Non-invasive quantification of knee kinematics:

A cadaver study

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Abstract

The ability to quantify kinematic parameters of the knee is crucial in understanding normal biomechanics, recognising the presence of pathology and its severity, planning treatment and evaluation of outcomes. Current methods of quantifying lower limb kinematics remain limited in allowing accurate dynamic assessment. Computer assisted surgery systems have been validated in quantifying kinematic parameters, but remain limited to the operative setting. Recently, image-free computer assisted surgery technology has been adapted for non-invasive use and validated in terms of repeatability in measuring coronal and sagittal femorotibial mechanical alignment in extension. The aim of this thesis was to develop and implement a set of validation protocols to quantify the reliability, precision and accuracy of this non-invasive technology in quantifying lower limb coronal and sagittal femorotibial mechanical alignment, anteroposterior and rotatory laxity of the knee by comparison with a validated, commercially available image-free computer assisted surgery system.

Pilot study confirmed feasibility of further experimental work and revealed that the non-invasive method measured with satisfactory precision and accuracy: coronal mechanical femorotibial alignment (MFTA) from extension to 30˚ knee flexion, anteroposterior translation in extension and tibial rotatory laxity during flexion.

Further experiments using 12 fresh cadaveric limbs revealed that the non-invasive method gave satisfactory precision and agreement with the invasive system measuring MFTA without stress from extension to 40˚ knee flexion, and with 15Nm coronal stress from extension to 30˚ knee flexion. Using 100N of anterior force on the tibia, the non-invasive system was acceptably precise and accurate in measuring sagittal tibial displacement from extension to 40˚ flexion. End of range apprehension, such as has been proven repeatable in measuring tibial rotatory laxity was used and the non-invasive method gave superior

precision and accuracy to most reported non-invasive devices in quantifying tibial rotatory range of motion.

Non-invasive optical tracking systems provide a means to quantify important kinematic parameters in health and disease, and could allow standardisation of knee examination increasing communicability and translation of findings from the out-patient to operative setting. This technology therefore could allow restoration of individual specific kinematics in knee arthroplasty and soft-tissue reconstruction.

Peer reviewed publications from this thesis

1: **Russell DF**, Deakin AH, Fogg QA, Picard F. Quantitative measurement of lower limb mechanical alignment and coronal knee laxity in early flexion. Knee. 2014 Dec;21(6):1063-8. doi: 10.1016/j.knee.2014.07.008. PubMed PMID: 25150912.

2: **Russell DF**, Deakin A, Fogg QA, Picard F. Non-invasive quantification of lower limb mechanical alignment in flexion. Comput Aided Surg. 2014;19(4-6):64-70. doi: 10.3109/10929088.2014.885566. PubMed PMID: 24856249; PubMed Central PMCID: PMC4266097.

3: **Russell DF**, Deakin AH, Fogg QA, Picard F. Repeatability and accuracy of a non-invasive method of measuring internal and external rotation of the tibia. Knee Surg Sports Traumatol Arthrosc. 2014 Aug;22(8):1771-7. doi: 10.1007/s00167-013-2812-5. PubMed PMID: 24370989.

4: **Russell DF**, Deakin AH, Fogg QA, Picard F. Non-invasive, non-radiological quantification of anteroposterior knee joint ligamentous laxity: A study in cadavers. Bone Joint Res. 2013 Nov 1;2(11):233-7. doi: 10.1302/2046-3758.211.2000199. PMCID: PMC3819608. PMID: 24370989

Presentations given at scientific meetings from this thesis

Non-invasive quantification of knee kinematics

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International Podium Presentation

12th Annual Meeting of the International Society for Computer Assisted Orthopaedic Surgery, Seoul, South Korea, 13th – 16th June 2012.

National Podium Presentation

6th Annual Congress of the British Society for Computer-Assisted Orthopaedic Surgery, 19th & 20th April, 2012.

Quantitative measurement of mechanical alignment and coronal laxity during early knee flexion.

D. Russell, A. Deakin, Q.A. Fogg, F. Picard.

Laboratory of Human Anatomy, University of Glasgow, Golden Jubilee National Hospital, Clydebank.

Regional Podium Presentation

Glasgow Meeting of Orthopaedic Research, 22nd March 2013.

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National Poster Presentation

1. *British Orthopaedic Association, Annual Meeting, Birmingham ICC, 1st – 4th October 2013.*
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2. *The British Association for Computer Assisted Orthopaedic Surgery, 7th Annual Congress, 21st – 22nd November 2013, The Royal society of Medicine, London*

Presentations given at scientific meetings from this work

(continued)

Non-invasive, non-radiological quantification of anteroposterior knee joint ligamentous laxity.

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1. *Scottish Committee of Orthopaedics and Trauma (SCOT) Meeting, Crieff, 25th February 2013.*

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1. *British Association for Surgery of the Knee Annual Meeting, 12th & 13th March 2013.*
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2. *British Orthopaedic Association, Annual Meeting, Birmingham ICC, 1st – 4th October 2013.*

3. *The British Association for Computer Assisted Orthopaedic Surgery, 7th Annual Congress, 21st – 22nd November 2013, The Royal society of Medicine, London*

Regional Poster Presentation

Glasgow Meeting of Orthopaedic Research, 22nd March, 2013

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Accompanying material

A CD ROM disc is included in a pocket secured to the rear binding. A spreadsheet summarising raw data from each experiment is included. Data from each separate experiment is contained in a labelled workbook. The raw data is not referenced in the text but made available for use as reference material to aid study following on from this work.

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Declaration

I declare that, except where explicit reference is made to the contribution of others, that this thesis is the result of my own work and has not been submitted for ay other degree at the University of Glasgow or any other institution.

Signature ____

Printed name ____

1 Introduction

Clinical examination of the human knee joint is important in diagnosis of disease and assessment of treatment success. Clinical examination is highly subjective, especially in terms of estimating parameters critical to diagnosis, or planning of treatment. Clinicians are poor at estimating specific parameters of knee kinematics, for example knee flexion angle (Watkins et al., 1991; Shetty et al., 2011), and errors tend to increase with increasing knee flexion angle (Shetty et al., 2011). In terms of diagnosis of ligament injuries, commonly used clinical tests such as the Lachman test for cruciate ligament integrity which is widely believed be sensitive in diagnosis of cruciate rupture (Kim et al., 1995) have been shown to have poor diagnostic reliability between testers (Cooperman et al., 1990).

Findings are difficult to communicate if not quantified, and decreasing subjectivity in the use of any diagnostic test is desirable (Edixhoven et al., 1989). Parameters essential to knee reconstruction include ligament laxity in the coronal, axial and sagittal planes, and mechanical alignment of the lower limb in the coronal and sagittal plane. A wide variety of radiographic, mechanical and more complex laboratory based methods of kinematic assessment are available. However, none of these comprehensively quantify the above mentioned parameters in real time and under loading in the clinical setting. Recently, three-dimensional optical tracking systems used for image-free knee navigation have been adapted both in terms of hardware and software to allow non-invasive registration of the lower limb. Recently published work by Clarke et al. (2012) reports precision and accuracy of this technology in measuring mechanical femorotibial alignment (MFTA) in knee extension and very early flexion. However no further validation *in vitro* or *in vivo* exists when measuring kinematics in flexion. The following series of experiments seek to quantify the precision and accuracy of this technology, and identify the obstacles to using skin-mounted tracking systems to reflect kinematics of bony anatomy.

2 Non-invasive quantification of knee kinematics

2.1 Introduction

Functional anatomy of the human knee has been the focus of much research across multiple scientific disciplines. Significant knowledge gaps exist in understanding normal knee kinematics and the influences of age, sex, ethnicity, disease and injury. Scientists and surgeons have sought to recreate surgically implantable reproductions of elements of this complex articulation in spite of major knowledge gaps in knee kinematics, using unrefined methods of kinematic estimation prior to and during knee reconstruction. This chapter reviews the relevant literature and summarises pilot experiments forming the basis of further work.

2.2 Knee kinematics

Kinematics refers to the branch of mechanics detailing the motion of objects without concern for the forces causing movement. The spatial relationships of the femur and tibia are important in diagnosis of knee pathology and surgical reconstruction. Patellofemoral kinematics are also important, especially in total knee replacement, but are not relevant to the aims of the work detailed here.

Kinematic parameters of the knee are considered in relation to the sagittal, coronal and axial planes as the femorotibial articulation moves in relation to each of these in terms of rotation and translation. This allows six degrees of freedom including three in orientation: flexion- extension, internal-external rotation, varus – valgus displacement; and three in translation including anteroposterior translation, medial-lateral translation and compression – distraction (Fu et al., 1994). Medial-lateral translation and compression – distraction are minimal and not routinely considered in clinical research and practice. The other parameters are relevant to surgical knee reconstruction and are reviewed below, along with current methods of kinematic quantification.

2.2.1 Defining lower limb alignment

The motion of the tibia relative to the femur in the coronal and sagittal plane is measured in terms of anatomical and mechanical alignment. Anatomical alignment uses the anatomical axes of the femur and tibia: a line drawn between two mid-cortical points to define the middle of the diaphysis. The mechanical axis of a bone or limb is sympathetic to the forces acting on load bearing surfaces of the bones i.e. the joints and must therefore always be represented as a straight line. The centre of the proximal and distal joint is used and a straight line connecting these points creates the mechanical axis.

2.2.1.1 Definitions of coronal alignment parameters

Six degrees of freedom allows the knee to move in three dimensions. However definitions of alignment refer to the bone / limb concerned in two dimensions, i.e. within one anatomical plane.

2.2.1.1.1 Varus and valgus

The term ‘varus’ comes from the Latin for crooked, ‘valgus from the Latin for twisted or bent. Respectively they refer to ‘bowlegged, or ‘knock-kneed’ deformity (Kamath et al., 2010). Varus and valgus refer to displacement of the distal part of the joint in the coronal plane toward or away from the midline of the body respectively.

2.2.1.1.2 Femoral mechanical axis (FMA)

A straight line in the coronal plane connecting the centre of the femoral head to the centre of the knee joint.

The centre of the femoral head can be found on anteroposterior radiograph using the circular edge of the femoral head and plotting the centre of a template circle.

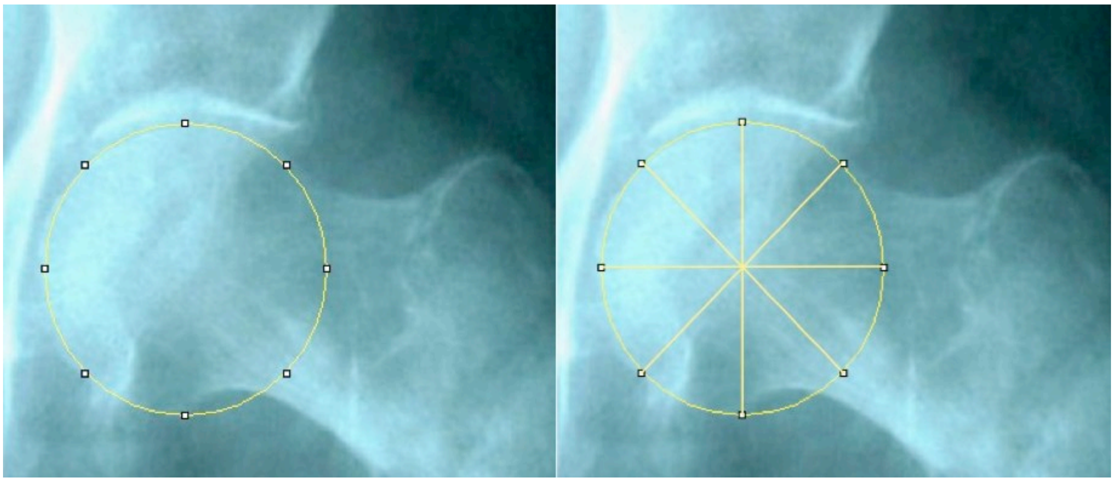

Figure 1 – Method of templating centre of femoral head.

The radiographic centre of the knee joint defined by Moreland, Bassett and Hanker (1987) used a midpoint from 5 suggested points considered as the anatomic centre of the knee. These included (Fig. 2): the centre between the soft tissue extremes, centre of femoral notch, centre of the tips of the tibial spines, the centre of the femoral condyles and the centre of the tibia.

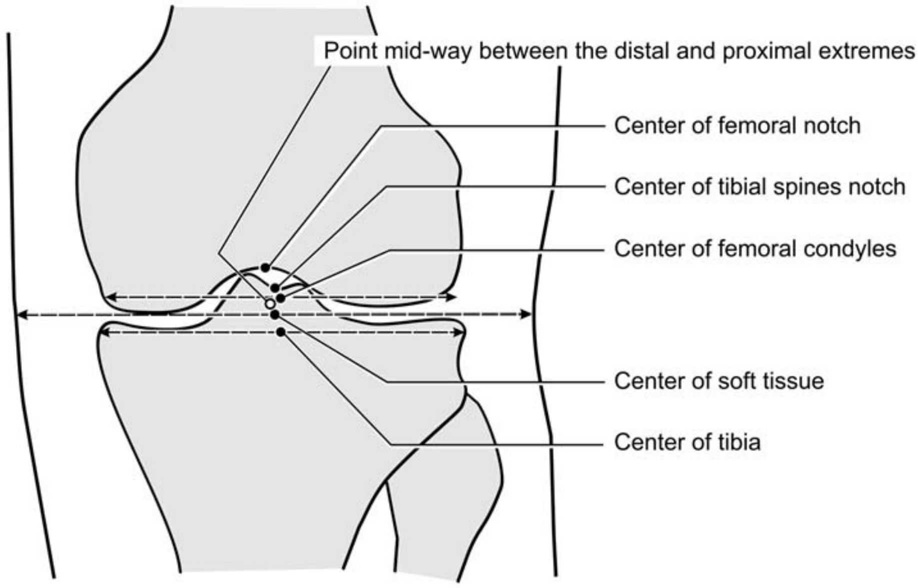

Figure 2 – Locating the centre of the knee. From Cooke et al. (2007).

2.2.1.1.3 Tibial mechanical axis (TMA)

A straight line in the coronal plane from the centre of the knee to the centre of the ankle. In a similar manner to the knee, Moreland, Bassett & Hanker (1987) define the centre of the ankle joint was taken as the midpoint between the malleoli just proximal to the cartilaginous space and the centre of the talus.

2.2.1.1.4 Mechanical femorotibial alignment (MFTA)

Mechanical femorotibial alignment is given by the lesser angle intersecting the mechanical femoral axis (line from centre of femoral head to knee centre) and mechanical tibial axis (line from knee centre to ankle centre). Authors may also refer to this as the hip-knee-ankle (HKA) angle, and in describing neutral alignment the larger angle of intersection (i.e. neutral MFTA =180˚), or the smaller angle of intersection (i.e. neutral MFTA = 0˚) may be used (Moreland et al., 1987; Cooke et al., 2007; Kamath et al., 2010). No uniform consensus exists on which terms to use as yet. Conventionally in knee reconstruction, the smaller value of intersection is used and varus angulation given as a negative value and valgus as a positive value, thus describing deviation from neutral alignment (Cooke et al., 2007). These positive and negative values will be used throughout.

Normal mechanical alignment of the lower limb in asymptomatic adults is variably reported. Long leg radiograph studies provide a range of reported mechanical alignment, however values are close to neutral in normal subjects.

Table 1 – Summary of literature reviewed on lower limb mechanical alignment from long-leg radiographs.

Author & Year	**Number of limbs studied**	**Ethnic Origin**	**Sex**	**MFT (˚)**	**SD**
Moreland et al. (1987)	25	Caucasian	M	-1.3˚	2.0
Hsu et al. (1990)	120	?	M & F	-1.2	2.2
Cooke et al. (1997)	75 (Healthy)	?	M & F	-0.97	2.86
	127 (Symptomatic OA)	?	M & F	-3.95	7.75
Tang et al. (2000)	25	Chinese	M	-2.2	2.7
	25	Chinese	F	-2.2	0.5
Wang et al. (2010)	50	Chinese	M	-0.7	2.3
	50	Chinese	F	0.2	2.5
Khattak et al. (2010)	40	Pakistani	M	-1.6	2.8
	19	Pakistani	F	0.0	3.0
Bellemans et al. (2012)	125	Caucasian	M	-1.87	2.42
	125	Caucasian	F	-0.79	2.13

Overall range of ‘normal’ reported mechanical alignment is from -2.2˚ (varus) to 0.2˚ (valgus), these most extreme mean values coming from two separate studies of Chinese population (Tang et al., 2000; Wang et al., 2010). It is interesting to note the high variation within studies amongst all groups and sexes, as indicated by the standard deviation. Slight differences in mean MFTA are present between subgroups of population. Cooke et al. (1997) observed that MFTA was significantly different in subjects with symptomatic knee OA by around 3˚ varus. MFTA may change with progression of OA, or varus malalignment may be a risk factor for initiation of pathogenesis and play a role in positive feedback of disease progression. Sharma et al. (2001) demonstrated in 230 individuals that baseline varus or valgus malalignment led to progression of medial or lateral compartment osteoarthritis respectively after as little as 18 months observation. In a further study (Sharma et al., 2010) of 2958 knees, findings from the initial study were confirmed with regard to direction of malalignment and risk of OA in the corresponding tibiofemoral compartment. Interestingly, varus but not valgus malalignment increased risk of incident knee OA. The risk of varus malalignment (2˚ or more from neutral) was associated with progression of OA, whereas 2˚ or more of valgus malalignment was not associated with disease progression. Biomechanically, the medial compartment will bear greater load during stance than the lateral compartment, even in a knee with neutral alignment (Morrison 1970; Andriacchi 1994), therefore any increase in adduction moment will markedly increase medial compartment contact pressure. Johnson et al. (1980) used gait analysis on 52 patients along with long leg radiographs to determine alignment. They found that when mechanical axis went through the centre of the knee, mechanical alignment of the lower limb was 5˚ valgus. Unless alignment was ≥5˚ valgus, the mechanical axis passed through the medial compartment. Engin & Korde (1974) performed biomechanical analysis on cadavers finding that 2.5˚ varus alignment increased medial condyle contact force by 70%, whereas 2.5˚ valgus alignment increased lateral contact force by 50%. Similarly, Brouwer et al. (2007) reported significant effect of varus malalignment on incidence of knee OA, whilst valgus malalignment had a borderline effect.

2.2.1.1.5 Femoral Anatomical Axis (FAA)

A line along the middle of the diaphysis of the femur. This line is usually offset from the FMA by 5˚ on hip-knee-ankle radiographs (Fig. 3) (Cooke et al., 2007).

2.2.1.1.6 Tibial Anatomical Axis (TAA)

A line along the middle of the diaphysis of the tibia (Fig. 3). This line has been shown not to differ significantly from the tibial mechanical axis in normal subjects (Oswald et al., 1993).

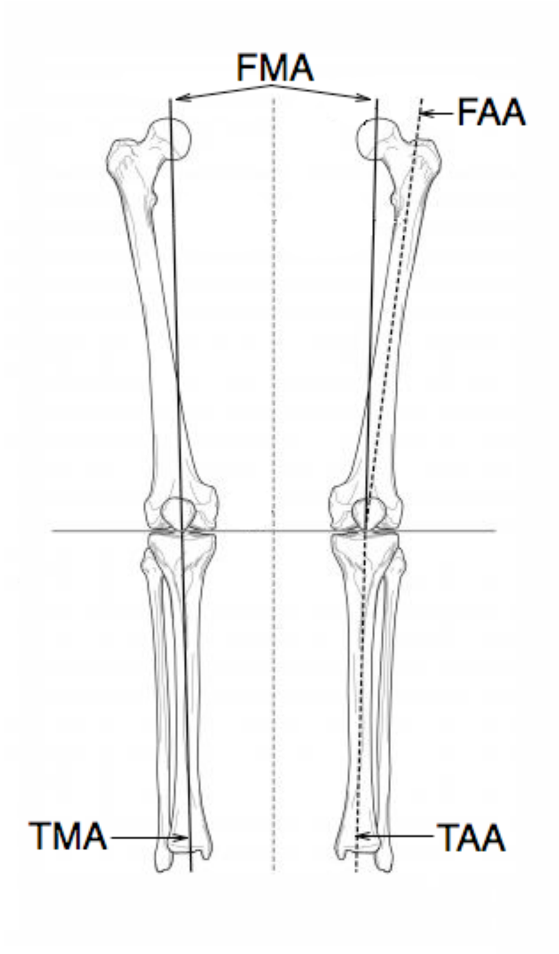

Figure 3 – Illustration of the femoral and tibial anatomical and mechanical axes Adapted from Pickering et al. (2012).

2.2.1.2 Definitions of sagittal alignment parameters

2.2.1.2.1 Femoral mechanical axis

A straight line from the centre of the femoral head to the centre of the knee joint. Radiographic acquisition of sagittal femoral mechanical axis requires a perfect lateral radiograph of the knee. Obtaining a lateral hip radiograph can be difficult, especially in obese patients (Sparmann et al., 2003). Two commonly used definitions of locating the knee centre radiographically are used (Chung et al., 2009). The first uses a point 1cm anterior to Blumensaat's line (a line extending through the intercondylar notch on a lateral radiograph of the knee) (Fig. 4).

