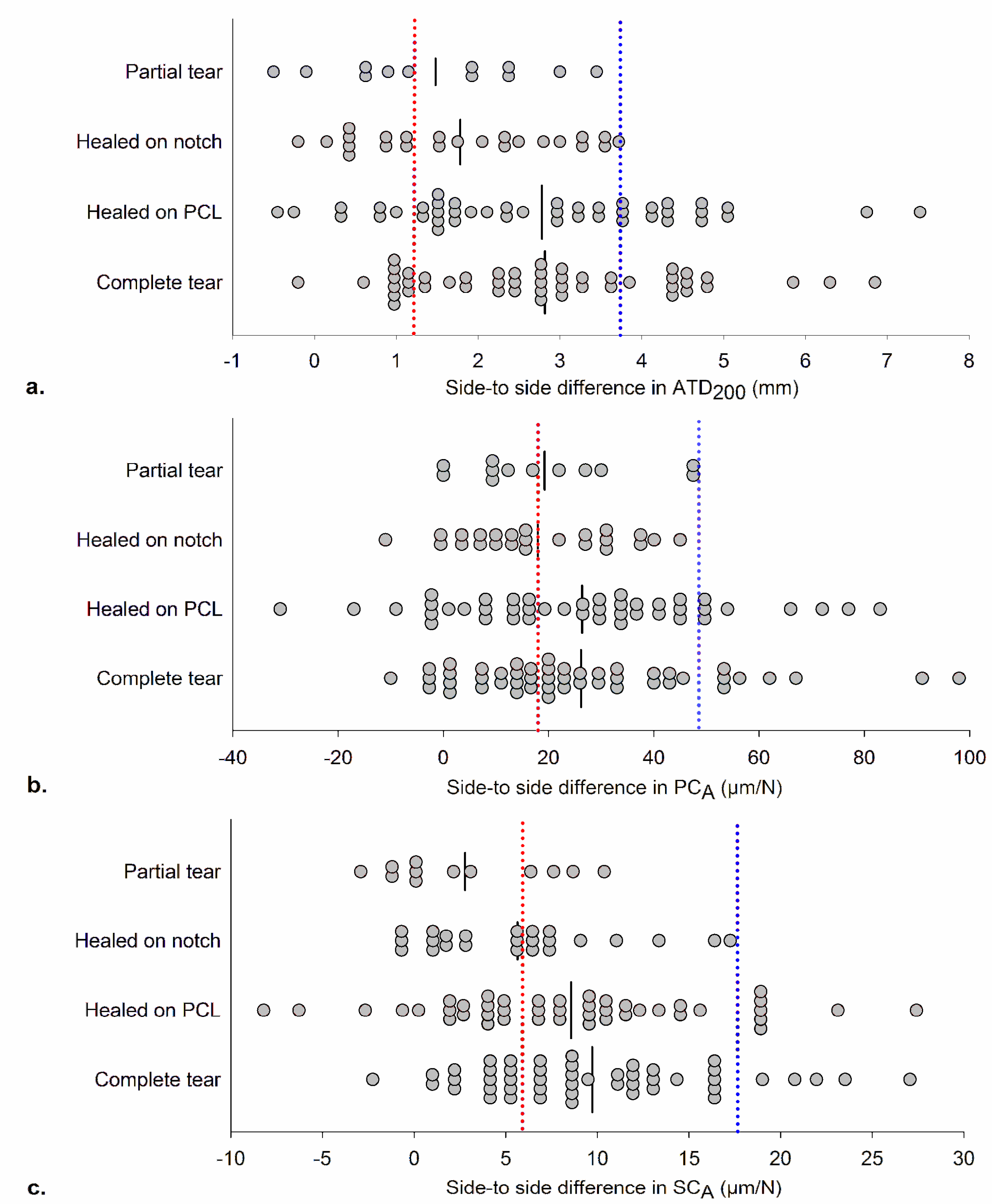
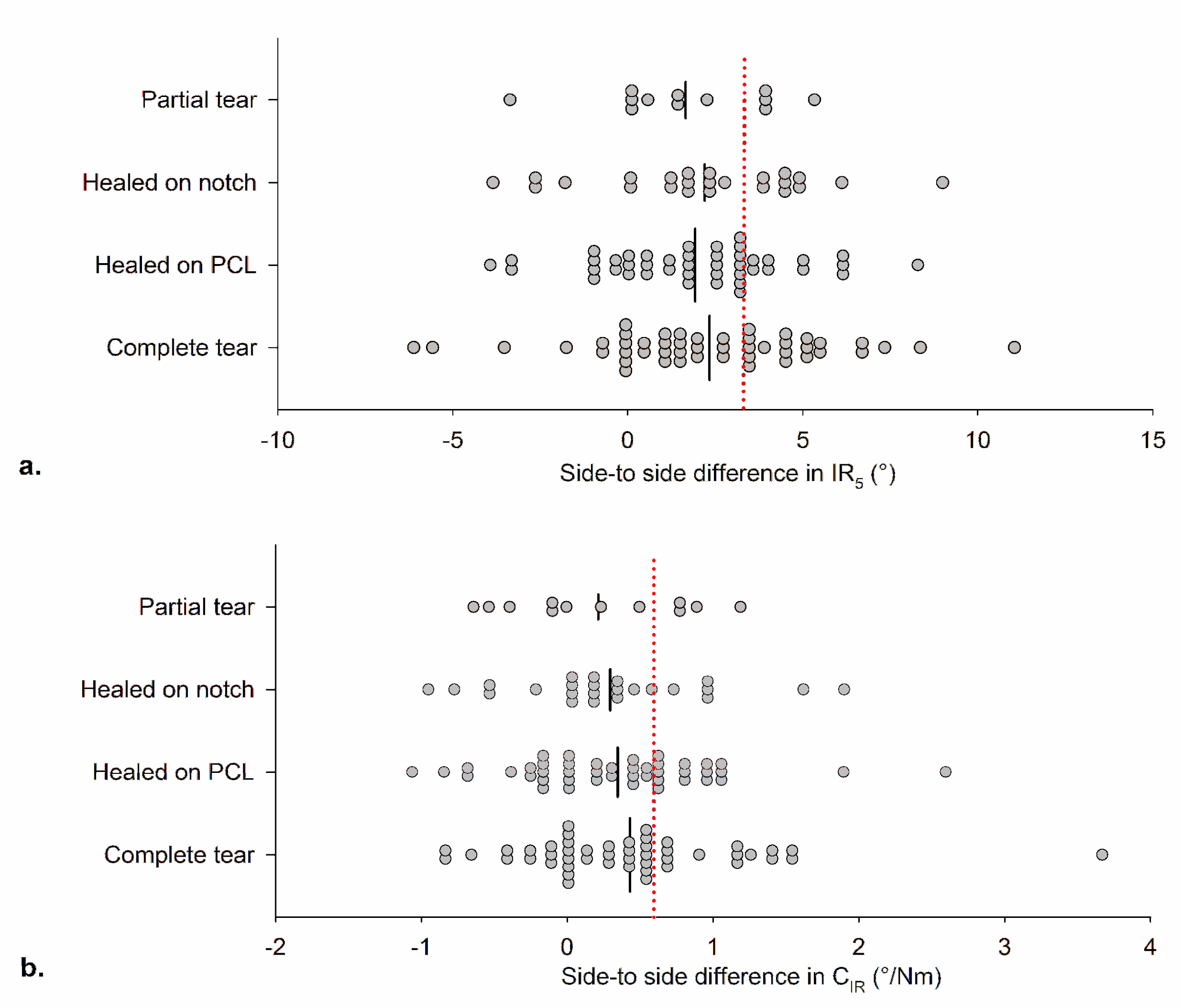