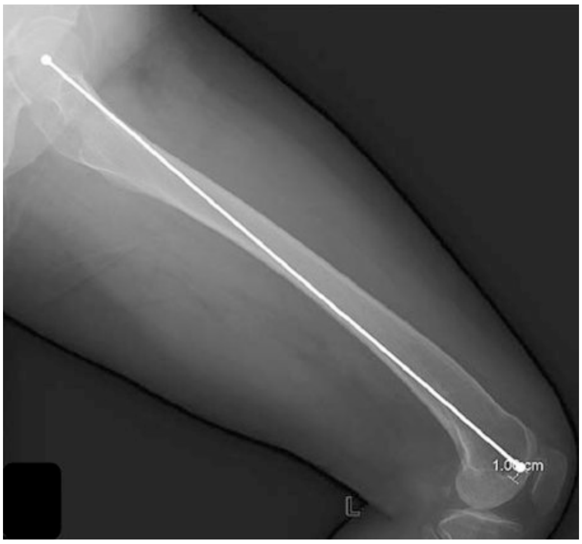

Figure 4 – Radiographic sagittal femoral mechanical axis
Lateral radiograph of the left femur with a line extending from the centre of the femoral head to a point 1cm anterior to Blumensaat'sline (the intercondylar notch). Illustration taken from Chung et al. (2009).

The second uses a point 65% of the distance from the anterior femoral cortex to the most posterior point of the medial femoral condyle (Fig. 5).

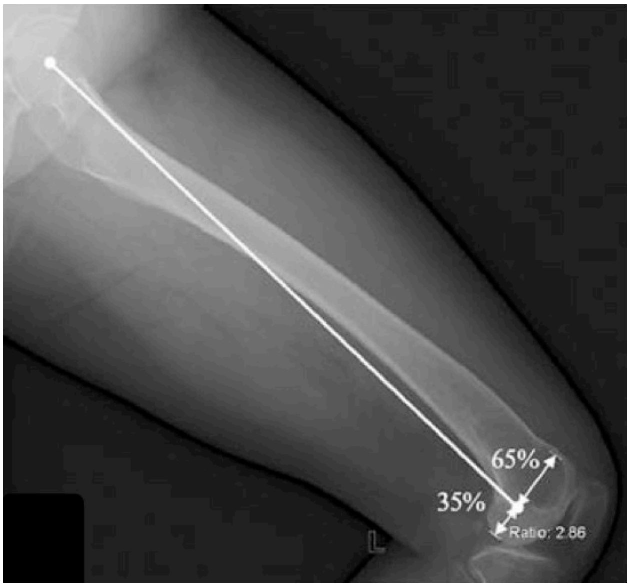

Figure 5 – Alternative radiographic sagittal femoral mechanical axis
The same radiograph as that seen in figure 4 with an alternative method of demonstrating the sagittal FMA; a line is drawn from the centre of the femoral head to a point 65% from the anterior femoral cortex at the widest point of the femoral condyles in the sagittal plane. Taken from Chung,. (2009).

2.2.1.2.2 Sagittal femoral anatomical axis

This is a curved line due to the anterior bowing of the femur. This axis is not referred to throughout this manuscript.

2.2.1.2.3 Sagittal tibial mechanical axis

Between 2004 and 2005 Han et al. (2008) performed computed tomography on 133 knees from 64 female and 8 male patients, mean age 69 (range 53 – 89 years). They defined tibial mechanical axis in the sagittal plane as a straight line from the midpoint of the tibial plateau to the mid point of the tibial plafond.

2.2.1.2.4 Sagittal tibial anatomical axis

Han et al. (2008) defined this as a line connecting the mid-diaphyseal points in the sagittal plane 7cm below the tibial plateau and 7cm above the tibial plafond. They found that the sagittal TMA and sagittal TAA were closely approximated with only 0.8˚±0.67˚.

2.2.1.2.5 Sagittal mechanical femorotibial axis

This is the intersection between the sagittal FMA and sagittal TMA. Functional motion of the knee (flexion – extension) occurs in this plane. When aligned, the flexion angle of the knee is 0˚ or in full extension. With flexion, i.e. the tibia moving posteriorly in the sagittal plane around the fulcrum of the knee joint centre, the angle is expressed as a positive value starting from 0˚. With hyperextension of the knee, i.e. the tibia moving anteriorly around the knee joint centre, the value is expressed as a negative, again from 0˚.

2.2.1.2.6 Sagittal load bearing axis

A straight line from the centre of the femoral head to the ankle joint centre as defined previously. In normal anatomy, the sagittal load bearing axis lies slightly anterior to the kinematic knee joint centre when the body is static and erect. As the posterior capsular structures of the knee are extremely stiff in resisting extension, the muscular effort required to maintain fully erect posture is minimised. Indeed, in slight hyperextension, the quadriceps femoris muscles are fully relaxed. Where full knee extension cannot be achieved, this increases muscular effort required to maintain a static standing position, as discussed in section 2.4. During locomotion, particularly weight acceptance and stance, the knee is in slight flexion and the load bearing axis moves posteriorly (Winter 1980).

2.2.1.2.7 Tibial slope (TS)

The lesser angle between a line perpendicular to the sagittal TMA and a line connecting the most proximal points of the anterior and posterior lateral tibial condyle. Han et al. (2008) demonstrated poor intra and inter-observer reliability in measuring medial tibial slope. Although no consensus exists on axes used when determining tibial slope value, use of the lateral tibial condyle has been suggested (Whiteside et al., 1988; Yoshioka et al., 1989; Kuwano et al., 2005; Han et al., 2008)

2.3 Clinical relevance of mechanical alignment

2.3.1 Mechanical femorotibial alignment and collateral ligament injury

The primary restraints to medial and lateral laxity in the knee are the medial and lateral collateral ligaments (Grood et al., 1981; Gollehon et al., 1987; Fu et al., 1994; Laprade et al., 2012). Trauma to these is usually the result of varus or valgus impact to the knee with or without rotatory force during sport (Phisitkul et al., 2006; Laprade et al., 2012). These structures do not act in isolation and do not have a single role. They assist in stability in various planes, supporting and being supported by other major stabilising structures of the knee.

Most biomechanical and anatomical evidence to support this comes from studies involving selective sectioning of capsular structures and observing the effect on stability. Gollehon et al. (1987) performed a study on 17 cadaveric knees involving selective section of the lateral collateral, popliteus-arcuate complex, anterior and posterior ligaments. Loading and rotation testing of the knees from 0˚-90˚ flexion demonstrated that the lateral collateral ligament acted in unison with the popliteus-arcuate (deep) ligament complex in resisting varus displacement and external rotation. The posterior cruciate was the primary restraint to posterior tibial translation. However at 0˚-30˚ knee flexion, sectioning the lateral collateral and deep ligament complex produced a similar increase in posterior tibial translation to that seen following sectioning of the posterior cruciate ligament. These results have been reproduced in other similar biomechanical cadaveric studies (Nielsen et al., 1984; Grood et al., 1988; Veltri et al., 1995; Veltri et al., 1996; Kaneda et al., 1997; Coobs et al., 2007) leading authors to consider injury resulting in varus instability as possibly involving both the lateral collateral ligament, lateral and posterolateral stabilising structures in the knee. From anterior to posterior, these structures include the patellar retinaculum, iliotibial band, and the arcuate complex. This complex is thought to function as a unit and includes the fibular collateral ligament, arcuate ligament and the tendoaponeurosis of the popliteus muscle. Biceps femoris, popliteus and the lateral head of gastrocmenius muscles provide dynamic support (Hughston et al., 1976). Studies suggest that approximately 55% of applied varus load in extension is resisted by the lateral collateral ligament load, however opening of the lateral compartment or varus deformity becomes markedly more significant when both the lateral collateral and posterolateral structures mentioned above are sectioned (Gollehon et al., 1987; Grood et al., 1988).

The medial collateral ligament differs in macroscopic structure from the lateral collateral in that it consists of three layers described by Warren & Marshall (1979). The superficial layer includes the crural fascia continuous with vastus medialis anteriorly and sartorius posteriorly, contributing to the patellar retinaculum. The middle layer is separated from the deep layer by a layer of fatty tissue and consists of the superficial portion of the medial collateral ligament. The majority of fibres are vertically orientated, and posteriorly this layer fuses with the deepest layer of the medial collateral ligament and is closely attached to the posteromedial meniscus. Posteriorly this structure receives fibres from the tendon of semimembranosus and is referred to as the oblique popliteal ligament (De Maeseneer et al., 1998). The deep portion is close to the medial meniscus with extensions to the femur and tibia are termed the meniscofemoral and meniscotibial (coronary ligament) extensions (De Maeseneer et al., 2000). A bursa exists between the superficial and deep portions of the medial collateral ligament (Lee et al., 1991).

The superficial and deep portions of the medial collateral are static stabilisers, along with the oblique popliteal ligament. The superficial medial collateral ligament is considered the primary static stabiliser resisting valgus displacement of the knee in the coronal plane (Warren et al., 1979). This is the largest of the ligamentous structures with one femoral attachment and two tibial attachments (Griffith et al., 2009). Grood et al. (1981) demonstrated that the medial collateral ligament provided 57% of the total restraint against valgus moment with the knee in 5˚ flexion, and 78% with the knee at 25˚ flexion due to decreased contribution from the posterior capsule. With continued stress causing rupture of the entire medial ligament complex, including the oblique popliteal ligament, the anterior cruciate ligament will eventually rupture during biomechanical testing. In vivo, this results in a more extensive injury; Fetto & Marshall (1978) reported from a series of patients with medial collateral ligament injuries that 78% of those with complete medial collateral ligament rupture had concomitant anterior cruciate ligament tear. The anterior cruciate ligament is termed a secondary stabiliser of the knee in terms of valgus laxity. Grood et al. (1980) published the concept of primary and secondary restraints to clinical examination by using a new method of biomechanical testing in determining the contribution of structures stabilising the knee. They highlight that previous methods of sectioning ligaments followed by measuring displacement are cutting order dependent, and proposed measurement of resistance to a displacement of 5mm at 30˚ & 90˚ knee flexion would eliminate this confounding factor. They found that the anterior cruciate ligament provided the primary restraint to anteroposterior translation, with the iliotibial band and medial capsular ligaments providing secondary restraint. A follow on study (Grood et al., 1981) examined medial and lateral laxity and found that at 5˚ and 25˚ the collateral ligament provided more than half of the total restraint. At 5˚ the posterior capsule and cruciate ligaments provided secondary restraint, with the contribution of the posterior capsule reducing significantly at 25˚ knee flexion as it reduced tension.

Collateral ligament injuries are currently assessed and graded using subjective clinical examination. This involves applying un-quantified varus/valgus stress in extension and early flexion and estimating the amount of joint opening. Patients may be very uncomfortable during this and require examination under anaesthesia. Again, this technique can be quite subjective, and examination of the contralateral limb is imperative given that the patient may have inherent soft tissue laxity. Furthermore, grading of these injuries is based on these clinical assessments (Wijdicks et al., 2010), meaning clinical decision-making regarding treatment and rehabilitation is being based on subjective testing. Stress radiographs can also be used, quantifying the amount of 'gapping' of the medial or lateral compartment when a varus/valgus stress is applied to the knee at 30˚ flexion. These radiographs must always be compared to the contralateral limb. LaPrade's group (LaPrade et al., 2008; Laprade et al., 2010) validated methods of applying quantified coronal stress (10 – 12Nm) with the knee in extension and 20˚ flexion with adjunct stress radiographs to detect medial and lateral collateral ligament sectioning in cadaveric models. Intra and inter-observer reliability was high for radiograph interpretation of the described tests in both studies, however this only relates to radiographic interpretation, the actual testing was not performed by a variety of investigators. Furthermore, the authors claim that opening of 2mm can indicate the degree of soft tissue injury, it could be argued that without robust inter and intra observer analysis of examination technique, force application and radiograph acquisition; examining radiograph interpretation alone is not sufficient to make this conclusion. Gwathmey et al. (2012) found that findings on stress radiography correlated with MRI findings in posterolateral corner injury. They acknowledge that MRI cannot give information about function or laxity.

Clarke et al. (2012) attempted to standardise examination of coronal laxity in vivo using a force application device to quantify varus and valgus forces, and an adaptation of image-free computer navigation technology. Results in early clinical testing were encouraging and will be discussed later.

At present, no routine clinical scenario or medical evidence exists within the out-patient or operative setting allowing quantification of varus/valgus laxity by determination of change in mechanical alignment following application of a known, standardised force. Real-time measurement of MFTA under a quantified load would allow communication of clinical findings between clinicians and researchers, and permit quantitative evaluation of treatment techniques within and between centres.

2.3.2 Mechanical femorotibial alignment and arthroplasty

The mechanical alignment of the lower limb has been demonstrated to be of critical importance to outcome following knee arthroplasty, and it is widely held that components should be placed perpendicular to the mechanical axis of the bone (Jeffery et al., 1991). The mechanical femorotibial axis (MFTA) following knee reconstruction will therefore be neutral i.e. 0˚. This is thought to minimise wear caused by unsymmetrical loading of the prosthesis, despite aforementioned disparity in compartment loading with neutral alignment.

Green et al. (2002) performed an in vitro analysis of 14-paired cadaveric knees. The right tibial component was implanted in neutral alignment and the left component in 5˚ varus. The components were lined with photoelastic coating and three times bodyweight loading applied simulating normal walking. Strain was determined across the tibial components which were divided into 12 zones. In the neutral aligned tibiae, strain was equal in the medial and lateral compartment. In the varus group, a significant concentration of strain was seen in the posteromedial tibial surface. Similar findings were reported by Werner et al. (2005) following in vitro loading of cadaveric knee implanted with components in varied amounts of varus and valgus malalignment. Following simulated gait loading, tibial components outwith 3˚ varus or valgus alignment demonstrated significantly altered pressure distribution across medial and lateral compartments. D'Lima et al. (2001) published similar findings from in vitro analysis of polyethylene wear from prostheses with simulated neutral alignment and malignment. Malaligned prostheses demonstrated significantly increased total wear, especially those in varus malalignment.

The orientation of total knee replacement components is described relative to the mechanical axis of the lower limb. Clinical studies reflect these findings, however the outcome measure used most frequently is implant survival. Ritter et al. (1994) reported a series of 421 total knee replacements carried out between 1975 and 1983. 27 of 38 (71%) of tibial component failures were found to be in varus malalignment (defined as >3˚ varus in relation to the mechanical axis of the tibia). Berend et al. (2004) reported outcomes of 3152 total knee replacements, 41 tibial components were revised, 20 for medial bone collapse. Mechanical alignment of the lower limb was significantly more varus in this group of 20 (mean 1.6˚ valgus vs 3.9˚ valgus in the entire cohort). Varus mechanical alignment of the lower limb was identified as a risk factor for medial bone collapse. Achieving neutral alignment of component position relative to the MFTA has been recommended in minimising failure rate of total knee replacement (Aglietti et al., 1988; Ritter et al., 1994; D'Lima et al., 2001; Green et al., 2002; Berend et al., 2004; Werner et al., 2005).

With respect to MFTA following total knee replacement, evidence indicates that alignment outwith 3˚ of neutral alignment (i.e. +/-3˚ of 0˚ MFTA) is a risk factor for early component loosening and failure. In 1991, Jeffrey et al. reported a series of 115 total knee replacements performed between 1976 and 1981. Long leg radiographs were used to identify components outwith the range of +/-3˚ of neutral. At median follow-up of 8 years, 24% of components outwith this range alignment demonstrated asceptic loosening compared with 3% of those aligned within 3˚ of neutral. This was the first study to analyse long-leg alignment radiographs. The margin for error on long leg radiographs is markedly smaller in analysing limb alignment than using short leg radiographs. A study by Abu-Rajab et al. (2009) demonstrated inter-oberserver agreement measuring mechanical axis of the lower limb on 20 long and short leg radiographs. Intraclass correlation coefficient for long leg and short leg radiographs was 0.95 and 0.51 respectively. Remarkably, most landmark studies making recommendations for total knee replacement alignment have used short leg radiographs to assess post-operative limb alignment and made up the body of evidence to support restoration of neutral mechanical alignment of the lower limb, and neutral alignment of components relative to the MFTA (Lotke et al., 1977; Bargren et al., 1983; Hvid et al., 1984; Rand et al., 1988; Ritter et al., 1994). More recently, Parratte et al. (2010) reported retrospective follow-up of 398 total knee replacements performed between

1985 and 1990. Using long-leg radiographs, the cohort was divided into those within 3˚ of neutral and those outwith this range (outlier group). No statistical advantage was seen in revision rate in patients with alignment within 3˚. Drawbacks from the analysis of this cohort include drawing conclusions from a relatively small sample size (59 revisions), and grouping those patients in valgus or varus mal-alignment within the 'outliers' category. Biomechanical and clinical studies suggest varus mal-alignment may be more problematic than valgus (Lotke et al., 1977; Bargren et al., 1983; Hvid et al., 1984; Jeffery et al., 1991; Ritter et al., 1994; D'Lima et al., 2001; Green et al., 2002; Berend et al., 2004; Werner et al., 2005). The authors conclude by rightly suggesting that an overall mechanical limb alignment as close to 0˚ as possible remains the target until more refined targets is suggested from future research.

When planning total knee replacement, clinicians will commonly examine the knee and describe alignment based on short or long leg radiographs. They will comment on appearance of the lower limb with the patient standing and supine in terms of obvious varus or valgus deformity, and estimate how 'correctable' the deformity is by applying an unquantifed stress to the knee, in extension where possible (however fixed flexion contracture is often present), and with the patient supine. This method of testing is highly subjective from many standpoints. Force application is unquantified and visual assessment of mechanical alignment is inaccurate (Shetty et al., 2011). Methods to standardise examination, provide descriptions or classification of laxity have been proposed, however it is difficult to communicate findings from examination which is not standardised, far less to make recommendations based on this as to how to proceed with management of soft-tissues during total knee replacement (Krackow 1990; Engh 2003; Ries et al., 2003). Advances in measuring static and dynamic MFTA are described below.

2.3.3 Measurement of MFTA

For many years, the definition by Moreland, Bassett & Hanker (1987) has been used. Studying radiographs of 25 healthy male volunteers, they found the MFTA to be a mean of 1.5˚ varus for the right leg (range 6.5˚ varus – 2˚ valgus) and 1.1˚ varus for the left leg (range 4.5˚ varus – 3˚ valgus). Van Raaij et al. (2009) found poor correlation between 68 short leg radiographs (i.e. focused on the knee and only displaying distal femur and proximal tibia) and long leg radiographs (r=0.34). Based on short leg radiographs, 15% of patients in this study would have been incorrectly classified as having a valgus alignment where the alignment was in varus. Nonetheless, many surgeons routinely plan total knee replacement procedures based on short-leg radiographs.

Long leg radiographs are prone to rotational error with abnormal rotation of a segment(s) such as the foot or tibia (Krackow et al., 1990; Hunt et al., 2006). Hunt et al. (2006) analysed three long leg radiographs taken on 19 lower limbs in the positions of feet pointing straight ahead, and feet internally and externally rotated 15˚. Mean difference in mechanical axis between the externally and internally rotated positions was 3.59˚ (CI 1.81˚ - 5.37˚). Internal rotation reduced varus alignment and external rotation increased varus alignment. Although a well-standardised approach to taking long leg radiographs can minimise error (Cooke et al., 1991; Cooke et al., 2007), patients with osteoarthritis and patients having had total knee replacement are often not able to achieve full extension of the knee; this has a large impact on accuracy of measurement of MFTA (Yaffe et al., 2008). Furthermore, the presence of varus or valgus deformity exacerbates the effect of error in MFTA measurement where the limb is internally or externally rotated whilst attaining long leg radiograph (Swanson et al., 2000). Authors have suggested that inaccuracy of radiographs in assessing MFTA, especially in those with flexion deformity may influence the results of studies comparing operative techniques (Mahaluxmivala et al., 2001; Yaffe et al., 2008).

In contrast to these findings, McDaniel et al. (2010) determined mechanical axis on 114 knees using 4 methods; long and short leg radiographs (short radiographs taken from the same image as the long radiograph), a short knee radiograph with the knee in slight flexion and manual examination using a goniometer. Correlations between MFTA from long leg radiograph and measurements obtained by the other methods ranged from r = 0.65 to 0.75. Despite the author's conclusion that knee alignment might be estimated by these alternative means, giving information on progression of disease, the absolute values obtained differed from MFTA on long leg radiographs by a mean of up to 4˚. This does not provide the level of accuracy required for surgical assessment. Authors state that the difference in absolute values of MFTA between methods was due to varying frames of reference. Authors used correlation coefficients to determine agreement, which is an inappropriate method of quantifying agreement between test methods (Bland et al., 1986). Similar studies by Hinman et al. (2006) and Navali et al. (2012) found the goniometer method to correlate poorly with MFTA. Despite concluding that short leg radiographs, caliper measurements to estimate joint centres and plumb line methods were valid alternatives to long leg radiographs, these contained similar weaknesses in data analysis and did not provide an alternative method of measuring MFTA which agreed sufficiently with long leg radiographs for use in the surgical setting, as admitted by the authors (Hinman et al., 2006; Navali et al., 2012).

Three-dimensional means of imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) can provide reliable measurement of MFTA. Liodakis et al. (2011) compared MFTA using upright MRI and long leg alignment films on 30 patient limbs demonstrating mean difference of 1.2˚ ± 1.1˚ (r = 0.95). This may be superior to previous methods of three-dimensional imaging as it allows weight bearing; however technology is not yet widely available. It may be possible to overcome the rotational problems associated with long leg radiographs using low radiation dose CT scanogram, however, using CT scanning devices common to the current clinical setting this again presents a static, non-weight-bearing evaluation (Henckel et al., 2006; Mohanlal et al., 2009). However, due to resources available in clinical units, CT scanning remain a common and reliable method of measuring limb alignment albeit with the limb in a non-standardised position of knee flexion, not weight bearing and supine; all of which potentially affect measurement of true mechanical alignment. CT scanning is very useful however for quantification of component position following arthroplasty (Jakob et al., 1980; Kim et al., 2012).

Other methods of measuring limb alignment and estimation of joint centres include gait analysis in a gait laboratory setting, estimation using surface anatomy, use of wearable accelerometers and gyroscopes and goniometers. These methods are not used in surgical planning as they do not as yet provide alignment data with a suitably low margin of error for surgical planning. They remain useful for analysing the effect of disease and surgical procedures on gait, and may be of use in certain clinical and research settings (McQuade et al., 1989; Kirkwood et al., 1999; Vanwanseele et al., 2009; Tao et al., 2012).