Figure 7.4: Side-to-side differences in rotational knee laxity for each ACL tear subtypes in a. Internal rotation at 5 Nm (IR_5) and b. Compliance in internal rotation (C_{IR}). The dotted red lines represent the threshold of 3.2° and 0.6 °/Nm determined for all categories of ACL injuries (see Table 7.2).



The combined analysis of several variables of the load-displacement curve increased the specificity to 100% both for the anterior and the rotational knee laxity tests. This combination of variables is of interest in the diagnosis of ACL injuries, especially to avoid false positives. Healthy knees never had more than 1 variable positive in the anterior or the rotational knee laxity test, such that 2 positive variables in one test confirmed the presence of an ACL tear. The fact that ACL-injured patients have several modifications of the load-displacement curve has never been reported before.

While anterior knee laxity measurement devices have been frequently described in the literature, efforts are still needed to develop reliable devices to measure rotational knee laxity. There is a great debate on whether static or dynamic measurements should be preferred in the evaluation of ACL injuries (Musahl et al. 2012). While static measurements may have less relevance to assess knee function, they may be particularly appropriate for the diagnosis of ACL injuries (Musahl et al. 2012). The increase in static internal rotation induced by isolated ACL injuries has been estimated to reach in average 3° (Markolf et al. 1984, Nielsen et al. 1984, Lane et al. 1994). The precision of the Rotameter has been found to be 4° for the SSD in IR_5 (Mouton et al. 2014), which may partly explain its low sensitivity of 38% for IR_5. A higher precision of the device may help to better discriminate between healthy and injured subjects and would likely also have an impact on the contribution of rotational knee laxity measurements in the diagnosis of ACL injuries. Nonetheless, although the sensitivity of this test is low, these results are still superior to the sensitivity of 24% reported for the pivot shift test in a previous meta-analysis (Benjaminse et al. 2006).

In anterior displacement at 200N, the current analysis revealed a sensitivity of 75% and a specificity of 95% for a threshold of 1.2mm. Robert et al. (Robert et al. 2009) reported a sensitivity of 70% and a specificity of 99% for a threshold of 3mm at 134N for complete ACL tears. The threshold was 1.5mm for partial tears to obtain a sensitivity of 80% and a specificity of 87%. Our threshold is far from the one of 3mm generally accepted by the orthopaedic community as described in the evaluation of the IKDC form (Hefti et al. 1993), which underlines the importance of reconsidering such standards. Still, the GNRB® displays a similar sensitivity compared to the Lachman test and to the KT-1000. A meta-analysis reported a sensitivity of 85% and a specificity of 94% for the Lachman test as performed by orthopedic surgeons (Benjaminse et al. 2006). Although we did not make a direct comparison between clinical tests and arthrometric measurements, the similarity in results appears to be striking. As for the KT-1000, its sensitivity has been reported to reach 72-82% in studies with a visual confirmation of ACL ruptures under arthroscopy and no apparent selection of the type of the ACL tear (Anderson et al. 1989, Anderson et al. 1992, Jonsson et al. 1993). The specificity of the KT-1000 has not clearly been established, as most studies did not include a healthy control group.

To the authors' knowledge, this is the first time that the diagnostic value of the GNRB® was assessed in different categories of ACL remnants. ACL remnants healed on the intercondylar notch and partial ACL tears displayed lower anterior laxity in comparison to complete ACL tears and ACL remnants which healed on the PCL (Crain et al. 2005, Panisset et al. 2008, Nakase et al. 2013, Di Iorio et al. 2014). The use of anterior knee laxity variables allowed to correctly identify 38% of the complete ACL tears or those that healed on the PCL. This information may be of help for surgeons in their decision making process. Nevertheless, the distinction between ACL injury categories was not optimal due to the high variety of the results inducing a great overlap of anterior laxity values between subtypes of ACL tears. So far, this overlap as well as the precision of the devices may prevent us from making clear distinctions between different types of ACL tears. Unlike anterior knee laxity measurements, rotational measurements were not conclusive to differentiate between any of the 4 categories of ACL injuries. Other authors hypothesised that ACL remnants may not stabilise rotational knee laxity because of their vertical position in the intercondylar notch (Nakamae et al. 2010). In a previous cadaver study using the first version of the Rotameter, resection of the posterolateral bundle indeed increased the tibiofemoral rotation significantly while the subsequent resection of the anteromedial bundle did not induce a further increase (Lorbach et al. 2010). As the anteromedial and posterolateral bundles of the ACL play different biomechanical roles (Zantop et al. 2007), it would be interesting to separate both types of tears and analyse the associated laxity measurements *in vivo*, provided that a greater number of patients with partial tears would be recruited and that a device with a greater precision would be developed.

The present study is not without limitations. The influence of associated injuries on knee laxity measurements was not considered although only 30% of ACL injuries are reported to be isolated (23% in the present study) (Maletis et al. 2011). Medial meniscus tears may influence anterior knee laxity measurements (Levy et al. 1982, Musahl et al. 2010, Ahn et al. 2011) while collateral ligament tears as well as lateral meniscus tears may influence rotational knee laxity (Musahl et al. 2010). Moreover, recent studies have shown that the frequently associated anterolateral ligament tears could be linked to the increased rotational knee laxity observed in ACL injuries (Claes et al. 2013). We decided not to analyse the influence of associated injuries on knee laxity measurements in this study because of the limited sample size for the resulting subcategories. Nonetheless, our approach demonstrates appropriate performance to diagnose ACL injuries, regardless of the associated injuries and the category of ACL injury.

5. Conclusion

The approach of combining static rotational laxity measurements as well as the slope of the load-displacement curve to the usual anterior knee laxity measurements improved the diagnosis of ACL injuries to a comparable extent than MRI or clinical examinations as reported in the literature. Several variables related to anterior knee laxity allowed to partially identify complete ACL tears as well as those, which healed on the PCL. Developing arthrometers with greater measurement precision and which allow to combine both anterior and rotational knee laxity has the potential to further improve the diagnosis of ACL-injuries in daily clinical practice.

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Chapter 8
Discussion, conclusions and future directions

A remarkable increase of publications on ACL injuries was observed between 1988 (n=149) and 2013 (n=1170) highlighting the growing interest (Vitzthum et al. 2009) from the medical and research communities on these injuries over the last decades. Despite the amount of ongoing research, few studies considered individual patient related factors. The general purpose of the present thesis was thus to propose a step towards an individualised approach of ACL injuries (1) through a systematic analysis of the demographic characteristics of ACL-injured patients and (2) through the implementation of individualised knee laxity profiles.

Since the development of knee arthrometers in the early 80's, the quantification of knee laxity has mainly been built on side-to-side differences (SSD) in anterior tibial displacement (ATD). Nevertheless, these devices are only used by a minority of surgeons on a systematic basis to evaluate knee laxities. Although knee laxity measurements are easy and quick to perform, current arthrometers have several limitations:

(1) No international consensus exists on which arthrometer to use. The KT-1000® is still widely used as a "gold standard" although its reproducibility has been criticised (Ballantyne et al. 1995, Sernert et al. 2007).

(2) Anterior knee laxity is not the only laxity that should be considered in ACL injuries. With the ongoing debate on the precision of ACL reconstruction techniques to restore normal knee kinematics, static rotational knee laxity has received an increased interest over the last decade (Bull et al. 2002, Isberg et al. 2011). An increased understanding of rotational knee laxity is still needed.

(3) A single measure of knee laxity may not be appropriate enough to describe knee laxity and/or injuries (Shultz et al. 2012, Di Iorio et al. 2014). As a consequence, a multiplanar approach combining anterior and rotational knee laxity measurements may provide a better description of an individual's knee laxity.