Computer assisted methods used in surgery and in clinical planning have been validated in measuring mechanical alignment, these will be discussed later (Haaker et al., 2005; Picard et al., 2007; Clarke et al., 2012).

2.3.4 Conclusion

The ability to determine dynamic, weight bearing mechanical alignment in a manner inconsequential to the patient would markedly advance assessment of patients with collateral ligament injury, and allow planning and evaluation before and after total knee arthroplasty in a manner most relevant to functional kinematic demands of the load-bearing knee. The ability to assess these parameters in health and disease, across gender, age and ethnic group would further enhance our understanding of pure knee kinematics, population variance and requirements in reconstruction.

2.4 Sagittal alignment

The sagittal plane passes anterior to posterior dividing the body into left and right sections. The major component of knee motion occurs in this plane (flexion and extension). Normal range of motion of the human knee has been quantified in young male subjects (n=90, 180 knees) by Rooas & Anderson (1982); flexion ranged from 115º - 160º (mean 143.7º) and extension from -10º - 0º (mean -1.6º). Minimum flexion values have been suggested to allow activities of daily living typical of western cultures. People require an estimated knee flexion of ~65° for walking, ~70° to bend down and lift objects, ~85°-90° for stair climbing, ~90°-95° to rise from a chair and 105° for tying shoelaces (Mulholland et al., 2001; Gonzalez Della Valle et al., 2007; van der Linden et al., 2008). Ability to maintain musculoskeletal fitness in terms of flexibility is beneficial in terms of overall health and quality of life (Kell et al., 2001).

Full extension of the knee joint is required to maintain a normal standing and walking posture (Su 2012). While minimal force is required to maintain knee extension and standing posture in an individual with full knee extension due to the lower limb load bearing axis passing anterior to the knee, flexion contracture places the load bearing axis behind the centre of rotation of the knee joint. The result is a large increase in forces required to support the body; at 15˚ flexion, it is estimated that approximately 20% of maximum quadriceps strength is required, at 30˚, this increases to 50% (Perry et al., 1975). Flexion contracture alters walking gait, with direct effect on the affected leg, adduction moment abnormality on the contralateral knee and abnormal moment on the spine (Su 2012)

2.4.1 Sagittal plane range of motion following total knee replacement and relevance to outcome

Knee flexion of up to at least 105˚ is necessary for common activities of daily living (Mulholland et al., 2001; Gonzalez Della Valle et al., 2007; van der Linden et al., 2008). The amount of flexion achievable following total knee replacement is a key component of functional outcome, characterised by ability in walking and stair climbing, and included in clinical outcomes scoring (Ritter et al., 1987). Chiu et al. (2002) reviewed articles focused on pre and post-operative knee flexion, most studies reported flexion angles of 100˚ and 115˚ following total knee replacement; they suggested that this be the general aim for total knee arthroplasty and that patients should typically be informed of this expected range of flexion and its significance in performing daily tasks at time of consent.

It is important to observe range of motion in the sagittal plane before, during and after total knee replacement surgery. Naylor et al. (2012) reported passive range of motion following total knee replacement at time of discharge from hospital; values at time of discharge; 102.9° (SD 15.4) flexion and 8.9° (SD 5.5) extension; at 1 year; 110.3° (SD 15.3) flexion and 4.6° (SD 5.4) extension. Measurements of flexion angle were determined using a non-validated, novel technique involving photograph interpretation. The method was standardised throughout the study with an independent rater performing all photograph measurements. Devers et al. (2011) graded 122 knees from 111 patients in terms of maximum passive flexion measured using a goniometer following arthroplasty: low ≤110º, mid 111º-130º and high flexion ≥130º. No relationship was found between high flexion and satisfaction; however patients in the high flexion group reported better fulfilment of expectations, ability to perform functional tasks and perception of their knee. This study was limited by retrospective methodology and incorporating 21 and 20 knees in the low and high flexion groups respectively. Furthermore, the 'low flexion' group included patients with the ability to flex from 100º-110º, the range in which most activities of daily living are possible (Rowe et al., 2000). Not all patients achieve this level of flexion (Chiu et al., 2002) and may be therefore be significantly more impaired than was suggested in the above study. A lower flexion angle boundary, for example <100˚ in the 'low flexion' group and a larger sample size would almost certainly have demonstrated a significant disparity in function and satisfaction between low and high flexion groups, and identified patients disabled by a level of flexion impairing activities of daily living. Furthermore, creating categories of patients beyond the range of flexion required for activities of daily living is highly unlikely to detect a difference in function and satisfaction (Meneghini et al., 2007; Thomsen et al., 2013).

Regarding the knee joint, the term stiffness will often be used by orthopaedic surgeons and physiotherapists to describe reduced range of motion. Even then, defined values of flexion and extension have not been universally agreed to categorise a knee as 'stiff'. Some definitions used in orthopaedic literature are as follows: Kim et al. (2012) and Yercan et al. (2006) define stiffness as involving flexion contracture of ≥10°, Nicholls & Dorr (1990) use flexion contracture ≥25° and/or maximum flexion ≤45°, Christensen et al (2002); range of motion total <70°. Bong & Di Cesare (2004) define stiffness as an inadequate range of motion (ROM) that results in functional limitations in activities of daily living.

In osteoarthritis, flexion contracture is very common, estimated to occur in up to 60% of patients (Su 2012). Functional consequences of flexion deformity heavily influence the capability of patients to mobilise. As the energy requirements to maintain standing posture increase with increasing flexion of the knee (Perry et al., 1975), increased energy expenditure generates fatigue on standing, walking, stair climbing and other activities of daily living (Su 2012). Furthermore, in a study by Harato et al. (2008) gait analysis using knee braces to simulate 15˚ and 30˚ of fixed flexion contracture in healthy volunteers resulted in mechanical overload in the contralateral, as well as the affected limb.

2.4.2 Sagittal alignment and aims in total knee arthroplasty

Unlike aims of total knee replacement in achieving neutral component and lower limb mechanical alignment, no fixed definition exists of an 'ideal' sagittal alignment to be used as a reference for total knee arthroplasty either on the femoral (Chung et al., 2009) or tibial side (Han et al., 2008).

Movement in the sagittal plane is very important and the amount of flexion and extension of the knee achieved before surgery relates to the amount of flexion achievable after surgery; this range of motion is critical to success of the procedure. The variable that consistently indicates post-operative range of motion in the knee is pre-operative range of motion. Nelson, Kim and Lotke (2005) analysed 1000 consecutive total knee replacements, 1.3% were diagnosed with post-operative 'stiffness' or reduced range of motion. These patients had significantly less pre-operative range of motion than those with good post-operative range of motion.

As discussed previously, achieving full flexion and certainly eliminating flexion contracture of ≥15˚ is crucial in terms of gait and walking ability (Su 2012). A series of 5000 total knee arthroplasty patients analysed by Ritter et al. (2007) indicate the rate of flexion contracture of ≥10˚ following surgery to be 3.5%. A series of 811 reported by reported a rate of 3.6%. In both studies, presence of this degree of deformity led to significantly reduced clinical outcome scores. Literature suggests that the most predictive risk factor for post-operative flexion contracture is pre-operative flexion contracture (Ritter et al., 2007; Su 2012).

A series of 104 total knee arthroplasty patients was retrospectively reviewed by Mitsuyasu et al. (2011), grouping the patients according to post-operative flexion contracture at 3 months, then reviewing the cohort at 2 years. It is stated that full extension was achieved following implantation of components on the operating table. At 2 years, 11/87 (12.6%) patients with flexion contracture of ≤10˚ had reduced deformity to ≤5˚, compared to none of the 17 patients who had flexion contracture of ≥15˚. The authors concluded that flexion contracture of ≥15˚ is likely to persist; this study was limited by relatively small sample size for subgroup analysis, retrospective design, and lack of independent patient assessment (assessments and measurements carried out by various investigators, including the surgeon). Furthermore, authors admit that use of a handheld goniometer is not very accurate in estimating knee flexion, and measurements were recorded in increments of 5˚, which may have led to bias. Lastly, no method of measuring knee range of motion at the time of surgery was given, and no data supported the statement that full extension was achieved at the time of surgery following implantation of components. Nonetheless these authors demonstrated that flexion contracture improves over time following total knee arthroplasty, but may persist if the deformity is significant.

Position of the femoral and tibial components in the sagittal plane may also influence outcome following total knee replacement. Excess flexion of the femoral component in relation to the anatomical axis of the femur will decrease the amount of knee extension following surgery. Conversely excess extension of the femoral component will decrease knee flexion, and also predispose the surgeon to removing excessive amounts of bone from the anterior femoral cortex (known as 'notching') thereby weakening the bone and increasing risk of supracondylar fracture (Laskin et al., 2004). Sagittal alignment of the tibial component is also critical. Whilst a neutral tibial component articular surface or tibial 'slope' is perpendicular to the anatomical axis of the tibia, elevation of the anterior tibial articular surface may influence the amount of knee flexion achievable following surgery. Laskin & Becksac (2004) suggest that the post-operative tibial slope should match the patient's pre-operative slope as much as possible as excessive deviation may limit range of motion. Bellemans et al. (2005) performed total knee replacement on 21 cadaveric knees, in each knee the tibial component was consecutively implanted with tibial components with a slope of 0˚, 4˚ and 7˚. Significant increases in achievable flexion were noted between each increment of increasing tibial slope. Points of criticism of this study include no available details of specimen-standardised load applied to perform flexion, and no account for creep in cadaveric tissue when performing repeated surgical simulations (creep is defined as progressive deformation of tissue under load which is below the load required to complete tissue failure (Shin et al., 2007)). Details regarding temperature of specimens and any manipulation to minimise the influence of tissue creep prior to the experiment are not given.

Shi et al. (2012) demonstrated a similar relationship between increasing tibial slope and knee flexion recently in a retrospective clinical follow up of 56 patients (65 knees). These were grouped according to post-operative tibial slope (group 1, 4˚ slope; group 2, 4˚-7˚ slope; group 3, >7˚ slope). A significant difference in post-operative flexion angle was noted between the groups, however no difference in clinical outcome score was observed. 1˚ increase in tibial slope resulted in a mean of 1.8˚ increase in flexion ($r^2 = 0.46$). Fujimoto et al. (2012) reported similar findings and highlighted the need for correct balancing and tensioning of the soft tissues especially the medial – lateral ligament balance during surgery.

2.4.3 Measurement of Range of Motion

Visual estimation of knee joint angle is unreliable (Watkins et al., 1991), margin of error of 5-10˚ was demonstrated by Shetty et al. (2011) when 52 orthopaedic surgeons attending a conference tried to place a skeleton model of the knee joint in full extension, 10˚ and 90˚ flexion. The majority of surgeons deviated by 5˚ and approximately a quarter deviated by 10˚ from the actual value obtained using a computer based optical tracking system; the degree of error reported increased with increasing flexion angle (Shetty et al., 2011). In clinical practice, recommendations have been made that a handheld goniometer is used, however most surgeons continue to rely on visual estimation (Watkins et al., 1991). Handheld goniometers result in a margin of error of at least ≥5˚ when compared to radiographic measurement of knee flexion angle, again, error increases with increasing knee flexion angle (Edwards et al., 2004).

Motion analysis is possible using gait laboratory equipment. The clinical applications of knowledge obtained are valuable however the equipment is not suitable for most clinical centres. Expense, portability and post-capture processing time prohibit routine clinical use (Tao et al., 2012). Gait analysis, including capture of sagittal plane kinematics is possible using accelerometers and gyroscopes, however this remains experimental

(Turcot et al., 2008). Rowe et al. (2001) validated electrogoniometers for use in measuring sagittal plane knee alignment on 5 healthy subjects, measurements were taken simultaneously with gait laboratory motion analysis using three dimensional arrangement of cameras. Differences in the system were ≤3˚, which is sufficient for clinical assessment. Further work has been carried out using electrogoniometers to assess knee range of motion during activities of daily living following arthroplasty (Rowe et al., 2005; Myles et al., 2006). Further work from this group used electrogoniometers as part of assessment of functional outcome between patients having had total knee replacement performed using conventional methods, or using computer assistance (CAS). No significant difference was noted bar an improvement in the pre-swing phase of gait and improved slope gait. (Smith et al., 2013). Piriyaprasarth et al. (2008) have demonstrated that improving protocol detail can improve measurement precision when using an electrogoniometer on the knee joint.

2.4.4 Conclusion

Clearly, it is important to be able to accurately measure range of motion before, during and after surgery. As yet, no non-radiological, non-invasive manner of measuring flexion and extension is sufficiently reproducible, versatile and available in a clinical setting. Non-invasive navigation based systems are capable of measuring coronal and sagittal alignment in early flexion, as will be discussed in section 2.5.10.

2.5 Anteroposterior translation of the tibia

Anteroposterior translation of the tibia relative to the femur occurs in the sagittal plane and is minimised primarily by the anterior and posterior cruciates, which limit anterior tibial translation and posterior tibial translation respectively. Stability in the sagittal plane is crucial in maintaining the integrity of the knee joint.

2.5.1 The anterior cruciate ligament

Both the anterior and posterior cruciate ligaments are considered ‘cord like’, similar to the lateral collateral ligament, in contrast to the medial collateral ligament, which is flat. From anatomical studies, we know that the anterior cruciate ligament consists of an entirely intra-articular anteromedial and posterolateral band or bundle (Furman et al., 1976). Norwood & Cross (1979) analysed 18 freshly amputated specimens, performing dissection in the axial plane to inspect the attachment points of the bundles of the anterior cruciate. They concluded that an intermediate bundle also exists. Further histological analysis of the bundles has suggested this subdivision may be arbitrary (Odensten et al., 1985). Biomechanical testing indicates that the posterolateral bundle is tighter and resists translation in extension, while the smaller anteromedial bundle resists translation in flexion (Sakane et al., 1997; Dargel et al., 2007). With rotational displacement of the tibia relative to the femur, the anterior cruciate and posterior cruciates tighten and provide restraint (Dargel et al., 2007). During anterior translation, the anterior cruciate ligament causes internal rotation of the tibia relative to the femur, thereby being a restraint to internal rotation (Fukubayashi et al., 1982). Markolf, Kochan & Amstutz (1984) found during biomechanical testing that anteroposterior translation of the tibia was at its peak at 20˚ of knee flexion when the anterior cruciate ligament was deficient and in normal healthy volunteers. In those patients who were anterior cruciate deficient, mean anteroposterior translation was 5.5mm at 20˚ knee flexion, compared to a mean of 3.5mm in normal subjects. A more recent biomechanical cadaveric study by Oh et al. (2011) studied the rotational effect of sectioning the anterior cruciate ligament. They concluded that sectioning of the ligament resulted in a 13% decrease in restraint against internal tibial rotation in a loading setup designed to simulate landing whilst pivoting on the leg.

The anterior cruciate ligament attaches to the posteromedial aspect of the lateral femoral condyle; the opposite end of the ligament attaches to the anterior tibial eminence. The fibres of the anteromedial bundle attach at the anterior portion of the femoral attachment and attach anteriorly and medially on the tibial attachment. The posterolateral fibres attach at the posterior portion of the femoral attachment and attach at the posterior and lateral portion of the tibial attachment.

The primary function of the anterior cruciate ligament is to prevent anterior translation of the tibia, secondarily it resists internal rotation and valgus angulation (Butler et al., 1980; Fu et al., 1994; Kweon et al., 2013). From biomechanical analysis of cadaveric knees by Butler, Noyes & Grood (1980), it is estimated that the anterior cruciate ligament conferred 85.1% (SD ± 1.9) of restraining force at 90˚ knee flexion.

Secondary restraint was conferred by the iliotibial band and medial capsule ligamentous complex. Methodological problems in this study include varied methodology throughout, resulting in conclusions on secondary restraints being based on six specimens when a total of 14 were used in the study. A further biomechanical cadaveric study by Christel (2012) involved applying 150N of force perpendicular to the longitudinal axis of the tibia through a screw attached to the tibial tuberosity at 30˚ of flexion. This was to simulate a Lachman test. Following this, the bundles of the anterior cruciate were sectioned and the test performed at 60˚ flexion and 90˚ flexion. They found that during the simulated Lachman test, lateral tibial translation exceeded medial translation (indicating internal rotation of the tibia during anterior translation), and that cutting the posterolateral bundle of the anterior cruciate did not result in increased translation. Cutting the anteromedial bundle however resulted in an almost identical degree of anterior translation compared to cutting the entire anterior cruciate ligament. A displacement of only 1.5mm occurred following section of the posterolateral bundle. This conflicts to some degree with earlier work by Markolf, Graff-Radford and Amstutz (1978) who quantified anteroposterior translation after dividing the posterolateral bundle in cadavers and applying 100N of quadriceps force, 100N anterior force and 5Nm internal tibial torque, who detected a 0.5mm displacement. Conflicting results possible highlight methodological differences, especially in loading and methods of measurement. Litner et al. (1995) performed staged section of the ligament bundles and found no significant difference in laxity between an intact anterior cruciate ligament, and that in which the anteromedial bundle had been sectioned. Again this conflicts with work by Christel et al. (2012). Wu et al (Wu et al., 2010) performed a similar study using robotic systems to measure the forces in each of the bundles at 30˚ knee flexion, in accordance with Christel et al. (2012), they found that the anteromedial bundle was under significantly greater tension than the posterolateral bundle in these conditions.

2.5.2 The posterior cruciate ligament

The posterior cruciate ligament consists of anterolateral and posteromedial bundles (Hughston et al., 1980). As is the case for the anterior cruciate, the posterior bundle is tight in extension, and the anterior bundle is tight in flexion (Fu et al., 1994). The posterior cruciate ligament attaches to the femur on the lateral aspect of the medial femoral condyle, and attaches to the tibia posterior and inferior to the tibial eminence, inferior to the articular margin. Two accessory ligaments, not present in all knees, pass from the posterior horn of the lateral meniscus and insert anterior and posterior to the femoral attachment of the posterior cruciate ligament. These are the ligaments of Humphrey and Wrisberg or meniscofemoral ligaments. If present, they act as secondary stabilisers to posterior tibial translation (Kweon et al., 2013). Butler et al. (1980) performed biomechanical loading tests on 14 cadaveric knees in which the anterior and posterior cruciate ligaments, along with other proposed ‘secondary’ restraints to anteroposterior translation were sectioned. They found that the posterior cruciate provided 95% of posterior restraining force. The major secondary restraints to posterior translation included the posterolateral structures, including the popliteus complex and the medial collateral ligament. As mentioned previously, Gollehon et al. (1987) found that at 0˚-30˚ knee flexion, sectioning the lateral collateral and deep ligament complex allowed a similar increase to posterior tibial translation to that seen following sectioning of the posterior cruciate ligament. These results agree with other similar biomechanical cadaveric studies (Nielsen et al., 1984; Grood et al., 1988; Veltri et al., 1995; Veltri et al., 1996; Kaneda et al., 1997; Coobs et al., 2007).

In the study by Butler et al. (1980), when only the posterior cruciate ligament was sectioned, increases were seen in external rotation and varus angulation which were also reciprocal to increasing knee flexion. Even so, with the knee at 90˚, the maximum flexion angle tested in this study mean increase and standard deviation of internal rotation following sectioning of the posterior cruciate only was 0.6˚±1.2˚, and 4.3˚± 0.9˚ for varus angulation. This study was limited by variation in the methodology throughout the study and obvious alteration in the relevance of kinematics studied in an in vitro setting, which is quite different from the normal in vivo setting due to specimen mounting and serial dissection of major restraining structures. In 1988, Grood et al. went on to report results of sectioning the posterior cruciate ligament on 15 cadaveric specimens in a biomechanical study. They concluded that removal of only the posterior cruciate ligament resulted in increased posterior translation of the tibia, however no additional rotational or coronal (varus/valgus) laxity; their findings correlated with other biomechanical studies at the time (Gollehon et al., 1987). Later, Logan et al. (2004) analysed the difference in knee kinematics in a case series of 6 patients with unilateral posterior cruciate deficiency against the normal knee using an open MRI scanner. During squatting, it was found that the medial femoral condyle was abnormally subluxed anteriorly in posterior cruciate ligament deficient knees (posterior subluxation of the medial tibial plateau), which would lead to abnormal medial compartment wear, a feature seen in patients with posterior cruciate deficiency.

Veltri et al. (1995, 1996) demonstrated that the popliteofibular ligament complex was found to be tight in all positions of knee flexion, as the ligament remains well aligned and functional in resisting external rotation throughout flexion. Sectioning the posterior cruciate ligament alone has little effect on external rotational laxity, whereas sectioning the posterolateral structures has a significant effect at 30˚ knee flexion. At 90˚ flexion, sectioning the posterior cruciate ligament a well as the posterolateral capsular structures causes a further increase in external rotation (Grood et al., 1981; Gollehon et al., 1987). This work forms the basis of simple clinical tests for discriminating posterior cruciate ligament and posterolateral structure pathology, such as the dial test. An increase in external tibial rotation at 30˚ of knee flexion compared to the normal side is diagnostic of posterolateral capsular structure injury. At 90˚ of knee flexion, further external tibial rotation indicates injury to the posterior cruciate ligament also (Miller et al., 2012).

The posterior cruciate ligament is involved in resisting hyper-flexion although it is not a major restraint to hyper-flexion in the normal knee (Vogrin et al., 2000). In the osteoarthritic knee, the posterior cruciate ligament may be shortened and rigid (Fujimoto et al., 2012). When not properly balanced during total knee replacement, this ligament may restrict flexion of the knee (Kim et al., 1997). This observation agrees with findings in biomechanical cadaveric studies that have demonstrated significantly increased strain on the posterior cruciate ligament during high flexion (Vogrin et al., 2000).