(4) Recent studies demonstrated that excessive physiological anterior knee laxity was a risk factor for non-contact ACL injuries (Uhorchak et al. 2003). Physiological laxity is complex to interpret as it may be influenced by several parameters such as gender, sex, body mass, bony anatomy, etc (Baxter 1988, Shultz et al. 2007a, Zyroul et al. 2014). As a consequence, it may be problematic to compare physiological laxity in individuals with different characteristics. Therefore, individual characteristics should be considered and normative references should be proposed.

(5) The analysis of knee laxity is currently based on the SSD in final displacement. Several studies reported that patients with an ACL injury displayed a modification of their knee stiffness, as represented by the slope of the force-displacement curve in knee laxity

(Markolf et al. 1984, Shino et al. 1987, Steiner et al. 1990). Its consideration may thus improve diagnosis and follow-up of knee injuries.

(6) Studies on the diagnosis of ACL injuries mainly deal with patients with isolated and complete ACL tears and do not consider other categories of ACL injuries (such as partial ruptures or ACL remnants). The diagnostic performance reported in the literature may thus not be adequate to apply in the daily practice.

The above-cited limitations can be overcome with a better understanding of arthrometers (precision) as well as an increased understanding of knee laxity in healthy subjects and ACL-injured patients. This knowledge can be gained through the establishment of individualised normative references and through a multiplanar approach of laxity. These two aspects were answered in the different chapters of the present thesis.

First, a description of the different profiles of ACL-injured patients and their treatment was proposed in ***Chapter 2***. Then, ***Chapter 3*** offered a comprehensive overview of rotational knee laxity. This knowledge allowed to properly establish individualised normative references for anterior and rotational knee laxity in ***Chapters 3, 4 and 5***. These findings were then applied to evaluate whether physiological laxity was higher in ACL-injured patients compared to controls in ***Chapter 6*** to verify whether knee laxity could be a risk factor for ACL injuries. Finally, in ***Chapter 7***, the performance of anterior and rotational knee laxity measurements were assessed together to diagnose ACL injuries.

1. ACL-injured patients: intrahospital registry and treatment decision

The goal of ***Chapter 8*** was to provide a picture of the ACL-injured population and its treatment. Current ACL registries rarely include nonoperatively treated patients which leads to an incomplete overview of the ACL-injured population and the treatment decision making process. As a consequence, an intrahospital registry was implemented in 2011 which included all patients with a clinically and radiographically (MRI) confirmed ACL injury. Patients were proposed to enter a systematic, prospective and standardised follow-up regardless of their treatment (operative or nonoperative). At their first visit at the physiotherapy department, patient were asked whether they would agree to sign a consent form. A home-made questionnaire gathered general information (height, weight …), data on sport participation before injury and during the follow-up, data on previous severe leg injuries and their treatment as well as data on the ACL injury (date, mechanism). If the patient underwent surgery, arthroscopic findings were gathered including information on the type of surgery.

The study included 423 patients of which 346 (82%) signed a consent agreement and thus agreed to participate. Significant age- and gender-related differences between patients could be identified. The inclusion of nonoperatively treated patients allowed to observe a new finding with a second peak of injuries in females over 35 years. The majority of these ACL injuries originated from alpine skiing. An analysis of these patients' activity profile revealed that the involved females were not practicing a regular sport or were involved in recreational sports such as swimming, cycling, and running before the injury. As such, these ACL injuries may partly be explained by a lack of physical fitness (Ruedl et al. 2011). For older patients with a lower activity, nonoperative treatment has proven to be efficient (Buss et al. 1995). These patients were thus mostly recommended for a nonoperative treatment.

Currently, no evidence-based argument exists to recommend a surgical reconstruction to every patient with an ACL injury (Smith et al. 2014, Eggerding et al. 2015). As such, the percentage of 74 % of operated patients in the current study seemed remarkably high. This was however comparable to both Frobell's (Frobell et al. 2010) and Grindem's (Grindem et al. 2014) studies who reported a similar percentage of nonoperatively treated patients of 30%. It did also correspond to Noyes et al. who presented the "rule of thirds" (Noyes et al. 1983). One third of patients are able to compensate adequately without any surgery, one third can compensate if they give up significant activities, and one third will perform poorly and require future surgery. By considering individual criteria like gender, age, previous ACL injury and preinjury level of practice, the decision-making equation revealed a complex picture of ACL-injured patients. Indeed, 8 profiles of ACL-injured patients could be identified. The percentage of surgical treatment was different within each profile. It was superior to 80% in patients under 35 years of age who were involved in a competitive sport (profiles 1 to 3). This percentage decreased to 60-80% in patients younger than 35 years who were not involved in a competitive sport and those who sustained previous ACL injuries (profiles 4 to 6). It was under 60% for patients above 35 years of age (profiles 7 and 8). In agreement with the literature (Collins et al. 2013), both gender and age influenced the decision for surgery. Males and younger patients were more likely to be operated than females and older patients. The preinjury level of practice explained to a large extent the decision for or against surgery, in accordance with recommendations for good clinical practice (Beaufils et al. 2009).

To our knowledge, this was the first time that all these parameters were prospectively assessed to improve the identification of clusters of patients with similar characteristics. The determination of typical profiles is innovative and may serve in the future as a basis to find the most adapted treatment for each patient.