2.5.3 Kinematics of the knee

The knee has been described as allowing motion in six degrees of freedom (Fu et al., 1994; Woo et al., 1999; Kweon et al., 2013); these include three translations, and three rotations as discussed previously.

The knee must accommodate high demand functional actions whilst conferring high levels of static and dynamic stability. Activities such as walking, and moreover, running, pivoting, weight bearing in flexion, ascending and descending slopes and stairs place large moments on the knee in all of these planes. The cruciate ligaments play a central role in kinematics of the knee. Having considered the major ligaments of the knee, the collateral and cruciate ligaments, we can briefly consider how these influence knee kinematics.

Due to the asymmetry of the anterior and posterior cruciate ligament attachments, the ligaments are under tension at different times during the range of knee flexion and extension. Standing with the knee in extension or hyperextension creates tension in the anterior cruciate, whereas the posterior cruciate remains relatively lax. Combined with the strong posterior capsular support of the knee, this mechanism, along with the congruence on the bony articulations and menisci allows for maintenance of erect, weight bearing posture with relatively little muscular effort, with these ligamentous structures resisting hyperextension. The tension of the anterior cruciate in extension can be demonstrated when mal-positioning or over-tensioning of anterior cruciate reconstruction graft occurs (Petsche et al., 1999), or in the instance of inter-condylar notch degenenerative disease resulting in intercondylar notch stenosis and anterior cruciate restriction (Leon et al., 2005). In both of these scenarios, extension of the knee is markedly limited.

During flexion of the knee, the posterolateral bundle of the anterior cruciate ligament reduces in tension, whilst the anterolateral bundle of the posterior cruciate ligament increases in tension. In mid-flexion (20˚ - 50˚), neither cruciate ligament is under maximum tension, and the knee is relatively less stable in the coronal and sagittal planes than when in full extension.

As the knee flexes, the anterior cruciate ligament becomes more parallel to the joint line, resisting forces of anteroposterior distraction, whereas the posterior cruciate ligament becomes more perpendicular to the joint line, resisting forces of femorotibial distraction (Kweon et al., 2013). This forms the basis of what has been termed the four-bar linkage system. This describes the interaction of the anterior and posterior cruciate ligaments in terms of their relative attachments and positions during flexion, resulting in the centre of rotation of the knee (dictated by the intersection of the cruciates during flexion/extension) moving posteriorly with flexion, while the ligaments ensure the femur does not sublux posteriorly or become disengaged from the tibia during late flexion by permitting rolling and sliding.

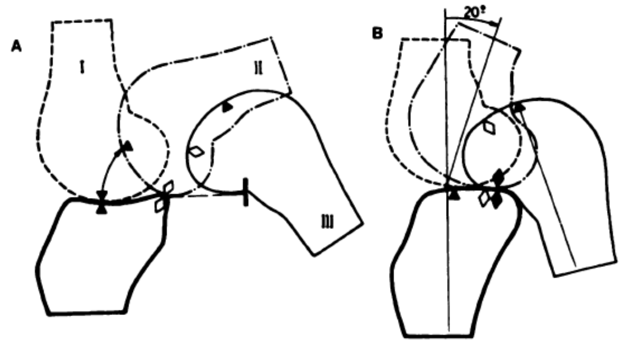

Figure 6 – Diagram illustrating rolling and sliding in the normal knee during flexion. If pure rolling (A) was to continue, the femur would roll off the posterior tibial plateau. The cruciate ligaments allow simultaneous rolling and sliding between the femur and tibia (B). Diagram taken from Fu et al. (1994).

2.5.4 Anteroposterior laxity and instability

The cruciate ligaments may be injured by abnormal loading of the knee in the coronal and sagittal planes, and this stress is often accompanied by excess rotational torque in the axial plane; typically loading of the knee in any direction whilst twisting. Frequently, multiple soft tissues of the knee are injured simultaneously, and associated chondral lesions are common.

Since the concept and development of complete and partial cruciate ligament repair, diagnosis of full and partial rupture of the cruciate ligaments has become important and will be discussed.

In cruciate deficient knees, intensive rehabilitation to maximise quadriceps and hamstring strength, including proprioceptive rehabilitation, improves functional outcome (McRae et al., 2011).

The long-term sequelae of cruciate injury include development of osteoarthritis. Authors suggest that 50% of individuals diagnosed with tear of the anterior cruciate ligament will develop symptomatic osteoarthritis at 10 – 20 years; variables influencing this include muscle strength, rehabilitation, obesity, age, sex, activity and re-injury (Lohmander et al., 2007). Still, little literature exists to strongly support reconstruction of the cruciate ligaments; well-designed randomised trials are scarce. One randomised trial began in 2008 in Sweden taking 121 young active adults with acute anterior cruciate ligament injury on a previously uninjured knee (Frobell et al., 2013). The patients were randomised to rehabilitation with early surgical reconstruction and rehabilitation with optional, later reconstruction. Of the 59 patients in the second group, 30 (51%) opted for later reconstruction; only seven of these were carried out beyond the two-year post-injury point. At five years, no difference in function, quality of life, activity levels or radiographic evidence of osteoarthritis was observed. Authors conclude that based on these results, clinicians should consider rehabilitation the primary treatment for anterior cruciate ligament injury, with the option of later reconstruction. The design of this trial highlights the difficulty in attempting to randomise patients into a treatment and optional treatment group; by two years, half of the delayed treatment group had received surgical reconstruction. Although the reported results are of interest, conclusions and recommendation for change in practice cannot be made at the five-year mark, as this is too early to examine the long-term sequelae.

A 15 years follow-up of patients (n=100) randomised to surgical treatment and rehabilitation indicated no difference in frequency of radiological evidence of osteoarthritis or activity level (Meunier et al., 2007). Patients in the non-surgical treatment group reported a slightly lower Lysholm score (this is a score designed to report functional symptoms in patients following anterior cruciate ligament injury). Notably, 16 of the 52 patients randomised to non-surgical treatment underwent surgical reconstruction for instability. The study indicates that functional instability may be a problem for a proportion of patients following anterior cruciate tear. Regardless of treatment, 50% of patients demonstrated osteoarthritic change on radiographs at 15 years, and 10% demonstrated severe disease.

A meta-analysis of 5770 patients demonstrated that at a mean of three years and five months following surgical reconstruction of the anterior cruciate, 63% of patients had returned to pre-injury activity level and 44% had returned to competitive sports (Ardern et al., 2011). This is consistent with other studies (Frobell et al., 2013). Although surgical reconstruction is recommended for those wishing to return to high levels of physical activity and competitive sport, it is no guarantee that this will be possible.

Natural history following isolated posterior cruciate ligament injury appears to be more encouraging. Shelbourne, Davis & Patel (1999) followed up 133 athletically active patients for a mean of 5.4 years following injury. No surgical intervention was performed in these patients. No correlation was found between clinical laxity and outcome score or return to sport. Half of the patients had returned to sport at the same or higher level, one sixth had not returned to sport. Nonetheless, biomechanical and clinical evidence suggests that complete tear of the posterior cruciate with associated posterolateral capsular injury / laxity, should be treated with surgical reconstruction to reduce articular cartilage damage and likelihood of secondary osteoarthritis (Matava et al., 2009). Authors admit that outcomes of surgical reconstruction are often unsatisfactory using current techniques, yet surgical reconstruction is undertaken, usually based on grading of injury severity, to maximise potential function (Matava et al., 2009; Maruyama et al., 2012). No high quality randomised trails of surgical treatment versus non-surgical treatment were found on reviewing the literature.

2.5.5 Assessment of anteroposterior knee laxity

It is clearly important to be able to assess anteroposterior laxity of the knee as a result of various ligamentous injuries. Methods of assessing cruciate ligament injuries include clinical examination, stress testing, magnetic resonance imaging and arthroscopic evaluation (Christel et al., 2012). Anteroposterior radiograph of the knee may reveal a small avulsion fracture from a site just distal to the lateral tibial plateau. This is known as a Segond fracture (Goldman et al., 1988; Hess et al., 1994; Campos et al., 2001). This avulsion is the distal attachment site of the iliotibial band and anterior oblique band of the fibular collateral ligament (Campos et al., 2001). This injury typically occurs when excessive varus and internal rotation is applied to the knee as opposed to the more usual mechanism of anterior cruciate rupture involving valgus stress (Goldman et al., 1988). Study of 151 patients with anterior cruciate ligament rupture revealed an incidence of 9% (Hess et al., 1994). Each of the above mentioned modalities for assessing the anterior cruciate is limited and using multiple methods of assessment is preferable. Controversy surrounds the definition of partial tear of the anterior cruciate ligament. A complete tear obviously refers to loss of integrity of the entire ligament. With increasing technical advances in repair techniques, including augmentation of partial tears, or repair of specific bundles of the anterior cruciate, there is an increasing need for reliable diagnostic tests. Functional laxity resulting in symptomatic instability during daily activities is more relevant to the patient's outcome and decision-making regarding treatment than simple demonstration of a degree of laxity in the clinical setting, however clinical tests to date focus on analysing the integrity of the ligament in a manner similar to biomechanical testing. The most common simple clinical tests include the Lachman test; the examiner maintains a knee flexion angle of 20 – 30˚; range of knee flexion angle for performing the test quoted in the orthopaedic literature is between10 - 30°, particularly in laboratory studies, however an angle of 20° flexion is generally accepted (Logan et al., 2004; Christel et al., 2012). The examiner uses one hand to stabilse the thigh, and then pulls anteriorly with external rotation on the proximal tibia, attempting to distract the joint in the sagittal plane. Feeling a 'solid' end point with similar translation to the contralateral (normal) knee is a negative test for cruciate insufficiency. The Lachman test is regarded as the most sensitive and specific simple clinical test to detect acute and chronic anterior cruciate ligament deficiency, with rates of both being between 85 – 98% in the reported literature (Torg et al., 1976; Donaldson et al., 1985; Zarins et al., 1986; Mitsou et al., 1988). The anterior drawer test is performed with the patient supine, hip flexed to 45˚ and knee flexed to 90˚. The foot is stabilised, usually by the examiner sitting on the foot, while the examiner uses both hands to pull the tibia anteriorly. Pushing posteriorly is referred to as the posterior drawer test. Again, comparison with the contralateral side in terms of translation and the presence or absence of a solid end point are the parameters used to detect pathology. The pivot shift test is more technically demanding and requires a great deal of patient relaxation, as such, it is best performed under anaesthesia. The patient is supine with the hip flexed to approximately 30˚. The examiner supports the lower leg applying internal rotation of the tibia and valgus stress. The examiner slowly flexes the knee. In the range of 30-40˚, during flexion the tibia may be felt to reduce from its subluxed position, during extension, subluxation may be felt. These indicate a tear of the anterior cruciate ligament, and possibly associated structures such as the posterolateral capsule, arcuate ligament complex or iliotibial band. Meniscal tears may limit movement during this test and guarding of the hamstring muscles due to pain and instability may make the test impossible to perform.

A large number of commercial devices have been developed to estimate anteroposterior translation and rotatory stability of the knee. They cannot all be examined in detail in this summary, however, the more common and thoroughly evaluated tools will be discussed in more detail. The KT-1000 (MEDmetric® Coroporation, California, USA) arthrometer is an instrument designed to quantify translation of the tibia in the sagittal plane. Authors studying the validity of the device have concluded that a translation of ≥3mm compared to the contralateral (normal) knee while applying a force of 133N is diagnostic of cruciate insufficiency (Daniel et al., 1985), other authors have used >2mm as the diagnostic threshold (Bach et al., 1990). No studies were identified in the literature specifically analysing the validity of the KT-1000 as a measuring tool of continuous anteroposterior translation, therefore its use as a measure of the continuous variable of translation in comparison of treatment outcomes is questionable, yet use in this manner is very prevalent in the literature pertaining to comparison of cruciate ligament reconstruction techniques (Jung et al., 2011; Hussein et al., 2012; Park et al., 2012). The KT-1000 has also been used evaluate normal population groups in terms of knee laxity (Brannan et al., 1995; Rosene et al., 1999), again the reliability of these data is questionable. A comparison of the KT-1000 and stress radiographs applying 9kg of anterior force to the tibia revealed no equivalence in absolute values of translation, and correlation coefficient between the two methods was weakly positive (0.67) (Lerat et al., 1993). Graham et al. (1991) concluded that the KT-1000 was “totally inaccurate” compared to the Lachman test when testing 21 individuals with cruciate insufficiency. The device was correct in 10 knees, diagnosed the contralateral (normal) knee as having cruciate deficiency in 8 tests, and provided equivocal results in three knees. Clinical studies indicate the device has a sensitivity of 0.9-0.97 using the criteria of a 2 or 3mm difference between the normal and pathological knee using a force of 133N (30 pounds) (Bach et al., 1990; Highgenboten et al., 1992). The device can only be recommended as a dichotomous diagnostic tool based on the current literature. Liu et al. (1995) compared the sensitivity of clinical examination using the Lachman, pivot shift and anterior drawer test, all without anaesthesia, magnetic resonance imaging and the KT-1000 arthrometer on 38 patients three days (range 1 -7) following complete tear of the anterior cruciate ligament (all of these patients had arthroscopically proven complete tears of the anterior cruciate at time of reconstruction, mean three weeks following injury). Using a force of 9kg anterior displacement and the KT-1000 device, 33 patients had a positive result (displacement ≥3mm compared to the normal knee (Daniel et al., 1985)). Without anaesthesia, Lachman test was positive in 36 knees, pivot shift in 25, and anterior drawer in 23. Magnetic resonance imaging was positive for tear in 37 of the 38 knees. Six of the 37 knees diagnosed with a tear were reported as partial tear by a radiologist following magnetic resonance imaging. In order of sensitivity; Lachman test conferred 95% sensitivity (CI 82 – 99), followed by KT-1000; 87% (72 – 96), magnetic resonance imaging; 82% (66 – 92), pivot shift; 71% (43 – 76) and finally, anterior drawer;

61% (54 – 85). Methodological concerns regarding the study by Liu et al (1995) include the subjective nature of clinical examination and reporting positive findings in the absence of normal (control) comparisons. It is therefore not possible to calculate specificity values (i.e. the rate of true negative results). Also, all the tests were performed in the acute phase, potentially limiting clinical examination due to guarding of the knee flexors. The study information does not provide information about patients with chronic cruciate insufficiency; in this setting, it is likely that manual clinical testing would be more sensitive for complete cruciate tears due to lack of pain. Sensitivity of manual clinical tests improves in the acute setting with patients being under anaesthesia, sensitivity of the Lachman test in anaesthetised patients has been reported at 100% (DeHaven 1980). More recently, Wiertsema et al. (2008) performed intra and inter-tester analysis to compare diagnostic findings by two physiotherapists performing the Lachman test, and using a KT-1000 arthrometer (9kg anterior force). Intraclass correlation coefficient for intra and inter-tester reliability for the Lachman test were 1.0 and 0.77 respectively, for the KT-1000; 0.47 and 0.14 respectively. These authors do not advocate use of the KT-1000.

Injuries of the posterior cruciate ligament are graded 1-3 according to the amount of posterior tibial translation. Grade 1: 1-5mm, grade 2: 6-10mm, and grade 3: >10mm (Shelbourne et al., 1999; Matava et al., 2009). Grade 1 & 2 tears are typically treated by conservative methods including quadriceps strengthening and rehabilitation. Grade 3 tears are often complex injuries with associated posterolateral capsular injury. These types of injuries tend to as a result of road traffic accidents and sport (Schulz et al., 2003). Little information exists on the natural history of such injuries. Biomechanical cadaveric studies indicate the resulting instability would lead to excessive wear of the medial compartment and these authors advocate surgical management as well as quadriceps strengthening (Skyhar et al., 1993; Harner et al., 2000). Clinical studies remain in the form of retrospective cohort analysis to date (Cross et al., 1984; Boynton et al., 1996; Strobel et al., 2003) and indicate variable outcomes, with a minority of patients experiencing severe symptoms, but evidence of medial compartment osteoarthritic degeneration with time in patients with this injury. Strobel et al. (2003) retrospectively analysed arthroscopy reports from 181 patients with conservatively managed posterior cruciate ligament insufficiency. In those individuals diagnosed ≥5 years prior to arthroscopic evaluation, 77.8% demonstrated degeneration of the medial femoral condyle articular cartilage, and 46.7% demonstrated degeneration of the patella. Surgical repair may therefore be considered on a case-by-case basis, taking into consideration the degree of injury, amount of anteroposterior and rotatory laxity, and any previous knee injury or surgery such as medial menisectomy.

Diagnosis of posterior cruciate ligament injury again can be divided into manual clinical examination, and examination using adjuncts such as arthrometers, stress radiography, and other imaging modalities.

Manual clinical tests include the posterior drawer test, posterior sag, active quadriceps test, reverse pivot shift and dial test.

During posterior drawer test, the patient's knee is flexed to 90˚ and a force directed posteriorly to the proximal tibia. Posterior sag simply compares the position of the tibial tuberosity with the patient supine and both knees flexed to 90˚. Absence of the posterior cruciate results in the abnormal knee 'sagging' posteriorly. Active quadriceps tests involves beginning with the knee at 90˚, the patient contracts the quadriceps or slides the foot down the examination table. In a posterior cruciate deficient knee, the tibia will reduce anteriorly from a posteriorly subluxed position. Reverse pivot shift involves the patient in a supine position, whilst the examiner applies external rotation to the foot. A valgus stress is placed on the leg and the knee extended from 80˚ flexion. If the tibia reduces at approximately 20˚ flexion, the test is positive (Colvin et al., 2009). The dial test has been described earlier. Neurovascular examination is extremely important in cases of suspected posterolateral rotatory instability, isolating and evaluating function of the tibial and peroneal nerves, and assessing the distal pulses.

Clinical examination can be variable and difficult in the acute setting (Colvin et al., 2009; Garofalo et al., 2009). In addition to these tests, and standard radiographs obtained at time of injury, authors have indicated that quantification of posterior laxity aids classification of the degree of injury, as described above, hence guiding treatment.

Stress radiography typically involves suspending a weight from the proximal tibia, or applying a load in a posterior direction, with the knee flexed at discrete intervals. Hewitt et al (Hewett et al., 1997) reported that this method diagnosed all (n=10) complete posterior cruciate ligament tears when using a threshold of ≥8mm posterior translation of the posterior aspect of the medial femoral condyle and posterior aspect of the medial tibia plateau. Mean posterior translation for the complete tears was 12.2mm (± 3.7mm). 11 partial tears were also assessed, mean translation: 5.6mm (±2.1mm). It must be noted that many positions and adjunct equipment have been advocated for use in performing stress radiographs (Huber et al., 1997; Garofalo et al., 2009), and that reliability may depend on the experience of those performing and interpreting the radiographs (Margheritini et al., 2003). One adjunct to stress radiography is the Telos device (Austin & Associates, Maryland, USA). This device secures the tibia whilst applying a force of 15N to the anterior tibia, after which a lateral radiograph of the knee is taken. Margheritini et al. (2003) reported intra-tester intra-class correlation coefficient of 0.95, and inter-tester intra-class correlation coefficient of 0.91 when evaluating 787 stress radiographs taken using the Telos device. Jackman et al. (2008) reported inter and intra-tester intraclass correlation coefficients of 0.97 and 0.96 in reporting stress radiographs using a kneeling technique and reported by three experts. However, Sørensen et al. (2011) evaluated the precision of the Telos device using radiostereometric analysis (RSA). RSA is an invasive technique involving implantation of tantalum beads and has an accuracy of 0.1mm (Selvik 1989). Bland-Altman plot of differences between the 1st and 2nd knee laxity measurements taken on 60 knees using the Telos and an improved limb positioning protocol demonstrated a mean difference of 0mm, and limits of agreement (95% prediction interval) of ± 5.2mm when measurements were taken using RSA. The authors concluded this clinical data conflicted with earlier animal studies which used RSA on goat limbs, reporting precision of ±1.77mm (Fleming et al., 2001); they conclude that the application of anteroposterior forces causes flexion and extension of the knee, along with the plasticity of soft tissues reducing how representative measurements taken superficial to the soft-tissues are compared to kinematics of the bony anatomy. These factors were deemed responsible for reducing precision of measurement, and the authors recommend that this device cannot be recommended for clinical use (Sørensen et al., 2011).

The KT-1000 has demonstrated poor precision in measuring pathological posterior tibial translation (Huber et al., 1997; Garofalo et al., 2009). Intraclass correlation coefficient for intra-tester reliability for an experienced and novice examiner: 0.74 & 0.7, inter-tester reliability: 0.29 (Huber et al., 1997). Stress radiographs have been demonstrated to provide superior reliability to the KT-1000 (Margheritini et al., 2003; Schulz et al., 2005).

Magnetic resonance imaging has sensitivity of 97%-100% in complete posterior cruciate ligament tears, but only 67% in partial tears (Gross et al., 1992; Patten et al., 1994).

Ultrasonography of the cruciates remains experimental, clinical studies have not been reported as yet (Hsu et al., 2005).

2.5.6 Other devices used in assessing cruciate ligament injuries

There are a large number of devices being developed and reported in the literature to assess kinematics of the knee in a non-invasive or minimally invasive manner. It is beyond the scope of this summary to examine each in detail.

The most prominent devices in the literature include the CA-4000 Electrogoniometer (OSI, Hay- ward, CA), Genucom Knee Analysis System (FARO Medical Technologies, Montreal, Ontario Canada), Kneelax3 (Monitored Rehab Systems, Haarlem, The

Netherlands), Rolimeter (Aircast Europa, Neubeuern, Germany), and Stryker Knee Laxity Tester (Stryker, Kalamazoo, MI), as well as the KT-1000 and KT-2000.