2. Precision of arthrometers

To date, the use of rotational knee laxity measurements is not considered in the medical practice as no device to measure knee rotation is yet commercialised. Furthermore, our knowledge on these measurements were poor at the beginning of the present thesis. To provide high quality research and be able to foresee the use of these measurements one day in the daily medical practice, we recommended, in ***Chapter 3***, a 5- step systematic approach. The first step was to evaluate accuracy, reliability and precision (MDC) of the instrument for the given setting. The second step was to establish normative references based on a healthy population. The 3 last steps dealt with injured or reconstructed patients to (3) evaluate diagnostic and (4) prognostic potential of these measurements and (5) to assess the influence of surgical techniques on static rotational knee laxity. Through the present thesis, the 3 first steps could be answered.
To evaluate the precision of the GNRB® and the Rotameter in ***Chapter 5***, the Minimum Detectable Change (MDC) was computed. The latter indicates whether a difference between 2 tests accounts for a true change or if it has to be considered as a measurement error. For the GNRB®, an inter-examiner precision of 1.2 mm and 1.5 mm was observed respectively for the absolute value and the SSD at 200 N. This precision is superior to those previously reported. The intra-examiner precision of the GNRB® was reported to reach 2 to 4 mm depending on the installation procedures (Vauhnik et al. 2013). These preliminary findings were similar to the precision reported for other arthrometers. With the KT-1000®, a precision of 2.9 mm has been reported for experienced examiners and of 3.5 mm for novice examiners (Berry et al. 1999). With the Genucom, a precision of 3 mm has been reported (McQuade et al. 1989). Our findings thus indicate that a rigorous protocol helps to improve the precision of the device.
Considering static rotational knee laxity measurements, the inter-examiner precision of the second version of the Rotameter was 4.2° in IR at 5 Nm for absolute measurements and 4.4° for the SSD (***Chapter 5***). A precision of 17° (McQuade et al. 1989), 5.1° (Tsai et al. 2008), 5 to 7° (Shultz et al. 2007b) and 6.9° (Branch et al. 2015) were reported using different methods of calculation for previous devices. As reported in ***Chapter 3***, there is a great variability between devices measuring knee rotation depending on: patient positioning, methods of measurement, examination protocols and data analysis. These differences may partly explain the wide range

of precision observed for the different devices. Compared to other devices, the Rotameter allowed for a standardisation of the hip and knee flexion angles, a parameter reported to influence rotation (Shoemaker et al. 1982). Moreover, the protocol of the Rotameter was optimised to measure rotation in a consistent way as advised in ***Chapter 3***: IR and ER were performed separately and includes 2 ‘‘preconditioning trials’ to avoid the hysteresis phenomenon when the tests encompass full cycles in IR and ER. Although we reported the highest precision in rotation compared to previous devices, our results need to be related to observations made in ***Chapter 7*** on the diagnosis of ACL injuries. For a threshold of 3.2°, we could observe a sensitivity of the Rotameter of 38%. Although this sensitivity is low, it is still superior to the sensitivity of 24 % reported for the pivot shift test in a previous meta-analysis (Benjaminse et al. 2006). A higher precision to measure knee rotation may help to better discriminate between healthy and injured subjects and would likely also have an impact on the contribution of rotational knee laxity measurements in the diagnosis of ACL injuries.

3. Knee laxity in healthy controls

Individualised normative references for knee laxity are missing in the literature. ***Chapter 4, 5 and 6*** therefore proposed an innovative approach to obtain individualised knee laxity profiles by considering both anterior and rotational knee laxity measurements.

3.1 Influencing factors

One goal of ***Chapters 4 and 5*** was to understand which individual characteristics amongst gender, age, height and weight influenced anterior and rotational knee laxity measurements. This could be achieved by measuring both laxities in a group of 104 healthy participants with no history of knee injury or surgery and by computing linear regression models to test the influence of gender, age, height and weight.

In ***Chapter 5***, anterior knee laxity measurements were not significantly influenced by gender: the difference observed between genders was of 0.5 mm. Although gender has been previously reported to significantly influence anterior knee laxity with the KT-1000® (Rozzi et al. 1999, Uhorchak et al. 2003, Shultz et al. 2007a, Zyroul et al. 2014), most of these studies reported a minor difference of less than 1.5 mm (Rozzi et al. 1999, Uhorchak et al. 2003, Zyroul et al. 2014). These differences are lower than the precision of the KT-1000® of 3 mm (Berry et al. 1999) so that they may not be clinically significant. As for rotational knee laxity measurements,

Chapter 4 and 5 confirmed literature findings (Hsu et al. 2006, Park et al. 2008, Branch et al. 2010, Almquist et al. 2013): being a female was associated with a higher internal (+3.7° compared to males, ***Chapter 5***) and external rotation (+6.4° compared to males, ***Chapter 5***). For internal rotation, the difference is however lower than the precision of the device and therefore may not be clinically significant.