Rotational laxity of the knee is another parameter exhibiting quantifiable change following anterior cruciate injury as will be discussed in section 6. Quantification of this parameter may be more relevant following treatment of anterior cruciate pathology than anteroposterior laxity in terms of prognosis; Kocher et al. (2004) examined 202 patients undergoing anterior cruciate ligament reconstruction 2 years following surgery. The degree of anteroposterior laxity was not associated with any symptom reporting or function ($p>0.05$), however pivot shift, which may be a more functional representation of stability, was associated with poor satisfaction, giving way and activity limitation, including sports ($p<0.05$). Authors have suggested that rotational laxity, not strictly anteroposterior laxity alone may be responsible for accelerated joint destruction and symptomatic instability, however no long term cohort studies are currently available to prove or refute this theory (Stergiou et al., 2007; Branch et al., 2010). Quantification of kinematic parameters including anteroposterior translation and simultaneous measurement of tibial rotation can be achieved using computer assisted surgery technology; this will be discussed later. Other devices have been developed to simultaneously quantify anteroposterior instability and rotational laxity, including electromagnetic systems (Hoshino et al., 2007; Kuroda et al., 2012). Initial tests prove that the electromagnetic non-invasive systems can detect differences in rotational acceleration of the tibia during a positive and negative pivot shift test. However limited inter-tester information exists in the literature (Hoshino et al., 2007; Kuroda et al., 2012). Furthermore, the pivot shift test is more difficult to perform and reliability between testers is more likely to be affected by this than errors within the system. Further work by this group (Araki et al., 2011) analysed anteroposterior translation during Lachman test between normal and cruciate deficient knees in 41 patients. Comparison was made with fluoroscopy and KT-1000. Significant differences existed between measurement using the electromagnetic device (EMD) and the KT-1000, but no difference was observed with fluoroscopy. Nonetheless, the authors conclude that strong correlations were observed between EMD and KT-1000 (r=0.64) and EMD and fluoroscopy (r=0.96): indicated that the EMD is 'as accurate' as fluoroscopy. This conclusion is of limited value in clinical practice; fluoroscopy is not a recognised gold standard in measuring articular excursion within the limits of precision and accuracy required for surgical practice. Quantified accuracy of mono-planar fluoroscopy ranges between 1-8mm for translation and 1˚-5˚ for rotation (Tersi et al., 2013) and with no reliable measurement of anteroposterior translation, no conclusions regarding accuracy can be made. Regarding precision, correlation coefficient is not sufficient to convey precision (Bland et al., 1986), and the appropriate statistics are not conveyed. We can only conclude that a strong correlation exists between EMD and fluoroscopy.

Other concepts in mechanical knee laxity testing have attempted to minimize the risk of rotational error and appreciating the influence of rotation. Mayr (2009) presented the concept of applying 2Nm external or internal rotation during anteroposterior laxity testing. This improved reliability from (intra-class correlation coefficient) 0.6 to 0.83 – 0.98. No published data has as yet followed this presented work. One potential problem with this type of system could be that with pathological rotatory laxity, a rotational force of 2Nm may not place the knee in a stable and reproducible position, thus decreasing reliability.

Authors have raised concerns over the subjective nature of force application during clinical examination and instrumented examination both in the out-patient clinic and operative setting (Robert et al., 2009; Branch et al., 2010), purporting the theory that standardised rate and quantification of load whilst maintaining a standardised limb position might increase reliability. Robert et al (Robert, Nouveau et al. 2009) developed the GNRB (Genurob, Montenay, France) in 2005. This device delivers a standardised load at a set rate to the posterior tibia whilst detecting anteroposterior tibial translation. Rotation of the foot/tibia does not appear to be standardised however. Reliability of the GNRB was significantly better than the KT-1000 testing normal healthy volunteers and those with complete anterior cruciate deficiency (diagnosed arthroscopically). Among the normal knees, no effect was seen between two testers of differing experience, this was observed using the KT-1000. Significantly more displacement was observed between knees in the normal volunteers using the KT-1000. At 134N force and using a differential threshold of 1.5mm between normal and affected knee in patients with partial (anteromedial bundle) anterior cruciate rupture, sensitivity for the GNRB; 80% and specificity; 87%. Using the same force in patients with complete tears however resulted in sensitivity of 70%, and specificity of 99% if differential tibial translation was at least 3mm. These results are superior to many reports of the KT-1000 (Forster et al., 1989; Graham et al., 1991; Wiertsema et al., 2008), however they are not superior to other methods of clinical examination such as the Lachman test (DeHaven 1980; Graham et al., 1991; Liu et al., 1995).

Further devices used to assess stability of the knee and integrity of the cruciate ligaments include the assessment of rotatory stability and are discussed below.

2.5.7 Tibial rotation

Rotatory stability of the knee has been discussed in part above (section 2.2). Estimation of 'normal' tibial rotation has been very difficult owing to the variables of knee flexion angle and test method used (Shoemaker et al., 1982; Zarins et al., 1983; Shoemaker et al., 1985; Uh et al., 2001; Almquist et al., 2002; Shultz et al., 2007; Shultz et al., 2007; Tsai et al., 2008; Diermann et al., 2009,McQuade, 1989 #1978; Shultz et al., 2010; Ahrens et al., 2011; Almquist et al., 2011; Shultz et al., 2011; Almquist et al., 2013). A variety of very different methods have been used with inconsistent results, as will be discussed.

The structures responsible for limiting rotation of the tibia in the axial plane include the cruciate ligaments and the lateral, posterolateral, medial, posteromedial capsule, and the menisci with dynamic/active restraint provided by the muscles crossing the knee (Markolf et al., 1976; Lipke et al., 1981; Shoemaker et al., 1985; Gollehon et al., 1987; Louie et al., 1987; Grood et al., 1988; More et al., 1993; Fu et al., 1994; Bodor 2001; Amis et al., 2003; Robinson et al., 2004). Internal rotatory laxity increases in early knee flexion, with the greatest range seen at 20˚ to 40˚ knee flexion, and biomechanical cadaveric studies indicate that sectioning of the medial collateral ligament increases internal rotational laxity much more dramatically than sectioning of the anterior cruciate, however sectioning either ligament increases internal rotational laxity (Lipke et al., 1981; Fu et al., 1994). Sectioning of the lateral and posterolateral structures in combination with the anterior cruciate ligament also increases internal rotatory laxity (Gollehon et al., 1987; Fu et al., 1994). Regarding external rotation, again this increases with knee flexion reaching a maximum at 30˚ - 40˚ of knee flexion (Fu et al., 1994). As the posterolateral capsular structures slant posteriorly as they pass distally, internal rotation slackens them and external rotation tightens them (Gollehon et al., 1987; Grood et al., 1988; Veltri et al., 1995; Veltri et al., 1996; Amis et al., 2003). Biomechanical studies have shown that the major restraint to external rotation of the tibia is the posterolateral capsule, and sectioning the posterior cruciate ligament has little effect on external rotatory laxity at low flexion angles. The lateral collateral ligament has been shown to provide the majority of restraint to external rotation in extension and very early knee flexion (Gollehon et al., 1987; Pasque et al., 2003; LaPrade et al., 2004; Lim et al., 2012). At 90˚ knee flexion, sectioning the posterior cruciate significantly increases external rotatory laxity of the tibia (Gollehon et al., 1987; Grood et al., 1988). Combined posterior cruciate ligament and posterolateral capsule injury results in the tibial plateau pivoting around the medial knee structures, causing excessive external rotation and abnormal articular wear (Amis et al., 2003).

A biomechanical study by Zantop et al. (2007) attempted to replicate combined stress on the knee in a manner similar to the pivot shift test involved placing cadaveric knees in a robotic measuring system and applying 134N anterior force, 10Nm valgus and 4 Nm internal tibial rotation. Following testing of intact knees, the investigators alternately sectioned the bundles of the anterior cruciate. Anterior translation increased with sectioning of the anteromedial bundle at 60˚ and 90˚ knee flexion. Sectioning of the posteromedial bundle increased anterior tibial translation and combined rotatory laxity at 0˚ and 30˚ knee flexion. The phenomenon of increased rotational instability appears to be related to the integrity of the postero-lateral bundle of the anterior cruciate ligament. Simulated in vitro pivot shift using robotic technology to compare intact knees, anterior cruciate deficient knees and following single bundle anterior cruciate reconstruction has shown a significant difference in anterior translation with deficiency of the anterior cruciate, but no significant increase in internal rotation between conditions of the anterior cruciate ligament integrity (Diermann et al., 2009). Authors have upheld the significance of rotatory instability over anteroposterior laxity (Stergiou et al., 2007; Branch et al., 2010), suggesting rotatory laxity is more disabling than anteroposterior laxity; Kocher et al. (2004) demonstrated that positive pivot shift test was associated with poor satisfaction, giving way and activity limitation, including sports ($p<0.05$). Jonsson et al. (2004)

assessed a relatively small cohort of 63 patients 5-9 years following anterior cruciate reconstruction, quantifying anteroposterior laxity with radiostereometry (RSA). Pivot shift test was documented for each patient at 2 years follow-up. Joint degeneration was quantified with radiographs and scintigraphy (radioisotope identification of increased bone physiological activity), and functional scoring. Functional scoring did not differ between patients with anteroposterior instability (defined as >2.5mm difference between the normal and operated knee on RSA applying an anterior force of 150N and a posterior force of 80N). Patients with a positive pivot shift had increased scintigraphic uptake at 5-9 year follow up, and poorer subjective knee function, activity and performance, but no increase in presence of osteoarthrosis. Increased joint scintigraphic uptake can indicate a pre-disease state (Hutton et al., 1986). When patients were grouped as having a knee which was stable or unstable in the anteroposterior plane, no difference was detected in scintigraphic uptake, presence of oseteoarthrosis or functional outcome scoring. The follow-up period for this cohort is quite short for analysing presence or absence of osteoarthritis following a surgical intervention, nonetheless it is interesting to note that presence of a positive pivot shift test may convey more information regarding functional ability and be of prognostic value. The ability to define the range of rotation, especially in a dynamic and real-time manner would be of use in research and clinical practice.

2.5.7.1Rotatory instability

Van der Hart et al. (2008) reported a cohort of 28 patients at a mean follow-up of 10.3 years following anterior cruciate ligament reconstruction. No significant correlation was seen between remaining anteroposterior laxity and grade of osteoarthritis. However the occurrence of osteoarthritis was significantly greater in the operated knee compared to the patient’s normal knee. While it is known from meta-analysis that cruciate ligament reconstruction does not appear to eliminate the risk of secondary osteoarthritis (Lohmander et al., 1994), the point of interest from the study by Van der Hart et al (2008) is the lack of correlation between anteroposterior laxity and occurrence of osteoarthritis, and the correlation between positive pivot shift and poor clinical and functional scoring in the study by Kocher et al. (2004); what is interesting is the question of whether rotatory instability is more important than anteroposterior instability in terms of satisfaction, function and pathogenesis of arthrosis. Both studies are limited by size, retrospective nature and the high incidence of concomitant meniscal pathology which will influence development of osteoarthritic change.

While it is clear from biomechanical and clinical studies that anterior cruciate deficiency results in anteroposterior laxity detectable by both clinical and quantified mechanical examination methods as discussed before, the increase in rotational laxity resulting from anterior cruciate ligament deficiency is small, owing to the fact that anterior cruciate is not the primary restraint to internal rotation. Sectioning of the anterior cruciate has been shown in biomechanical studies to increase internal rotation between only 2-4˚ when the knee is in early flexion (20˚ - 30˚) (Lipke et al., 1981; Nielsen et al., 1984; McQuade et al., 1989; Lane et al., 1994; Andersen et al., 1997). The posterior cruciate ligament is even less involved in rotatory stability, only demonstrating significant effect at 90˚ knee flexion (Gollehon et al., 1987; Grood et al., 1988). Devices with an aim of detecting cruciate ligament pathology or dysfunction would have to be very sensitive compared to those detecting anteroposterior instability. It may indeed be more useful to detect anteroposterior instability for diagnosis of cruciate pathology and develop non-invasive means of quantifying rotatory stability in a dichotomous manner to evaluate surgical reconstruction of the cruciate ligaments and functional outcome.

Rotatory instability of the knee can of course be caused by injury to a number of soft-tissues. The biomechanical literature suggests that no one ligament is primarily responsible for rotatory stability, rather structures in the posterolateral and posteromedial corners of the knee act in synergy with the cruciate ligaments, collateral ligaments, menisci and surrounding musculature (LaPrade et al., 2004; Robinson et al., 2004). Whilst detecting rotatory stability may of some diagnostic use, imaging such as magnetic resonance imaging remain the primary diagnostic modality, especially in multi-ligamentous capsular injury of the knee (LaPrade et al., 2007). Methods of assessing rotatory instability would be of value in evaluating surgical repair methods. Should this be available in the intra-operative setting, the surgeon would be able to evaluate surgical repair on the operating table. Strictly this would require quantification of applied rotatory force and laxity values from the contralateral knee. A non-invasive device would therefore be ideal, as invasive methods would add to surgical morbidity if the contralateral knee was being tested.

2.5.7.2 Assessment of rotation & rotatory instability

The earliest attempts at assessing rotatory stability of the knee were complex and encountered difficulty adjusting for soft tissue movements around the femur and tibia, and excursion of the ankle soft tissues Shoemaker & Markolf (1982). These investigators found that the range of rotation of the tibia was greater with the knee at 90˚ of flexion than at 20˚, this was at odds with previous biomechanical studies (Lipke et al., 1981; Fu et al., 1994). They also detected differences in range of rotation due to flexion angle of the hip, suggesting that hamstring muscle tension and tone may influence rotatory laxity. They found that with the hip extended, rotation of the tibia was greater than when flexed at 90˚. The authors also noted that when applying 10Nm of torque to the ankle joint, significant excursion occurred independently of the tibia. They estimated this to be up to 66% of the measured range of tibial motion, especially at extremes of range. Early attempts to detect differences between knees with anterior cruciate ligament injury and the contralateral knee suffered from methodological difficulties associated with measuring the applied torque and standardising lower limb position, making interpretation of differences unreliable (Zarins et al., 1983; Markolf et al., 1984). Early studies presented a wide variability in range of motion and few trends in normal and pathological knees, most likely due to the difficulties described (Shoemaker et al., 1982; Zarins et al., 1983; Markolf et al., 1984; Almquist et al., 2002).

Almquist et al. (2002) developed a device called the Rottameter. A platform for the subject to sit on was adjustable in terms of angle allowing adjustment of knee flexion angle. Two side supports for the thigh and a foot and ankle support attached to a rotating footplate secured the leg. Torque was applied using an adjustable spanner, with an indicator from the footplate displaying angle of rotation. Five male subjects with tantalum beads inserted during previous anterior cruciate ligament reconstruction were tested. The beads allowed radiostereometric analysis (RSA) to be carried out as a gold standard comparison. The Rottameter was found to overestimate range of total range of rotation at torque values of 3Nm, 6Nm & 9Nm by 12˚, 20˚ & 35˚ respectively; this was also overestimated in internal and external rotation. Later, intra and inter-tester reliability was calculated (Almquist et al., 2011) using torques of 3Nm, 6Nm & 9Nm as well as examiners 'end feel'. For the flexion angles tested (30˚, 60˚ & 90˚): between week intra-tester reliability ranged from (ICC) 0.22 – 0.84, same session intra-tester reliability 0.59 – 0.94, and inter-tester reliability 0.49 – 0.87. The least reliable variables in measurement conditions were low torque (3Nm) and testing at 30˚ & 60˚. Testing total range of rotation at 90˚ with 9Nm torque appeared to be most consistent and reported ranges were between 70˚ - 79˚. Interestingly, using 'end feel', one week apart reliability at 30˚, 60˚ & 90˚ was (ICC) 0.82, 0.76 & 0.65, conveying reasonable reliability without standardising torque application. Despite initial limitations in accuracy (Almquist et al., 2002), this device was used recently on normal subjects to report range of motion (Almquist et al., 2013). 120 healthy subjects were tested at the same flexion angles as used previously, but not with 3Nm torque in this study. No difference was seen between left and right knees, and females demonstrated 10 – 20% larger range of motion than males. Using the overestimation demonstrated in the earlier study using RSA in individuals with anterior cruciate ligament reconstruction (Almquist et al., 2002) as a constant for adjustment of Rottameter readings, Almquist et al predicted that at 90˚ knee flexion and with 9Nm torque applied, total range of tibial rotation in females in their study population of 120 volunteers was 33˚- 44˚, and 30˚ - 38˚ in males.

Musahl et al. (2007) reported initial and in vivo (Tsai et al., 2008) results of assessing rotational laxity using a simple portable device consisting of a pneumatic lower leg brace and a handle are with torque sensor attached. This device did not permit standardisation of knee flexion angle and has not been used in clinical practice.

Robotic systems have been reported in the literature (Park et al., 2008; Branch et al., 2010). Park et al. (2008) also demonstrated increased laxity in female tibial rotation using a motorised device. Assessing 10 healthy male and female volunteers, a mean difference in tibial rotation of 6˚ was observed in external rotation, with no significant difference in internal rotation. No data was available on validation of this device Branch et al. (2010) report between day and inter-tester correlation coefficient of at least 0.97 using a robotic laboratory based device which controls rate and torque during testing of rotational laxity of the tibia. This device can facilitate measurement of both limbs simultaneously. Once again, validation of this device was not discussed. These authors also noted increased total range of rotation in females, however only four females were included in the control group; total tibial rotation males 35.2 ± 7.0, females; 42.0 ± 7.1 (Branch et al., 2010). The device has been used to demonstrate increased internal rotation with reduced external rotation in the ‘normal’ knee of individuals with a history of anterior cruciate injury compared to healthy controls (Branch et al., 2010). Whilst these findings may point toward those at risk of anterior cruciate ligament injury, this technology remains out with the clinical domain at present. Once again, excursion of the ankle joint whilst measuring tibial rotation remained a noted challenge; authors estimated tibial rotation using electromagnetic sensors on the most superficial part of the bone anteriorly. It was estimated that 48.7% of the total range of tibial rotation measured was attributable to ankle joint excursion.

The ‘Vermont knee laxity device’ was initially presented as a method of measuring anteroposterior displacement, however this remained laboratory based (Uh et al., 2001). The device used a complex patient positioning, loading of the limb to simulate weight bearing and electromagnetic position sensors. No data was available in validating this device for discrete measurement of tibial rotation, comparisons had been made to radiographs in determining anteroposterior translation (Uh et al., 2001). One group used the device to compare male and female subjects, and analyse the effect of menstrual cycle on laxity (Shultz et al., 2007a; Shultz et al., 2007b; Shultz et al., 2010; Shultz et al., 2011). No literature was available validating the device for discrete measurement of internal and external tibial rotation in terms of accuracy. Reliability of the device ranged from (ICC) -0.28 to 0.92. No relationship between menstrual cycle and knee laxity was identified; females were found to have significantly increased total tibial rotation compared to males (27.5˚ ± 7.5˚ v 20.2˚ ± 4.1˚)

A further device to quantify rotation has been developed known as the Rotameter. This device is designed to assess rotational laxity, allowing quantification of manually applied torque. The system is designed specifically for assessing pathology of the anterior cruciate, or evaluation of reconstruction techniques. In a paper detailing the initial validation process, Lorbach et al. (2009) tested 17 amputated cadaveric knees using the rotameter and simultaneous image free navigation. The navigation system is capable of high levels of accuracy and provided a gold standard against which the rotameter could be tested. Despite high levels of correlation between readings from each system (Pearson coefficient at 5Nm, 10Nm & 15Nm; 0.95, 0.9 & 0.9 respectively): the Rotameter appeared to grossly overestimate rotation with higher levels of applied torque. At 15Nm external rotation, the Rotameter recorded 41˚± 12.1˚, and the navigation system: 26.8˚ ± 8.8˚; internal rotation at 15Nm; 39.2˚ ± 8.8˚ & 27.9˚ ± 8.4˚ respectively. With 15Nm torque applied, the Rotameter measured a mean total range of internal and external rotation of 80.2˚ ± 20.9˚, and the navigation system 54.7˚ ± 17.2˚. Significant differences in measurement of up to 42˚ between the two systems are observed on Bland-Altman plots. At lower torque values of 5 & 10Nm the Rotameter overestimated range of motion by approximately 5˚ & 15˚ respectively. No upper limit or cut off value for precision or accuracy is given prior to testing in order to accept or reject the device and/or methodology. This would have been desirable but is irrelevant to the analysis performed as no coefficient of repeatability or limits of agreement (Bland et al., 1986) are calculated to convey definitive values for precision and accuracy of the device at various torque values. It is clear the limits of agreement would be very large from these data. Yet the authors conclude that the most important observation is a high Pearson correlation coefficient. One major point which is unclear in the methodology of this pilot study is the accuracy and precision of the navigation system used, the authors reference a paper by Columbet et al. (2007) which used whole cadavers to test a different image free navigation system and validate its use in assessment of anteroposterior laxity. The registration process in the study by Columbet et al. (2007) is carefully described, highlighting that although the experiment was carried but in whole cadavers, the hip centre was not registered, only a cloud of points at the knee and kinematic registration of the knee. The system used by Lorbach et al. (2009) placed optical trackers in amputated limbs. No details are given regarding an adjusted registration process or the precision and accuracy of this, accuracy values quoted refer to the same hardware being used in a different registration process for total knee replacement surgery, which involves registration of the whole limb; it is not clear whether this is important, and no reference is given for the quoted accuracy values. Furthermore, extensive dissection of the soft tissues around the knee was performed, which may further limit applicability to the in vivo setting. Despite the authors claim that this system is less prone to soft tissue error compared to skin mounted tracking systems such as electromagnetic sensors, this has not been tested, as most of the soft-tissue was absent from these limbs. No reason is given in the methodology for this. A further cadaveric study (Lorbach et al., 2010), this time analysing the effect of sectioning the cruciate ligament revealed significant differences in rotational laxity between intact knees and subsequent sectioning of the posterolateral bundle. No effect was observed on sectioning the anteromedial bundle. Again, only correlation, not agreement was described regarding measurements taken with the Rotameter and a navigation system. The conclusion of this paper is sound in that the Rotameter may be able to detect rotational laxity due to cruciate insufficiency given the results of an in-vitro study, and the difference in sectioning the posterolateral and anteromedial bundles is interesting; however once again, accuracy of the system is questionable and a robust analysis of precision is not available.