In ***Chapter 4 and 5***, increased body mass was related to lower knee rotation. Body mass did not influence anterior knee laxity measurements and height did not influence neither anterior nor rotational knee laxity. Previous studies had investigated BMI (Shultz et al. 2012, Zyroul et al. 2014). Shultz et al. showed that subjects with increased rotational knee laxity tend to have a lower BMI. The authors however did not report any absolute differences. It is thus difficult to verify whether this effect was important or not. For anterior knee laxity, one study reported a significant influence of BMI on these measurements (Zyroul et al. 2014). The results were however inconsistent as they were only significant in men and not in women (Zyroul et al. 2014). Moreover, the influence of BMI in men was minor as, for each BMI increase, the anterior knee laxity was reduced by 0.04 mm only. As such, our finding that body mass has no influence on anterior knee laxity measurements is relatively consistent with the literature.

In ***Chapter 4 and 5***, age did not influence anterior or rotational knee laxity measurements. Zyroul et al. also reported no effect of age on anterior knee laxity in a study with 521 healthy subjects aged from 15 to 74 years (Zyroul et al. 2014). A similar pattern was observed for rotational knee laxity, no significant influence of age could be observed both in males and females (Almquist et al. 2013). Our results are thus consistent with the literature.

In summary, anterior knee laxity was not influenced by gender, age, height or body mass. For rotational knee laxity measurements, gender and body mass were found to significantly influence its measure: it explained a non-negligible variability of internal, external and total rotation from 46 to 60% (***Chapter 5***). Our results are however probably more consistent than previous studies due to the higher number of healthy subjects studied (n=104) and to the large range of age (11-59), height (150-198 cm) and body mass (42-106 kg) studied.

3.2 Individualised references and knee laxity profiles

To improve the understanding of normality in knee laxity, the second goal of ***Chapter 5*** was to calculate individualised and standardised laxity scores for anterior and rotational knee laxity measurements taking into account influencing characteristics. The different scores were combined to establish knee laxity profiles which description was the third aim of ***Chapter 5***.

Scores were calculated as a z score for anterior knee laxity with the average value and standard deviation observed in the cohort. For rotational knee laxity measurements, which are influenced by gender and body mass, the predicted value given by the model and the standardised residuals obtained from the statistical software were used to calculate the standardised score.

For each laxity, the score established in ***Chapter 5*** represented the distance of one individual to the average of the healthy control group with the units being the standard deviation of the healthy control group. As standard deviation has already been previously used as a threshold (Uhorchak et al. 2003), we decided to use it to categorise knees as being hypo- (score < -1), normo- (score between -1 and 1) and hyperlax (score > 1). It should be highlighted that the proportion of hyperlax knees found in healthy subjects for ATD, IR and ER of about 15% is influenced by the normal distribution of knee laxity measurements. Under normal distribution, it is indeed recognised that about 16% of cases will be above 1 standard deviation above the average.

Anterior and rotational knee laxity scores were poorly correlated (r<0.24; p=0.02) in agreement with the literature (Shultz et al. 2007a). Within rotational knee laxity, internal and external rotation were moderately correlated (***Chapter 5***: r=0.60; p<0.01). These low correlation suggests that anterior displacement, internal and external rotation yielded complementary information. Interestingly, when combining the anterior displacement to internal and external rotation, only 32% of the participants showed a normal knee laxity profile (all 3 scores >-1 and <1), 33% were concerned by hyperlaxity (at least one score >1), 40% by hypolaxity (at least one score <-1) and 5% by both (one score >1 and one <-1).

Through the standardisation of the score, comparison of rotational knee laxity of an individual to a general population became possible irrespective of differences in gender or BMI. The normative data presented here may allow improving the comprehension of physiological and pathological laxity. Indeed, while the existence of specific laxity profiles has been previously suggested (Shultz et al. 2012), their distribution in a general population had not yet been reported. The diversity of laxity profiles found in ***Chapter 5*** highlights both the complexity of the interpretation of multidirectional knee laxity and the necessity for individualised care of knee injuries and diseases. Further investigations are however needed to understand the influence of such diverse knee laxity profiles on knee function and injuries.

4. Knee laxity in the non-injured knee of ACL-injured patients

In ***Chapter 4 and 6***, we hypothesised that the ACL-injured patients would be more likely to have increased knee laxity profiles in their contralateral knees than healthy control knees. Independent t-tests allowed to compare knee laxity scores between a group of healthy subjects and a group of healthy contralateral knees of ACL-injured patients. ROC curves were computed to differentiate knee laxity between groups.

The non-injured knee of ACL-injured patients displayed increased anterior laxity compared to healthy knees of a control group. A subject with an anterior laxity score above 0.75 were 2.97 (95% CI: 1.68-5.24) more likely to be in the group of ACL-injured patients. These results are in line with prior findings (OR=2.6) (Uhorchak et al. 2003).

Regarding static rotational knee laxity, in ***Chapter 4***, we did not find any difference in rotational knee laxity between healthy controls and the non-injured knee of ACL-injured patients. However, we highlighted that the power analysis did not exceed 0.5. In ***Chapter 6***, with a much greater number of subjects (104 healthy controls and 171 healthy contralateral knees of noncontact ACL-injured patients), we could confirm that the internal rotation score was in average greater in the non-injured knee of ACL-injured patients compared to healthy controls. This finding is in agreement with the literature (Branch et al. 2010). However, unlike Branch et al. (Branch et al. 2010), ER was similar between both groups in ***Chapter 6***. These authors observed that the non-injured knee of ACL-injured patients displayed less ER than healthy control knees. This lower ER counterbalanced for the higher IR in the non-injured knee of ACL-injured patients so that the total range of knee rotation did not differ between the non-injured knee of ACL-injured patients and healthy control knees (Branch et al. 2010). The reason for this finding remains unclear.