The follow-on clinical study (Lorbach et al., 2012) analysing reliability of the device between testers in an in vivo setting gives high intra-class correlation (inter-observer reliability 0.94 – 0.98, intra-observer reliability 0.67 – 0.93) and concludes that reliability of the device is sound. The only reference to the validation study is again the Pearson coefficient. Intra-class correlation between left and right knees testing healthy young adults was 0.95 – 0.98; authors conclude that the high correlation validates the device for use in testing patients with an abnormal / knee with suspected laxity or following surgical cruciate reconstruction, against the patients normal knee. Finally, a clinical study of 52 patients 6 months following anterior cruciate reconstruction was performed. No difference between operated and normal knee was found throughout the cohort. Differences were in the region of 0.2˚ - 1˚. Patients with a positive pivot shift test following surgery, indicating a possible functional laxity had slightly more difference between knees in terms of rotational laxity: a mean difference of 4.1˚ at 10Nm force. The authors conclude that this device could be used in objective quality control in examining knee ligament injuries and evaluating treatments, such as single versus double bundle anterior cruciate reconstruction.

The device may be reliable between testers and moderately reliable within tests performed by a single investigator, and may therefore be used as a stand alone assessment of rotational laxity in order to discriminate between a normal and abnormal knee given the ability to quantitatively apply torque and obtain an estimate of range of rotation (Lorbach et al., 2010). However, as outlined above, precision of this device compared to a gold standard has not been analysed in a robust manner using tests described by Bland & Altman such as coefficient of repeatability (Bland et al., 1986). Also, as discussed above, the accuracy of the system has not been robustly analysed, and the raw data from the validation study puts in serious doubt the relevance of any absolute value of rotation given by the Rotameter. Absolute values certainly could not be used in comparison of two test subjects. The device may best be used as a dichotomous tool to analyse relative laxity between a single individual's normal and abnormal knee.

Despite flaws in the methodology and analysis of this series of experiments, the concept of comparing a thoroughly validated device such as an image-free navigation system to any novel system measuring the same kinematic parameters is sound. Provided a thorough analysis of repeatability and agreement between the two systems is carried out, this would be a robust method of validation.

2.5.7.3 Conclusion

Devices allowing quantification of tibial rotation have great potential in pure research of physiological variation and collecting of reference data. In clinical practice, identifying those 'at risk' of ligamentous injury, diagnosis of injury, evaluation and follow-up of non-surgical and surgical treatments would be useful adjuncts to current methods of clinical examination. Computer-assisted surgery technology has the ability to quantify tibial rotation, however this is invasive, can only be used in a surgical setting and data obtained is not standardised by consistent force application, and is not functionally relevant due to the effect of anaesthesia and, in a proportion of cases, surgical approach.

It remains unclear whether enough difference exists in rotatory instability between normal knees and those with a cruciate tear, as can be appreciated by mechanical testing for anteroposterior translation. Furthermore, a device would need to display high levels of precision when testing the patient's normal and abnormal knee in order to be sufficiently sensitive.

A reliable non-invasive device with thorough validation prior to in vivo testing is not yet available, and as a result, knowledge gaps exist in defining normal and abnormal rotational knee laxity.

2.6 Computer Assisted Surgery in Knee Reconstruction

Computer Assisted Surgery (CAS) includes the use of computer navigation systems, as well as robotics (DiGola et al., 2004). The list of technologies and applications is expanding, however all systems have been designed to aid the surgeon in increasing precision and accuracy and reduce 'outliers' in terms of surgical results. Specific to reconstructive surgery of the knee, CAS supports the surgeon in recreating normal anatomy as closely as possible, despite disruption of normal anatomy though disease and surgical approach, and the use of artificial implants.

2.6.1 History of CAS

The first use of CAS was in the field of neurosurgery, using pre-operative data acquired from three dimensional computer tomography (CT) scanning to map the brain prior to minimally invasive biopsy. Using stereotactic techniques, the pre-operative scan with a specialized rigid frame clamped to the skull allowed creation of coordinates using specially designed software and guidance of specialized minimally invasive hardware via the frame to biopsy lesions in the brain thus minimizing damage to surrounding structures. This technology was developed further using binocular infrared cameras with instruments and pointers capable of being tracked by the 3D camera integrated with software to match pre-operative CT images with real-time position of tracked instruments. The first orthopaedic applications of this technology were in spinal surgery (Jenny 2006). These technologies provide the basis for currently used orthopaedic navigation systems. In general they can be divided into image-based and image-free.

2.6.2 Image-based navigation

Image based navigation in orthopaedics is a direct adaptation of the technology discussed above where intra-operative guidance of tools marked with specific trackers is based on data acquired prior to surgery, usually from CT scan. Other imaging modalities may also be used, including intra-operative fluoroscopy (Reinhold et al., 2008). Image based technology remains popular in spinal and cranial surgery, however image-free technology remains the main method used in computer assisted orthopaedic surgery.

2.6.3 Image-free navigation

This method was first developed for reconstruction of the anterior cruciate ligament (Dessenne et al., 1995). Reference markers were placed on the femur and tibia followed by anatomical localization of the proximal and distal attachments of the ligament using a pointer. This allowed optimisation of the relative position of the femoral and tibial channel to minimize complications from impingement and inappropriate tensioning of the ligament (Jenny 2006), initial comparison study suggested that this technique enhanced results in terms of reducing variability in graft positioning (Klos et al., 1998).

This concept was more thoroughly developed for application in total knee arthroplasty (Delp et al., 1998). Image-free navigation in total knee arthroplasty uses reference markers invasively attached to the femur and tibia involves placement of invasive trackers in the femur and tibia. The hip, knee and ankle centres are determined by a combination of prescribed limb movements from which the software determines the joint centres from analysing the kinematic data, and use of a pointer used to identify anatomical landmarks. The mechanical alignment of the lower limb can then be determined. Initial randomised controlled trial demonstrated the technology to be as precise and accurate as conventional methods performed by an expert surgeon (Saragaglia et al., 2001). Further studies on this technology will be discussed later in this section.

2.6.4 Tracker types

Various types of tracker are available with corresponding locator systems. Broadly, electromagnetic and infrared (IR) are available, with IR being subdivided into active and passive. Active IR trackers are powered, emit light and require power cable or batteries. Passive trackers consist of a specific configuration of rigid body with mounted with spheres lined with reflective material (Fig. 7). The reflective material presenting in a specific configuration is recognised by the localiser. Experiments demonstrate acceptable levels of precision and accuracy using the various types of commercially available trackers and localisers for purposes of surgery (Wiles et al., 2004; Elfring et al., 2010; Rudolph et al., 2010). Passive trackers are becoming more widely used in the surgical setting. Trackers are mounted onto the femur and tibia via the bone screws and tracker mounting (Fig. 7). A further tracker is mounted onto a specifically engineered pointer or probe (Fig. 8). This device has a specific geometry, the position of the pointer tip relative to the rigid body specified for use on the pointer can be detected by the localiser to an accuracy within 1mm (Picard 2007).

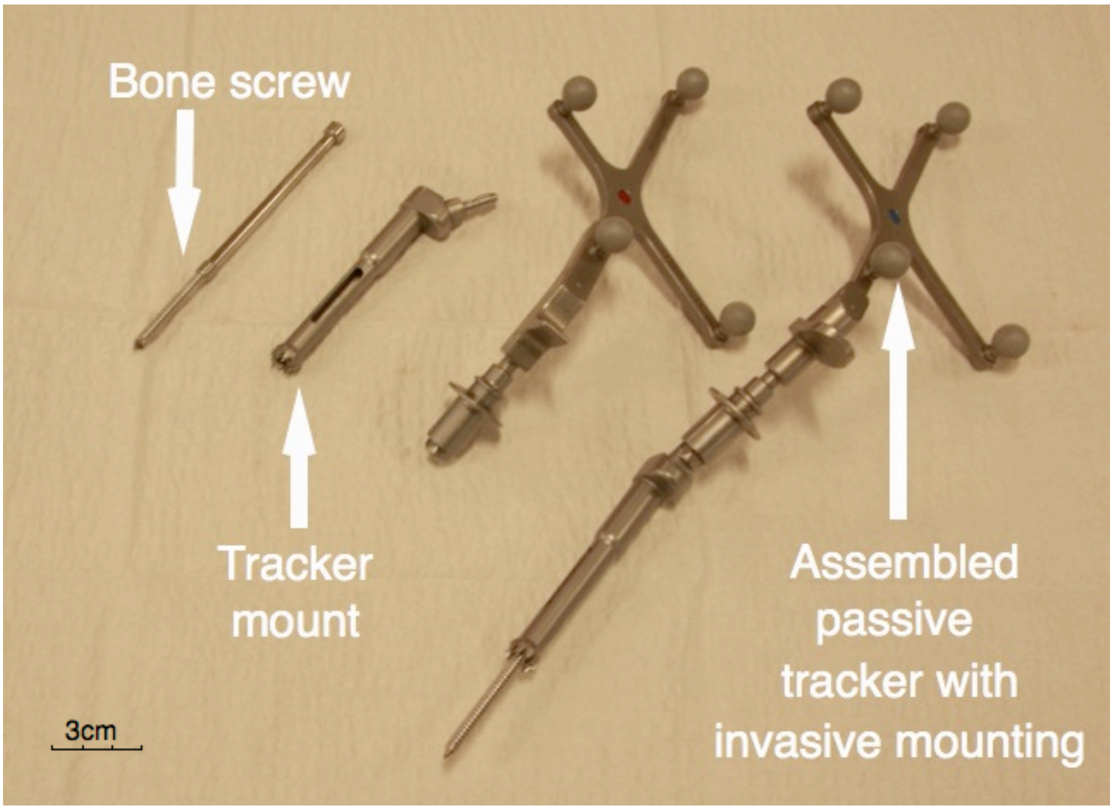

Figure 7- Components of invasive optical tracker mounting.
Components of invasive method of passive tracker mounting, with an assembled passive tracker on invasive mounting. The four spheres on each passive tracker are lined with highly reflective material.

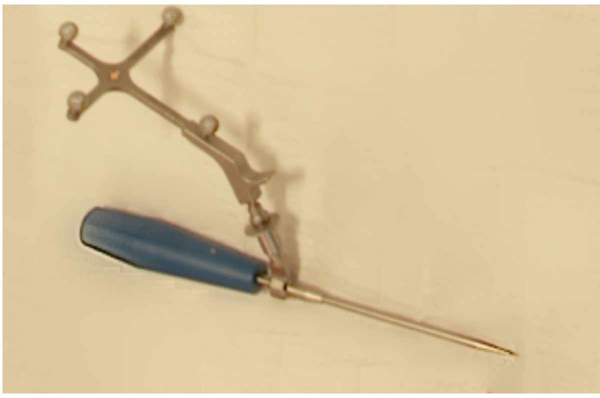

Figure 8 – Hand-held pointer

The hand-held pointer is used to register location of anatomical landmarks, note rigid body with reflective spheres attached (Fig. 8).

2.6.5 Localiser

The localising device (Fig. 9) uses a binocular IR camera and emits IR light from the area surrounding the lens. Passive trackers reflect this light from the reflective spheres (Figs 7 & 8) allowing the localiser to detect their position in three-dimensions using both lenses.

The line of sight must not be obstructed during use. Electromagnetic tracker precision and accuracy is affected by metal implements used during the operative procedure (Glossop 2009).

Figure 9 – Localiser of optical trackers.
Localiser: A – binocular camera, B – touchscreen, C – computer, D – foot pedal.

2.6.6 Computer

The computer (Fig. 9) is linked to remote control via foot pedal and touchscreen (Fig. 9). The foot pedal is critical in allowing the operator to remain free to use their hands during a surgical or experimental procedure. The computer processes information from the localising camera and instructs the user and / or relays kinematic data in real time via the touchscreen or display screen. The computer uses software designed to be used with all of the above purpose specific hardware and uses algorithms to determine lower limb kinematics.

2.6.7 Validation

The image-free concept has been developed and thoroughly validated to allow acquisition mechanical alignment of the lower limb using kinematic data acquired during registration (Picard 2007). Technically, CAS localizing and tracking systems can repeatedly measure a point with precision and accuracy of <1mm & <1˚ (Wiles et al., 2004; Picard 2007; Rudolph et al., 2010). The majority of error comes from human input and misuse; care must be taken especially during registration to maximise accuracy of output data (Amanatullah et al., 2013). This highlights two separate areas in which CAS systems must be validated; technical and clinical (DiGioia et al., 2005). Typically, manufacturers validate CAS subsystems and evaluate end-to-end validity of the device for use. Concerns have been raised over the number of systems available and proposals were made to create standardised testing and reporting of precision and accuracy. As yet this has not been established. In the independent laboratory setting, Pearle et al. (2007) demonstrated very high correlation between output from a computer navigation system and validated robot senor in reporting multiplanar knee motion in 6 cadaveric lower limbs. In the clinical setting, computer navigation has been demonstrated to allow the surgeon to reliably place components within an optimum range of coronal and sagittal alignment and axial rotation, as measured following surgery by CT scanning in multiple large studies (Sparmann et al., 2003; Bathis et al., 2004; Stockl et al., 2004; Matziolis et al., 2007; Czurda et al., 2010; Kim et al., 2012). These data provide the main clinical evidence supporting clinical use of CAS systems (DiGioia et al., 2005). Martin et al. (2006) prospectively performed total knee replacement on 22 patients using an image-free CAS system and 22 with a CT-based CAS system. Radiographic outcomes including mechanical alignment, tibial slope, femoral and proximal alignment angle were similar between the two types of system.

2.6.8 Role in total knee replacement

2.6.8.1 CAS and implant coronal and sagittal alignment

Following registration the surgeon uses the navigation system output which provides lower limb mechanical alignment, flexion of the knee, bony resection measurements and can help position arthroplasty components according to pre-operative planning aims (DiGola et al., 2004). This is one of the primary objectives of CAS, to maxmise the ability of the surgeon to fulfill the pre-operative plan and maxmise implant longevity. The 'optimum' range for lower limb mechanical alignment has been reported as neutral mechanical axis +/- 3°; this is achieved in approximately 75% of cases using conventional instrumentation (Mahaluxmivala et al., 2001; Bathis et al., 2004). Alignment out with the range of +/- 3° has been associated with increased early asceptic loosening. (Jeffery et al., 1991; Berend et al., 2004)

CAS has been shown to improve post-operative mechanical alignment. Bathis et al. (2004), prospectively studied 160 consecutive patients and randomised them between conventional and CAS TKR. 96% of the CAS group demonstrated post-operative lower limb alignment within 3° of neutral compared to 78% of the conventional group; this was a significant difference. These findings have been confirmed by similar studies (Sparmann et al., 2003; Matziolis et al., 2007; Mullaji et al., 2007). Meta-analyses on this topic concur that CAS reduces outliers in mechanical alignment +/-3° from neutral mechanical alignment (Bauwens et al., 2007; Mason et al., 2007; Brin et al., 2011).

2.6.8.2 CAS and component rotation

Component rotation is important in total knee arthroplasty; Bell et al. (2012) found excessive internal rotation of both the femoral and tibial components was linked to increased pain following total knee arthroplasty. Malrotation affects flexion stability, tibial, femoral and patellofemoral kinematics and alignment in flexion (Feeley et al., 2009; Glossop 2009; Victor 2009; Lutzner et al., 2010; Merican et al., 2011)

Limited evidence exists to demonstrate that CAS improves rotational alignment of the tibial and femoral components. Kim et al. (2012) demonstrated a marginal improvement in consistency of femoral rotation with CAS compared to conventional surgery. Czurda et al. (2010) reported a case control study with 123 patients having had image-free CAS versus 207 conventional total knee replacements that no significant difference was found in terms of component rotation however malrotation of the femoral component ≥3˚ in either group was associated with post-operative pain. Stockl et al. (2004) found use of CAS improved femoral rotation and flexion angle of the femoral component in a prospective study of 64 patients using computer tomography. Tibial component rotation remains variable with and without the use of CAS (Siston et al., 2006).

High quality prospective randomised controlled trials confirm CAS improves alignment in the coronal and sagittal plane, but not in axial rotation. (Matziolis et al., 2007; Barrett et al., 2011; Cheng et al., 2011). Meta-analysis looking specifically at image-free CAS including 29 quasi-randomised and randomised controlled trials and 11 prospective comparative studies demonstrated improved mechanical alignment with CAS but no difference in component rotation (Cheng et al., 2012).

2.6.8.3 CAS and soft tissue balancing

Before the knee can be balanced, it is important to quantify coronal laxity of the normal and pathological knee. Okazaki et al. (2006) analysed coronal laxity in 50 (34 male) normal knees from a Japanese population at 10˚ flexion. Mean age 25.9y (SD ± 7.5y, range 19-59y). A 15kg force was applied and radiograph taken. Mean varus laxity was 4.9˚ with varus stress and 2.4˚ with valgus stress. A similar study by Heesterbeek et al. (2008) examining 30 healthy knees in a slightly older Caucasian population (15 male, mean age 62y, SD ± 6.4, range not given, authors invited participants aged 50-75y) used a 15Nm load in extension. They reported a mean valgus laxity of 2.3˚, and varus laxity of 2.8˚. Comparisons are difficult as force application is not the same in each study as well as differences in study population.

The ability to quantify mechanical alignment during surgery allows the surgeon to categorise extent of deformity. Furthermore, following application of varus/valgus stress, the surgeon can differentiate between those knees which can be corrected to neutral alignment, and those which require more extensive soft-tissue release to eliminate deformity. Algorithms have been devised to standardise intra-operative soft-tissue management (Picard et al., 2007; Unitt et al., 2008; Hakki et al., 2009; Jenny 2010; Lehnen et al., 2011; Aunan et al., 2012; Moon et al., 2013). Collateral ligament release is performed if the knee cannot be corrected manually to 0˚ mechanical alignment. Rates of release vary in these studies with the procedure being performed in 11 – 25% of cases. This is an evolving area in the understanding of total knee replacement surgery. Unfortunately, studies to date do not use standardised force application in measuring the envelope of varus/valgus laxity and establishing whether deformity is correctable. It is therefore difficult to draw comparative conclusions from these studies. Authors have suggested that achieving neutral alignment with an envelope of 3˚ varus/valgus tilt on manual stress in extension ought to be the target in balancing knee soft tissues (Unitt et al., 2008). Again, it is difficult to adopt these values to current surgical practice owing to lack of standardised force application during intra-operative assessment.

2.6.8.4 CAS and implant survivorship

Survivorship of the implants is a major outcome in joint replacement. CAS technology does not have a long enough track record to date to allow analysis of its impact on long-term (15 – 20 year) survivorship in cohorts of meaningful quantity. Schnurr et al. (2012) reported reduced asceptic loosening and revision rates using CAS compared with conventional instrumentation, however this was an uncontrolled retrospective series. From the prospective trials currently collecting follow-up data, no difference in medium term survivorship has been identified, however these authors acknowledge further follow-up is required before conclusions can be made (Konyves et al., 2010; Kim et al., 2012). In a study from South-Korea, Kim, Park and Kim (2012) reported results of 452 female and 68 male patients following bilateral knee replacements. One knee was performed using computer navigation, the other using conventional instrumentation. The Kaplan-Meier survivorship with revision as the end point at 10.8 years was 98.8% (95% CI, 0.96 to 1.00) in the computer-navigated total knee arthroplasty group and 99.2% (95% CI, 0.96 to 1.00) in the conventional total knee arthroplasty group. Also of note, the authors found no difference in clinical function or alignment.

Norwegian arthroplasty register data actually indicated an increase in early revision when using a specific design of implant with CAS. The cause for this has not been identified on further analysis and is still being investigated at the time of writing this manuscript (Gothesen et al., 2011).

2.6.8.5 Functional outcomes in CAS and conventional knee arthroplasty

Very few studies have demonstrated an improvement in patient reported outcomes following knee arthroplasty using CAS. There is no evidence of poorer function following surgery using CAS technology. However, as is the case with implant survival and time to revision, longer term follow up of the larger high quality randomised controlled trials will be required until conclusions can be made.

A retrospective study by Ek et al (2008) of two matched cohorts consisting of 50 patients who underwent computer assisted and 50 underwent conventional total knee replacement found significant improvement in overall KSS (CAS group: 164±67, conventional: 106±43, p 0.002) and physical component of the physical component of the Short Form-12 score (CAS group: 41±9, conventional: 37± 8), as well as improved component and limb alignment in the CAS group. A prospective cohort study by Lehnen et al (2011) found a significant improvement in functional outcome scoring (WOMAC & KSS scores) at 12 months when comparing computer-assisted total knee replacement with conventional technique. Although the authors mention a significantly lower BMI in the CAS cohort, they did not purely study the difference between CAS and conventional surgery, as the CAS group also underwent a specialized protocol for soft-tissue tensioning, gap balancing and tissue release using a spring loaded tension sensor. This intervention may be responsible for the difference in clinical outcome. Outcomes such as mechanical alignment are not documented. The potential for bias in this study is significant due to lack of randomisation, especially when it is impossible to blind the operating surgeon to which surgical procedure is being carried out. Patients were not blinded to treatment type, nor is it clear whether the research nurse scoring the patients at one year was blinded to treatment type. Short to medium term randomised controlled trials mentioned above found no difference in patient outcome. (Czurda et al., 2010; Schmitt et al., 2011; Kim et al., 2012). Reporting medium term follow-up of 1040 knees at a mean of 10.8 years, Kim, Park and Kim (2012) found no statistically significant difference in total knee scores, knee function scores, pain scores, WOMAC scores, knee motion, and activity.

Hoffart, Langenstein and Vasak (2012) hypothesised that CAS would give a superior clinical outcome at every stage over five years of follow-up and on analysis of their results concluded that a significantly better outcome in terms of mean KSS, function and knee score was observed. The authors randomised 195 knees to CAS (n=97) and conventional (n=98). At five years they retained 62% of patients and reported improved total knee society score (KSS) in the CAS group as well as further separating this scoring system down further into it’s components (Lingard et al., 2001): ‘knee score’ and ‘function score’ to detect superior results from the CAS group. They conclude that at five-year follow-up, marginal linear model analysis gave significantly better mean ‘knee’ and ‘function’ components of the KSS score in the CAS group, however the pain component of the KSS indicated no significant difference. These figures are not quantified in the paper. Model-based results were used to analyse the effect of time on scores: ‘pain’ and ‘knee’ score components of the KSS remained constant over time and a statistically significant difference is stated between the CAS and conventional groups. For pain, this difference equates to 2 of a maximum possible 50 points. ‘Knee’ score, of which the pain score makes up 50%, the CAS group was a mean of 3.62 higher out of a possible 100. Total KSS and ‘function’ scores altered with time, with the CAS group having a higher score on immediate discharge, then less difference between the groups over time. Although the absolute score values are not given, graphs provided in the paper indicate that CAS patients had a better KSS and ‘function’ score of approximately five points at five years. To put these mean differences in context, whilst the statistical tests may convey a significant difference, the maximum possible score for KSS is 200 and 100 for ‘knee score’, which is a component of the KSS. Intervals between grades of function on the scoring system are 10 points apart. Although statistically significant, these are unlikely to represent a significant clinical difference.

The authors conclude that the difference in function cannot be attributed to improved alignment, as no difference in alignment was detected using radiographs. They state that the improved KSS scores may be attributed to improved component rotation. However, the methodology of this study mentions that in the CAS group, only the femoral component was placed using navigation, and component rotation was not measured at follow-up. Further, more robust study is needed before the statements made in this study can be affirmed or refuted. At present no other studies indicate improved function using CAS for total knee replacement.

In terms of biomechanical function, Smith et al. (2012) analysed well matched groups from a double-blinded, prospective RCT including 102 CAS and 98 conventional knee arthroplasty patients using flexible electrogoniometry during a range of activities of daily living. They found significant improvements in level and slope gait cycle and pre-swing phase in the CAS group, however they conclude these differences are unlikely to affect patient activity levels and functional ability.

2.6.8.6 Role in collateral ligament reconstruction

Computer navigation systems are not currently routinely used in the diagnosis, surgical management or follow-up of collateral ligament injuries. Feeley et al. (2009) used a computer navigation system to demonstrate increased valgus opening and external rotation in grade 3 medial collateral ligament injury in a cadaveric setting, and analyse reconstruction techniques using CAS based biomechanical testing on cadavers following simulated reconstruction. CAS systems can provide objective measurement of mechanical alignment and quantify knee laxity, ideally under controlled loading; this has application in diagnosis, intra-operative and post-operative assessment. Commercial systems used in the clinical setting are currently limited to intra-operative use due to the requirement for invasive tracker placement.

2.6.8.7 Role in cruciate ligament reconstruction

Using CAS, two types of measurement are possible whilst measuring flexion angle; tibial rotation and anteroposterior translation. These variables can be sought individually by performing tests such as the Lachman test for anteroposterior translation, or simple tibial rotation to quantify range of rotation. It is also possible to combine measurements and measure rate of rotation during more complex maneuvers such as the pivot shift test (Koh 2005; Lopomo et al., 2010; Colombet et al., 2012). Motion analysis of this test has demonstrated poor inter-tester reliability, once again owing to a lack of standardized forces and technique (Noyes et al., 1991). CAS technology does allow tracking of multiplanar movements and the rate at which movements take place. Lane et al. (2008) performed 24 examinations under anaesthetic with navigation to track movement during pivot shift test. A characteristic P shaped motion was created by the system tracking during pivot shift. This angle of P provided a means of characterising the point of tibial reduction in relation to it's motion path in the sagittal plane prior to reduction. They found a high correlation between clinical grading of pivot shift and angle of P (R^2=0.97). Moderately good correlation was found between clinical grade of pivot shift and tibial rotation (R^2=0.77), and maximum anterior tibial translation (R^2=0.87). The authors concluded that CAS used intraoperatively could facilitate evaluation of anterior cruciate reconstruction.

Whilst non-invasive systems are still in development, CAS remains limited to intra-operative use as invasive placement of trackers is required. Pre-operative examination and grading of anteroposterior laxity correlates very strongly with intra-operative laxity values using CAS (Yamamoto et al., 2010). Intra-operative use of CAS has been demonstrated to provide quantitative data on pre and post-operative kinematic parameters relevant to anterior cruciate ligament reconstruction in a precise and accurate manner (Zaffagnini et al., 2006; Martelli et al., 2007; Bignozzi et al., 2010). One of the most important developments in use of CAS to evaluate cruciate reconstruction has been in demonstrating the advantages of double bundle technique in reducing rotational laxity and restoring kinematics (Plaweski et al., 2011; Lee et al., 2012). Although no obvious functional benefit of anterior cruciate ligament reconstruction using CAS has been demonstrated to date, tunnel placement is more consistent using CAS (Hart et al., 2008). Long-term comparison data between reconstruction with and without CAS is not available at the time of writing.

2.6.9 Conclusion

The evidence to justify either CAS or conventional instrumentation as superior in use for routine arthroplasty is still far from fully formed, mostly owing to the lack of long-term follow-up to date. It is not entirely clear at present whether any benefit in function or survivorship can be gleaned in the short or medium term using technology that exists at present as highlighted by recent meta-analysis (Xie et al., 2012). Further technical and technological development in CAS and analysis of current randomised controlled trials in years to come may indicate whether the demonstrated reduction in alignment outliers improves long-term function and time to revision. There are a number of instances where navigation continues to be very useful and superior to total knee arthroplasty using conventional instrumentation; for example in post-traumatic deformity and cases where conventional instrumentation is difficult owing to congenital or acquired deformity (Fehring et al., 2006).

2.6.10 Non-invasive image-free navigation

The main obvious obstacle to non-invasive quantification of limb kinematics is that soft-tissues displace independently of the underlying bony anatomy to some extent during active or passive movement of the limb creating artefacts when using methods of surface mounted tracking. Soft-tissue artefacts are a well-recognised and thoroughly researched area preventing measurement of bony displacement and therefore limb kinematics. Radiological quantification can overcome this but is limited by consequences of ionising radiation to the patient and where this is not the case, such as with magnetic resonance imaging, very few specialised devices exist to allow dynamic scanning.

Stagni et al. (2005) studied two subjects with implanted total knee replacements, combining three dimensional fluoroscopy and radiostereometric analysis to analyse multi-planar bony displacement relative to skin mounted markers during active lower limb movement. Standard deviation of skin marker movement relative to bony anatomy was up to 31mm in the thigh and 21mm in the lower leg. Kuo et al. (2011) expanded a similar methodology to 10 subjects and again found significant soft tissue artefact in the thigh, more than the lower leg, which was also significant in flexion, extension and internal rotation of the tibia. Soft-tissue artefacts were greatest toward the end of range. A study by Benoit et al. (2006) using intra-cortical pins in direct comparison to skin mounted trackers also concluded that skin mounted trackers are not representative of underlying bony movement. Development of systems that can use surface mounted tracking to represent the underlying bony anatomy is an area of on-going research.

The KneeKG system has been developed extensively from early attempts to reduce soft-tissue artefacts by fixing tracking devices, initially magnetic, to a form of exoskeleton. Initial attempts (Sati et al., 1996) led to refinement of the device (Ganjikia et al., 2000). Ganjikia et al (2000) compared this exoskeleton device to markers placed directly on the skin by analysing displacement relative to that of the bony anatomy by fluoroscopy, concluding that the device reduced three-dimensional displacement error by a factor of six in four out of the five of the subjects tested. In vivo analysis demonstrates good reproducibility of results (Hagemeister et al., 2005; Labbe et al., 2008). Hagemeister et al. (2005) demonstrated repeatability of tibial rotation of 0.4˚ - 0.8˚ and 0.8mm – 2.2mm for anteroposterior translation. These kinematic measurements were obtained while the subject waked on a treadmill and do not refer to any form of clinical testing, nor is there any comparative method of measurement to determine accuracy of this device in vivo. Sudhoff et al. (2007) analysed the stability of three separate methods of optical tracker attachment concluding by way of radiographic analysis following 50 gait cycles that the KneeKG system was the most stable, and that all systems were relatively poor at controlling stability in the transverse plane. No further literature is available on the KneeKG and the system has not been adopted for further clinical or biomechanical use at the time of writing. It should also be noted that throughout its development, slight variations of the tracker attachment and mounting system have been used (Ganjikia et al., 2000; Hagemeister et al., 2005; Sudhoff et al., 2007; Labbe et al., 2008).

Clarke (2012) developed a method of attaching active optical trackers to the lower limb using fabric strapping and a baseplate. This method was compared to flexible electrogoniometry to quantify knee flexion angle (Clarke et al, 2012a). Between extension and 100˚ flexion at 1˚ increments, discrepancy between the systems was ± 1˚. A validated force application device (FAD) was used to apply a force of 18Nm. Three clinicians performing six examinations to determine the MFTA whilst applying quantified varus and valgus stress on 1 volunteer gave a standard deviation ≤1.1˚ for each clinician. Values of MFTA obtained across the examinations varied by 1˚. Further work by the group (Clarke et al., 2012b) using this non-invasive device on 30 volunteers, performing two registrations and during each registration, MFTA was measured supine, with coronal stress, and standing. Repeatability of measuring MFTA within one registration episode was ± 1˚, with a 0.5˚ loss of repeatability following coronal stress manoeuvres and 0.2˚ following stance. Between registrations, sagittal alignment limits of agreement were within ± 2.3, for coronal lower limb mechanical alignment, limits of agreement ±1.6˚. Varus and valgus stress measurements agreed to within ± 1.3˚ and ± 1.1˚ respectively. Force application was not standardised during testing. When standing, sagittal and coronal alignment limits of agreement between volunteers was ± 5.0˚ and 2.9˚ respectively, the authors suggest this may have reflected variation in gait between episodes of stance.

Clarke went on to test patients with osteoarthritis to ensure the method would work on subjects with knee symptoms, potentially higher BMI and poorer soft-tissue elasticity. Although a force application device had been developed, volunteer testing demonstrated that a single clinician could reproduce ± 1˚ repeatability when performing varus / valgus stress manoeuvres, a value which is within limits of precision of the non-invasive tracking system. It was decided not to use the force application device to save time. The non-invasive method was compared to intra-operative, invasive measurements using bone screws and long leg radiographs taken before and after surgery.

The non-invasive method displayed satisfactory inter-registration agreement measuring MFTA pre and postoperatively; limits of agreement ≤1.8˚ measuring MFTA, for sagittal alignment, ≤4.4˚. Mean difference and standard deviation in measurement of MFTA using the non-invasive system and intra-operative invasive system was 0.5˚ (SD±2.8˚) for the pre-operative comparison and 0.5˚ (SD±1.4˚) for the post-operative comparison. For sagittal alignment testing these values were -5.2 (SD±4.3˚) and -7.2˚ (SD±4.7˚) respectively. Applying a varus stress, mean difference between pre and intra-operative measurements; -1.5˚ (SD±2.4˚), and post-operative invasive and non-invasive comparison; 0.3˚ (SD±1.4˚). Applying a valgus stress, pre and intraoperative mean difference; 1.6˚ (SD±1.6˚), following procedure mean difference 0.9˚ (SD±1.3˚).

Pre-operative non-invasive standing alignment differed from long leg radiographs with a mean difference of 1.8˚ (SD±4.1˚), post-operative non-invasive standing alignment and long leg radiograph differed even more with a mean difference of 2.9˚ (SD±3.3˚). Interestingly, supine intraoperative invasive pre and post procedure measurements of MFTA were compared more favourably with pre and post op long leg radiographs showing mean difference of 0.2 (SD±3.7˚) prior to total knee replacement and 0.6˚ (SD±2.7˚) after total knee replacement. The main drawbacks in the methodologies used include no direct comparison for the non-invasive system with a known 'gold standard'. As highlighted previously, electrogoniometers and long leg radiographs suffer from inherent error, limiting their use as a comparator. Furthermore, comparing non-invasive measurements with those obtained intra-operatively is limited by the influence of anaesthesia, presence of arthrotomy and therefore lack of filled joint capsule intra-operatively and most likely a significant swelling six weeks following surgery with presence of acute inflammatory fluid and tissue. The author acknowledges these points highlighting that the aim in the patient cohort was not to test reliability of the device as this had been covered by earlier work (Clarke et al., 2012b); rather to standardise a method of pre and post-operative assessment which correlated sufficiently with intra-operative findings.

As such, no direct comparison has been carried out between non-invasive and invasive methods of optical tracker fixation.

At the time of writing, preliminary evidence is available indicating that ultrasound based mapping of bone could allow both visualisation of landmarks and mapping of joint position if used in concert with navigation based technology (Tretbar et al., 2002; Wang et al., 2005; Keppler et al., 2007; Swiatek-Najwer et al., 2008; Krysztoforski et al., 2011; Masson-Sibut et al., 2012). At present this technology is still being developed prior to clinical trial, however combining imaging modalities which confer minimal consequence to the patient with technology capable of three-dimensional position capture is an obvious and exciting next step to refine acquisition of bony anatomy in the lower limb in a non-invasive manner.

2.6.11 Summary

Establishing the 'normal' static and dynamic alignment of the lower limb is an area of ongoing research (Tang et al., 2000; Bellemans et al., 2012; Nicolella et al., 2012; Orishimo et al., 2012; Whatman et al., 2012), with authors noting ethnic variance (Tang et al., 2000) and questioning what is 'normal' mechanical alignment (Bellemans et al., 2012). Bellemans et al. (2012) revealed that 32% of males and 17% of females from a cohort of 250 young adults had varus alignment of ≥3˚ measured on long-leg standing radiographs. Non-invasive, non-radiological methods of determining MFTA both in supine and weight-bearing conditions (Clarke et al., 2012) may help determine variation in 'normal' alignment, whether this relates to development of osteoarthritis (Hunter et al., 2007) and evaluating current aims in restoring neutral versus 'constitutional' alignment in total knee arthroplasty (Bellemans 2011; Lombardi et al., 2011). Controversy also exists with regard to the recommendation that final alignment of the lower limb following total knee replacement to within +/-3° of neutral (Mahaluxmivala et al., 2001; Bathis et al., 2004) affects clinical outcome (Matziolis et al., 2010) or survivorship (Parratte et al., 2010). These studies are based on static measurements of MFTA. A method allowing dynamic assessment of MFTA in the early functional range may help in establishing the relationships between final mechanical alignment, function and survivorship in total knee arthroplasty.

The ability to develop a standardised method of coronal knee laxity quantification which is available in the out-patient setting prior to surgery would be a major advance in operative planning, and allow further development of soft-tissue balancing algorithms based on the presence of deformity and whether this is fixed, or correctable (Luring et al., 2005; Briard et al., 2007; Claus et al., 2007; Hakki et al., 2009; Mihalko et al., 2009; Heesterbeek et al., 2010). This technology would also be of use in sports injury. As mentioned previously, current assessment of knee collateral ligament injury relies on subjective clinical examination and stress-radiographs (LaPrade et al., 2008; Laprade et al., 2010; LaPrade et al., 2010). Despite numerous innovations to measure kinematics of the knee in a clinical setting, no non-invasive instruments have been developed which are capable of conveying parameters quantifiable by intra-operative navigation technology with the precision and accuracy required for surgical planning. Quantification of lower limb MFTA on dynamic weight bearing and clinical examination would aid diagnosis, surgical planning, follow-up and research evaluating treatment modalities.

Soft-tissue artefacts remain the barrier to development of systems that are feasible for clinical use. The parameters of lower limb sagittal and coronal alignment, anteroposterior translation of the tibia and tibial rotation are all very important in establishing normal and pathological kinematics; they are routinely used for purposes of diagnosis, and in evaluation of treatment modalities. At present, there are numerous separate methods of estimating these parameters, with mixed reliability. Most frequently, clinical examination and various radiological methods are used with the problems of reproducibility and lack of dynamic assessment whilst quantifying alignment. Literature concerning the use of non-invasive devices to measure lower limb kinematics as discussed above has revealed the importance of determining precision of new devices in a robust manner, and determining to what extent they agree with a validated method of measurement prior to performing any in vitro or in vivo population study, comparative anatomical analysis and certainly diagnostic testing and treatment evaluation.

Recent adaptation of image-free navigation technology to quantify mechanical alignment with and without coronal stress has been validated in early flexion only (Clarke et al., 2012). The non-invasive method can be used to measure other kinematic parameters such as MFTA in flexion, sagittal alignment, anteroposterior translation of the tibia and tibial rotation; however no such validation is reported in the literature. This technique uses similar frames of reference to those used in intra-operative navigation. The software workflow is based on validated software currently used during computer-assisted high tibial osteotomy and anterior cruciate ligament reconstruction. Should the non-invasive method prove valid, it would allow for the first time direct matching of dynamic, non-ionising pre or postoperative kinematic assessment and intraoperative evaluation, especially if concurrent methods of force application could be used in both the out-patient and surgical setting. Surgeons are already familiar with this type of technology, and should the method prove reliable, it could be used to quantify variety of important kinematic parameters with powerful application in diagnosis and operative planning in a manner directly related to intra-operative computer assisted measurement. The device would also be of use in research in evaluating treatment methods, and progress knowledge of kinematics of the knee in health and disease, as well as establishing differences between genders, age groups and different ethnic groups.

Preoperative non-invasive kinematic assessment could also overcome the disadvantages inherent to using intraoperative navigation based measurements to guide soft-tissue algorithms including: un-quantified influences of anaesthesia, non-standardised passive examination forces with the patient supine and non-weight / non-physiological load bearing, and the unknown effect of arthrotomy on alignment and laxity measurements. Parameters such as mechanical alignment in flexion, tibial anteroposterior translation and rotation have not been tested using this non-invasive method.

Non-invasive attachment of optical trackers and their movement relative and representative of the bony anatomy of the lower limb is an area of on-going research (Sudhoff et al., 2007; Lustig et al., 2012). Various materials have been proposed for attachment of non-invasive trackers including fabric strapping which has been validated (Clarke 2012; Clarke et al. 2012a, 2012b), and rubber strapping (Stulberg et al., 2002). Rubber strapping has the advantage of being less expensive allowing new strapping to be used on each subject. Fabric strapping may be more expensive and may have to be used on multiple individuals which has implications for infection control in a clinical setting (Department of Health Estates & Facilities Division 2007; Shuman et al., 2012).

Image-free navigation technology has been thoroughly validated in measurement of the kinematic parameters of interest. This involves invasive placement of optical trackers. Direct comparison of this method with the proposed non-invasive method is feasible in the in-vitro setting only provided all attempts are made to maintain integrity of the bony and soft-tissue anatomy, thus replicate kinematics of the knee in vivo as closely as possible. Developers of image-free navigation technology have from the outset sought to "establish a reliable and direct link between pre-operative planning and the process of surgery" (Picard 2007). The non-invasive method of image-free acquisition of lower limb kinematics could provide discrete parameters used for pre-operative planning, intra-operative processes and post-operative assessment and evaluation of practices. Validation of the non-invasive method has been carried out in early flexion measuring coronal and sagittal alignment of the lower limb. The method has not been validated to date measuring anteroposterior translation or rotation. Determining the validity of the non-invasive method of image-free navigation measuring all of these parameters throughout knee flexion would progress current knowledge in methods of quantifying of knee kinematics.

2.7 Aim

The primary aim of this pilot study was to determine the validity of using a non-invasive system based on image-free navigation technology as described by Clarke et al. (2012a, 2012b) in measuring a variety of kinematic parameters of the knee throughout flexion. Specifically, this method was to be directly compared in a cadaveric setting with a validated and commonly used intra-operative computer navigation system in terms of repeatability and agreement when measuring: MFTA, tibial anteroposterior translation and rotation throughout flexion, as well as maximum flexion and extension.

The secondary aim was to compare proposed methods of non-invasive tracker attachment; firstly using a previously validated fabric strap (Clarke, 2012), then using a rubber strap.

2.8 Materials and methods

6 embalmed cadaveric knees from 4 cadaveric specimens were selected for the pilot study. Average age of specimens was 77.8 years (range 57 – 90 years), 2 were female. Selection of the embalmed knees was based on finding those with the most range of motion. Embalmed cadaveric knees are inherently stiff, however for the pilot study, they were deemed appropriate as the experiment protocol would need to be refined prior to using more valuable fresh specimens should the method prove reliable. All specimens were free from signs of previous dissection or surgery to the pelvis and lower limbs.

An image-free OrthoPilot navigation system (B. Braun Aesculap, Tuttlingen, Germany) was used with passive optical trackers. Experimental software based on algorithms from ‘KneeSuite High Tibial Osteotomy’ and ‘KneeSuite ACL’ was used for the experiments. The software was named ‘PhysioPilot v1.0’. This software has not been validated for use with non-invasive (strap-mounted) tracker fixation, however the algorithms are used in the ‘KneeSuite’ software, designed for use during surgery using invasive (bone screw mounted) optical trackers. The software is therefore validated for use with the invasive hardware.

2.8.1 Experiment Protocol

The registration process was carried out with the cadaver intact and supine. The specimen number, date of testing, which side of the body was being tested and sex of the specimen were recorded. The optical camera was positioned 1.9m meters from the specimen. This could be measured using a setup screen at the beginning of testing. The specimen table and Orthopilot wheels were locked. Temperature of the laboratory was consistent throughout the testing process. The specimens were not refrigerated or used for any other purpose between testing sessions. The test limb was put through 24 cycles of hip circumduction, followed by knee and ankle flexion and extension to minimise tissue creep during the experiment.