As we did not observe any difference in ER between the healthy contralateral knee of ACL-injured patients and the healthy control group, we then only compared the association of anterior laxity and internal rotation laxity scores between both groups. An individual with both laxity scores above established thresholds was 3.18 times more likely to be in the group of the non-injured knee of ACL-injured patients (***Chapter 6***). The combination of anterior and rotational knee laxity led to a higher odds ratio (3.18) than when considered separately highlighting the potential interest of combining knee laxity measurements obtained from different planes (2.97 for anterior knee laxity and 2.45 for internal rotation). Knee laxity profiles differed between patients and controls in 2 associations: the non-injured knee of patients were less likely to be normolax in anterior displacement associated with hypolaxity in internal rotation and more likely to be hyperlax in anterior displacement associated with normolaxity in internal rotation.

The case-control design of ***Chapter 6*** however did not allow to conclude on a causal relationship between the different knee laxity profiles and the risk to sustain an ACL injury. It was the first time that the differences in knee laxity profiles between healthy controls and the healthy contralateral knees of ACL-injured patients were reported. Future prospective investigations are needed to analyse how these knee laxity profiles characterise the risk of an individual. Within the context of the present thesis, it would have been difficult to recruit a sufficient amount of participants and observe enough ACL injuries to get a reasonable power analysis.

5. Knee laxity in the injured knee of ACL-injured patients

The purpose of ***Chapter 7*** was to determine whether a combination of variables derived from the load–displacement curves of anterior and rotational knee laxity measurements would improve the instrumental diagnosis of ACL ruptures. Both the GNRB® and the Rotameter were performed in a group of healthy controls and a group of ACL-injured patients with an arthroscopically confirmed ACL injury. Both the final displacement and the slope of the load-displacement curves were considered. A second aim of Chapter 7 was to determine whether combined knee laxity measurements would provide sufficient precision to detect different subtypes of ACL tears.

For the ATD at 200 N and an optimal threshold of 1.2 mm, sensitivity and specificity of the GNRB® reached respectively 75% and 95% for all types of ACL tears and regardless of associated injuries. Robert et al. reported a similar sensitivity of 70 % and specificity of 99 % for a higher threshold of 3 mm at 134 N for complete ACL tears only (Robert et al. 2009). Our threshold to detect ACL injuries is far from the one of 3 mm generally accepted by the orthopaedic community as described in the IKDC classification (Hefti et al. 1993) but highlights well that the current "gold standard" in the diagnosis of ACL injuries needs to be redefined.

Static rotational knee laxity, as measured by the IR at 5 Nm, associated to the ATD at 200 N increased the sensitivity of the diagnosis from 75 to 84%. Considered alone, rotational knee laxity may have a limited value in the diagnosis of ACL injuries. For internal rotation at 5 Nm and a threshold of 3.2°, sensitivity and specificity reached 38% and 95%. This sensitivity is surprisingly low. However, a meta-analysis revealed that the pivot-shift test without anaesthesia had a lower performance with a sensitivity of 24% and a specificity of 98% (Benjaminse et al.

2006). As explained earlier in this chapter, a higher precision of the Rotameter may help to better discriminate between healthy and injured subjects and would likely also have an impact on the contribution of rotational knee laxity measurements in the diagnosis of ACL injuries.

The slope of the load-displacement curve associated to final displacement increased the specificity of the diagnosis as shown in ***Chapter 7***. No false positive result occurred when the diagnosis was based on several characteristics of the load-displacement curve both for anterior and rotational knee laxity measurements. In other words, a test with more than one parameter being abnormal indicated with certainty a patient with an ACL injury. These findings highlight that healthy knees never have more than one parameter of the load-displacement curve being modified/abnormal.

The concomitant analysis of anterior and rotational knee laxity measurements as well as the concomitant analysis of the SSD in final displacement and of the slope of the load-displacement curve further improved the diagnosis of ACL rupture. With this combination, a positive result was correct in 100% of patients and a negative result in 84% (sensitivity: 81%, specificity: 100%), regardless of the subtype of the ACL tear and the associated injuries. This performance is similar to the one reported for MRI (sensitivity: 81%, specificity: 96%) (Rayan et al. 2009).

ACL remnants which healed on the notch and partial tears were more stable anteriorly in agreement with the literature (Crain et al. 2005, Panisset et al. 2008, Nakase et al. 2013, Di Iorio et al. 2014). A threshold of 3.7 mm in the anterior displacement at 200N allowed to detect 27% per cent of complete tears and ACL remnants which healed on the PCL. Unlike anterior knee laxity measurements, rotational measurements were inconclusive to differentiate between the different types of ACL tears. Other authors hypothesised that ACL remnants may not stabilise rotational knee laxity because of their vertical position in the intercondylar notch (Nakamae et al. 2010). To date, arthrometers may not be precise enough to make a better distinction between subtypes of tears.

It was the first time, to our knowledge, that sensitivity and specificity of rotational knee laxity measurements were reported alone and in combination with anterior knee laxity measurements with the consideration of different characteristics of the load-displacement curve. The efficient approach of the diagnosis of ACL injuries with arthrometers, as proposed in ***Chapter 7,*** may encourage physicians to systematically consider knee laxity measurements in their diagnosis. This may specifically be of value in these cases where neither the clinical nor the MRI diagnosis are sufficiently conclusive. Further studies are required to understand whether concomitant injuries to the ACL influence knee laxity measurements and whether current arthrometers are precise enough to detect them. The analysis of concomitant injuries was unfortunately not possible in ***Chapter 7***. Due to the diversity of associated lesions observed in ACL-injured patients, this would have led to a low power analysis.

6. Conclusions

- Systematic data collection allowed to identify specific subtypes of ACL-injured patients according to gender, age, previous ACL injury and preinjury level of practice, for which the percentage of surgical treatment varied significantly. The diversity of patient subtypes suggests that there is no such thing like a single ACL injury and that there is a need for a better understanding of patients at risk for ACL injuries.

- Regarding knee laxity measurements, the GNRB® displayed a higher precision than previously reported provided that care is taken to have a standardised evaluation protocol. The Rotameter also displayed higher precision than previous arthrometers. The latter indeed display highly variable testing procedures which may have influenced the reproducibility of previous devices.

- Physiological knee laxity in healthy controls revealed to be complex. Anterior knee laxity was not influenced by individual characteristics such as gender, age, height or body mass. Rotational knee laxity was greater in females compared to males and negatively influenced by increasing body mass. The influence of individual characteristics as well as the high inter-subject variability observed in rotational knee laxity measurements prevent its direct comparison between heterogeneous groups of subjects. As such, the use of individualised normative references may be critical in the future.

- The interpretation of multidirectional knee laxity is even more complex as anterior and rotational knee laxity are poorly related to each other. The diversity of laxity profiles observed in healthy subjects suggest that an individualised approach of knee laxity may be also necessary in patients to achieve the best treatment outcome.

- The healthy contralateral knees of patients with noncontact ACL injuries displayed both increased internal rotation and anterior displacement compared to a group of healthy control knees hence indicating that genetic and anatomic factors may be related to the occurrence of noncontact ACL injuries. The identification of knee laxity profiles may thus be of relevance for primary and secondary prevention programs of these injuries.

- In ACL-injured patients, the combination of anterior and rotational knee laxity measurements lead to excellent diagnostic value for ACL injury, provided that both the slope of the load-displacement curve and the final displacement are considered together.

- Overall, the recent development of new arthrometers has offered the possibility to improve the understanding and to draw solid conclusions on physiological, pathological and reconstructed knee laxity. Knee laxity measurements may not replace the manual clinical evaluation in the future but may complete the diagnostic and therapeutic follow up of knee injuries.

7. Future directions

The challenge for the future will be to provide an individualised management of ACL injuries through a deeper understanding of the type of ACL-injured patients and their knee laxity.

The best treatment strategy of ACL injuries for each patient subtype and the most important parameters to consider in the decision making process remain, to date, unknown and still need to be investigated. In addition to gender, age and sport practice, knee laxity and associated lesions may be considered in the decision to operate a patient or not. However, a greater understanding of these parameters are needed.

To improve our understanding of knee laxity measurements in the healthy knee, the inclusion of varus-valgus laxity and genu recurvatum in knee laxity profiles may provide additional information. Further studies may also focus on a specific population such as children, for which the concomitant evolution of knee laxity and of neuromuscular control is still poorly understood.

Prospective studies are needed to confirm that anterior and rotational knee laxity and/or certain knee laxity profiles place a subject at risk for a non-contact ACL injury, be it for a primary or even a recurrent or contralateral tear. If so, it may become possible in the future to evaluate a subject’s risk to sustain a first or recurrent ACL injury. To assess this risk, a multifactorial analysis including anatomical, biomechanical and neuromuscular risk factors would be mandatory.

A link between excessive knee laxity and at risk movement for ACL injuries as well as poorer proprioception and poorer ACL reconstruction outcomes remain to be confirmed to make knee laxity become of particular interest for primary and secondary prevention programs. The influence of exercise and fatigue on anterior and rotational knee laxity and its consequence on knee movement may also be foreseen. If associations would be confirmed, patients with higher knee laxity may benefit from an adapted care compared to other patients such as an adjusted rehabilitation or reconstruction procedure.

Our current understanding of knee laxity measurements after ACL injuries and reconstruction is still poor. Associated lesions, despite their large numbers and their influence on knee laxity, remain insufficiently investigated in the diagnosis and follow-up of ACL injuries. Moreover, respective outcomes of surgical techniques in terms of knee laxity are still debated and the restoration of knee laxity by the ACL reconstruction remains insufficiently known on an individual basis.

In that sense, knee laxity measurements may have the ability to improve the management of

ACL injuries. Finally, whereas investigations were focused on ACL injuries, the role of knee laxity in other knee injuries and diseases like osteoarthritis and posterolateral corner injuries needs to be investigated further.

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