A 3cm incision was made down to bone 12cm proximal to the proximal pole of the patella just medial to the anterior midline. Tissues were gently separated around the bone and a hole drilled beginning with the drill bit 30˚ toward the midline of the specimen. This angle was to compensate for the backward tilt of the passive tracker, maximising the profile of the passive tracker facing the camera

A 3cm incision was made 7cm distal to the tibial tuberosity followed by clearance of the soft and periosteal tissues and again the drill bit, again angling the drill bit 30˚ medially for the reason described above.

The bone screw secured tracker mountings were assembled and trackers fitted. Care was taken to ensure the reflective tracker ball lining was intact and clean. The bone screws were then inserted through both cortices and trackers attached (Fig. 10)

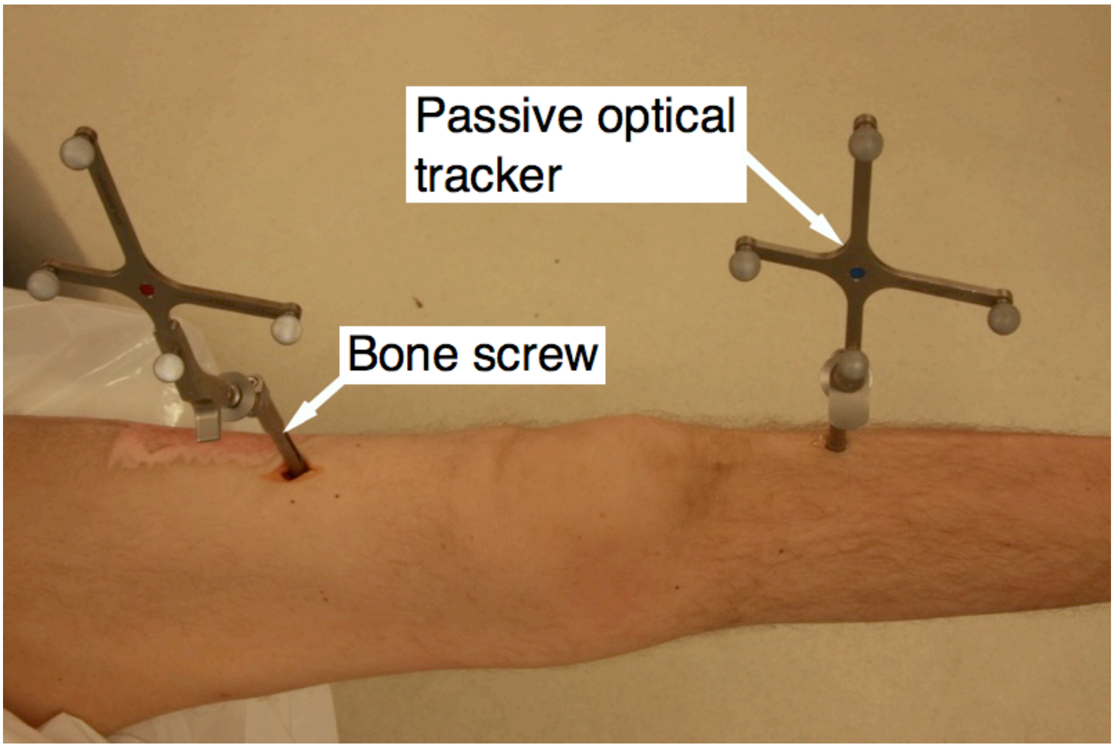

Figure 10 - Position of bone screws with optical trackers mounted.

Registration screens prompted specific movements to allow recognition of each joint centre. Failing to perform complete or smooth motions resulted in a failure to register the limb. This is less difficult in a cadaveric specimen than a living subject. Hip registration involves maintaining the pelvis absolutely still while circumducting the limb smoothly through 360˚, this was always performed in a clockwise direction.

The knee registration included marking the position of the medial and lateral epicondyles with the leg in extension and, on the next screen tool, the centre of the patella using the pointer mounted with a passive tracker but with the knee flexed to 90˚. The next screen prompt involved putting the knee through its entire range of motion. Range of motion was limited with the embalmed cadavers owing to stiffness however enough data could be gathered for registration in each case. Ankle joint registration involved marking position of the most medial and lateral points on the malleoli, followed by the midpoint between these two using a further screen tool. The final screen prompted full internal and external rotation of the tibia. This is an identical procedure to that which would be followed during intra-operative registration of a lower limb. Care was taken to identify the bony landmarks (medial and lateral epicondyles and malleoli), as these positions were the basis for marking the centre of patella and ankle respectively. To minimise error in the experiment protocol, pinpoint skin incisions were made over all of the bony landmarks required for registration, with a permanent marker used to highlight the position of this small incision. The incision was not made down to bone, but sufficient enough for the end of the pointer to rest in a consistent position during repeated registrations, maximising consistency in the limb registration data.

Limb alignment was recorded in extension. Throughout the entire study, valgus limb alignment was recorded as positive and varus as negative (e.g. Fig. 11 screenshot: 2˚ varus = '-2°').

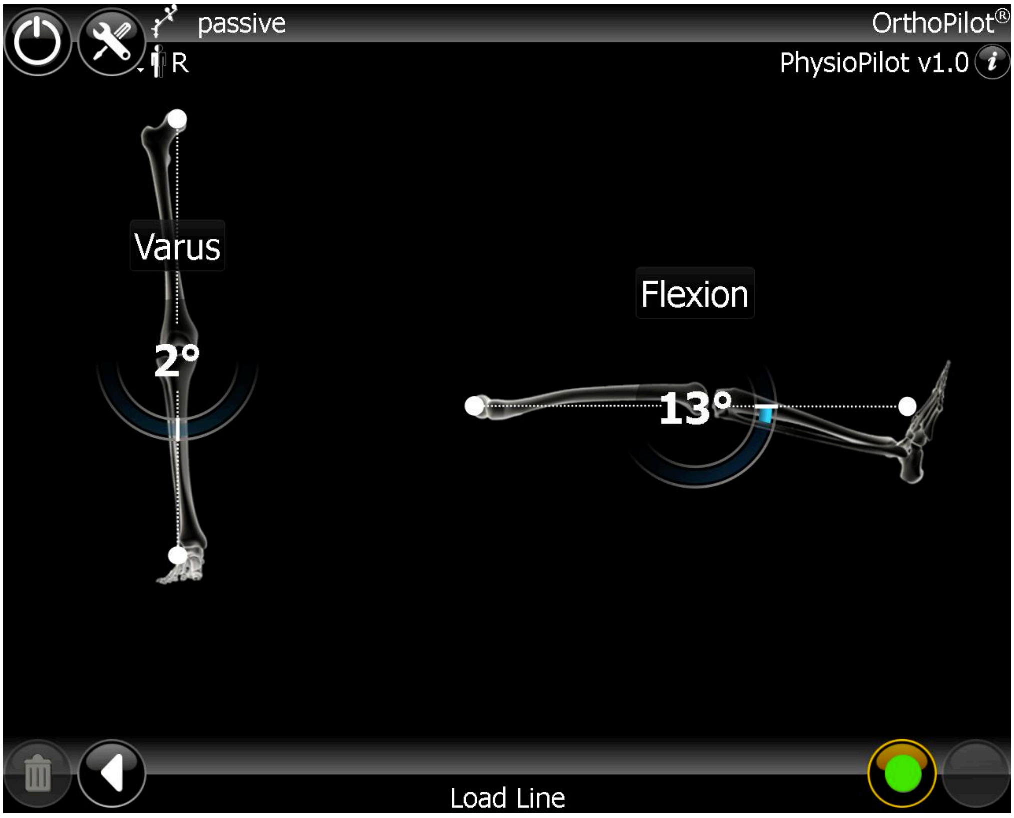

Figure 11 - Screenshot displaying MFTA (˚) (left) and knee flexion angle (˚) (right).

A series of recording screens were then available. For the first invasive (bone screw tracker mounting) registration, MFTA was recorded on paper and the entire registration process repeated using the same invasive tracker mountings. Once 2 registrations recorded MFTA within 2˚, recording commenced. The investigator was not blinded to readings during this experiment.

MFTA was recorded in maximum knee extension. The knee was then stabilized in a manner similar to clinical examination with one hand supporting the posterior knee, and the other used to produce a varus/valgus moment on the distal tibia. The MFTA was recorded with valgus and varus stress applied to the knee using the 'Load Line' screen. This process was carried out in full extension, and at 10˚ intervals from 30˚ - 60 of knee flexion. 30˚ of flexion was selected to account for flexion deformity of some of the embalmed cadavers. 60˚ flexion was selected as during the gait cycle the knee does not generally exceed 60˚ flexion (Roda et al., 2012). One specimen had a maximum mean flexion of 58.8°, not reaching 60°.

To record anteroposterior translation of the tibia, a further screen option was selected and the knee was placed in the required flexion angle (Fig.12). With one hand to support the thigh, the proximal tibia was pulled anteriorly in a manner similar to clinical examination (Lachman test).

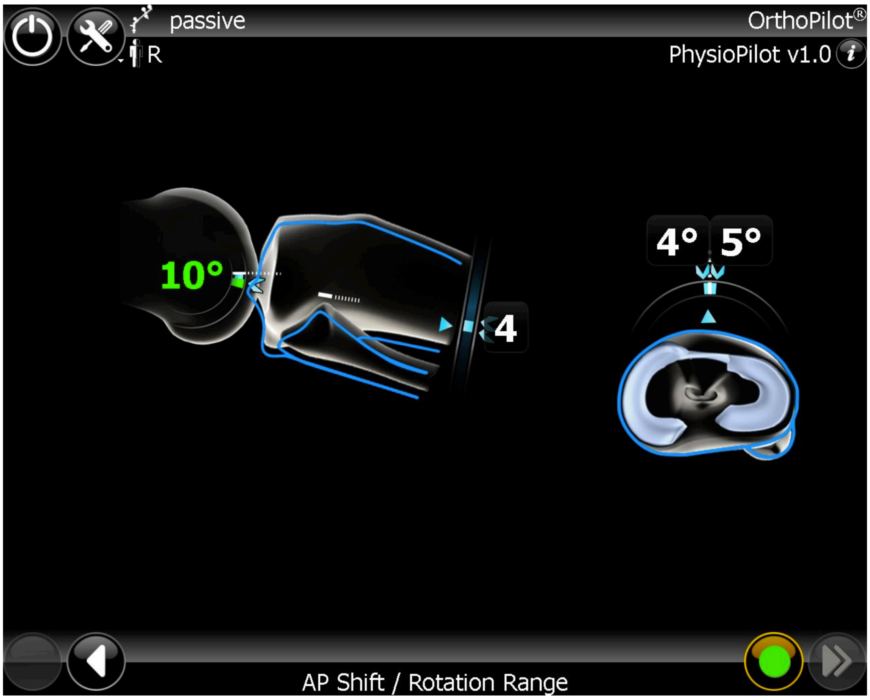

Figure 12 - Screenshot showing knee flexion angle (˚), anteroposterior translation of the tibia (mm) and internal & external rotation (˚)

Following this, the knee flexion angle was maintained while full internal and external rotation of the tibia were carried out (Fig. 12).

Maximum achievable flexion angle was recorded (Fig. 13).

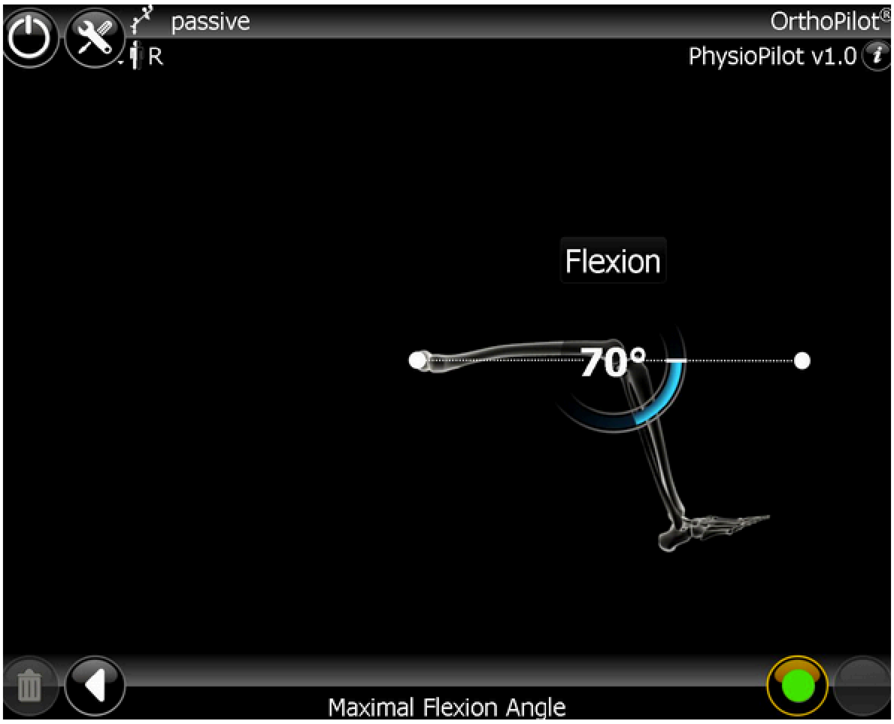

Figure 13 - Screenshot of maximum flexion angle (˚)

Three separate methods of tracker fixation were used: standard bone screws, a previously untested rubber strap securing a standard baseplate, and fabric strap securing the baseplate (Fig. 14). The fabric strap and baseplate used in this study had been validated previously (Clarke, 2012). This fabric strap (542, E&E Accessories, UK) was made of elastic webbing, was broader (45mm) and less elastic than the rubber strap. The non-invasive trackers were secured 8cm proximal to the proximal pole of patella overlying the distal vastus medialis obliquus muscle, and 4cm distal to the tibial tuberosity, again on the medial aspect of the lower limb to maximise tracker exposure to the camera (Fig. 14). Registration was then carried out as described above.

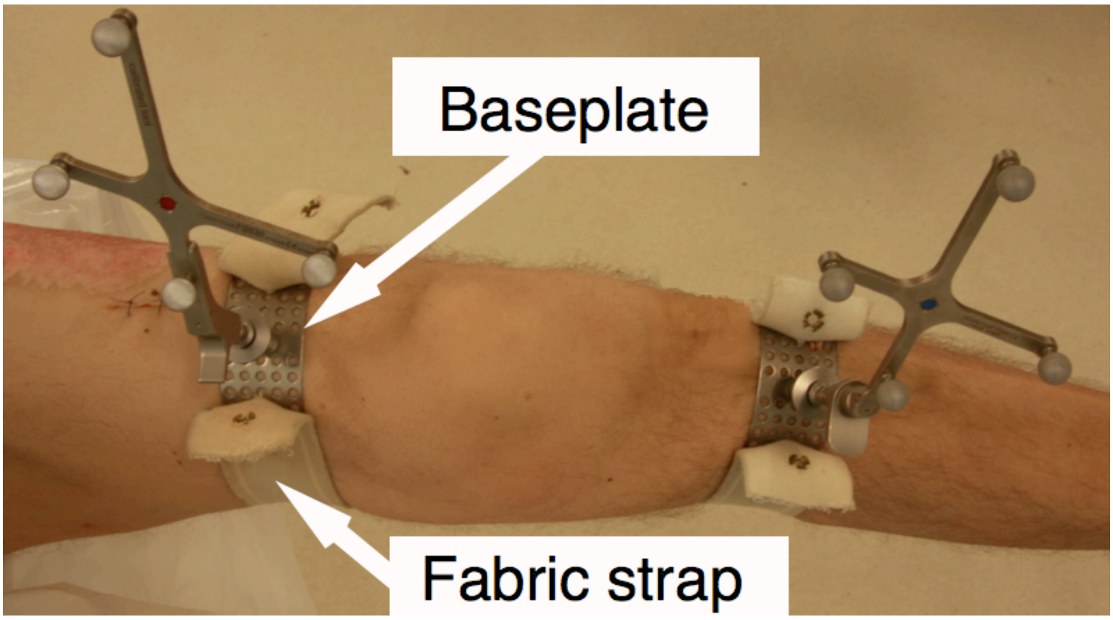

Figure 14 - Positioning of non-invasive fabric strapping, identical positioning was used for rubber strapping

Several runs of the protocol were performed on a specimen unsuitable for the experiment due to stiffness. This highlighted any problems with the protocol and reduced the effect of learning curve.

The experiment protocol was repeated four times on each of the six knee specimens with each type of tracker mounting (bone screws, rubber strapping and fabric strapping. Between each run of the protocol the non-invasive trackers were taken off, relocated and a new registration performed. Separate registrations when using the invasive method of tracker fixation did not include relocation of the bone screws.

This created 72 separate episodes of registration. During each of these, 25 data points were recorded. The protocol design allowed analysis of the effect of knee flexion and type of tracker mounting on repeatability as four values were obtained with all independent variables of degrees of knee flexion, tracker mounting and knee specimen remaining constant. The only change between these four points was a new system registration to minimise potential random error from a single erroneous registration (Taylor 1997).

2.9 Statistical Methods

Calculation of intraclass correlation coefficient (ICC) was performed using IBM SPSS® Statistics 17.0 software (IBM Corp., Armonk, NY, USA), all other simple calculations were performed using Microsoft Excel® (Microsoft Corp, Redmond, Washington, USA) Reliability within each method of tracker fixation used in measuring MFT (°), tibial rotation (°) and tibial translation (mm) was analysed by calculating ICC. (Shrout and Fleiss 1979). A coefficient of 0.75 demonstrates good reliability (Fleiss 1981; Portney and Watkins 1993). Repeatability coefficient was calculated to demonstrate repeatability between test – retest measurements within each method of tracker fixation (Bland and Altman 1986). The 4 recorded data points with all variables constant across the 6 specimens were divided into 2 pairs (test 1 & 2, test 3 & 4) to allow calculation. The repeatability coefficient defines interval within which 95% of test – retest differences lie, i.e. within 2 standard deviations of the test - retest differences (Bland and Altman 1986). Image free navigation systems have been demonstrated to have accuracy within 1˚ (Haaker et al., 2005) and 1mm (Stockl et al., 2004).

A repeatability coefficient of ≤2° (i.e. ± 1°), therefore demonstrates excellent precision. In the clinical setting, MFTA following total knee replacement out with the range of +/- 3°

has been associated with increased early asceptic loosening (Jeffery et al., 1991; Berend et al., 2004). The value of +/- 3˚ has become a widely used reference for comparing results of alignment when using conventional and computer assisted methods in performing total knee replacement surgery (Mahaluxmivala, Bankes et al. 2001; Bathis, Perlick et al. 2004). It is therefore critical that the device be able to measure MTFA precisely within this range. A repeatability coefficient of 3°conveys that 95% of all measurements are within a range of +/-1.5°.

With regard to translation of the tibia on the femur during cruciate ligament testing, mechanical devices such as the KT 1000 are accepted as demonstrating cruciate insufficiency if anterior tibiofemoral translation is ≥3mm compared to the contralateral (normal) knee during dichotomous testing (Arneja and Leith 2009). We therefore accept a repeatability coefficient of ≤3mm as demonstrating clinically relevant precision. Again, a repeatability coefficient of 3mm conveys that 95% of all measurements are within a range of +/-1.5mm.

To compare reliability of measurements between invasive and the two non-invasive methods of tracker mounting, ICC was calculated. Bland-Altman plots were generated as a visual representation of the limits of agreement. In calculating standard deviation of the differences, the 95% limits of agreement, calculated using the corrected standard deviation of the differences (SD_c) as described by Bland and Altman (Bland and Altman 1986), (mean difference +/- 1.96 SD_c), were calculated to analyse agreement between the invasive and two non-invasive methods of tracker fixation. Acceptable limits of agreement were once again set at 3° for measurements of MFTA, and 3mm for AP translation. No reference is available in the literature for acceptable limits of agreement regarding measurement of tibial rotation. Most systems measure within the limits of +/- 10˚, however this is a general estimate of systems discussed in section 2.5.7. Results will be discussed in the context of previously reported findings.

2.10 Results

Each specimen exhibited a degree of fixed flexion deformity when measured using the invasive method. Mean fixed flexion for the six specimens was 12.8° (range 5° - 18°). Mean maximum flexion using invasive trackers was 68.2° (range 58° - 95°). All measurements of maximum flexion using invasive trackers for specimen 1 were 58°, therefore we could not measure kinematics at 60° knee flexion in this specimen.

2.10.1 Reliability measuring MFTA

Table 2 – ICC measuring MFTA in all conditions of coronal stress (pilot study).

	Measuring MFTA no applied stress		
	ICC each method of tracker fixation		
	Bone screw	Fabric strap	Rubber strap
Mean	0.877	0.928	0.811
Range	0.801 - 0.991	0.891 - 0.963	0.166 - 0.982
	Valgus stress		
Mean	0.903	0.920	0.631
Range	0.784 - 0.963	0.839 - 0.988	-0.456 – 0.995
	Varus stress		
Mean	0.852	0.898	0.631
Range	0.757 - 0.957	0.822 - 0.98	-0.218 - 0.917

Measurements taken in all conditions of flexion and coronal stress displayed very good reliability (ICC ≥0.75) when using bone screws and fabric strapping (Table 2). Rubber strapping did not display acceptable reliability with coronal stress applied. Throughout the series of results, 95% confidence intervals have been examined for the ICCs calculated for every single condition and are included in the appendix (Appendix 8.1).

2.10.2 Repeatability measuring MFTA

The graphs in figures 15 - 17 demonstrate the effect of flexion with no stress, and varus/valgus stress on precision by displaying the repeatability coefficient in conditions of flexion and coronal stress.

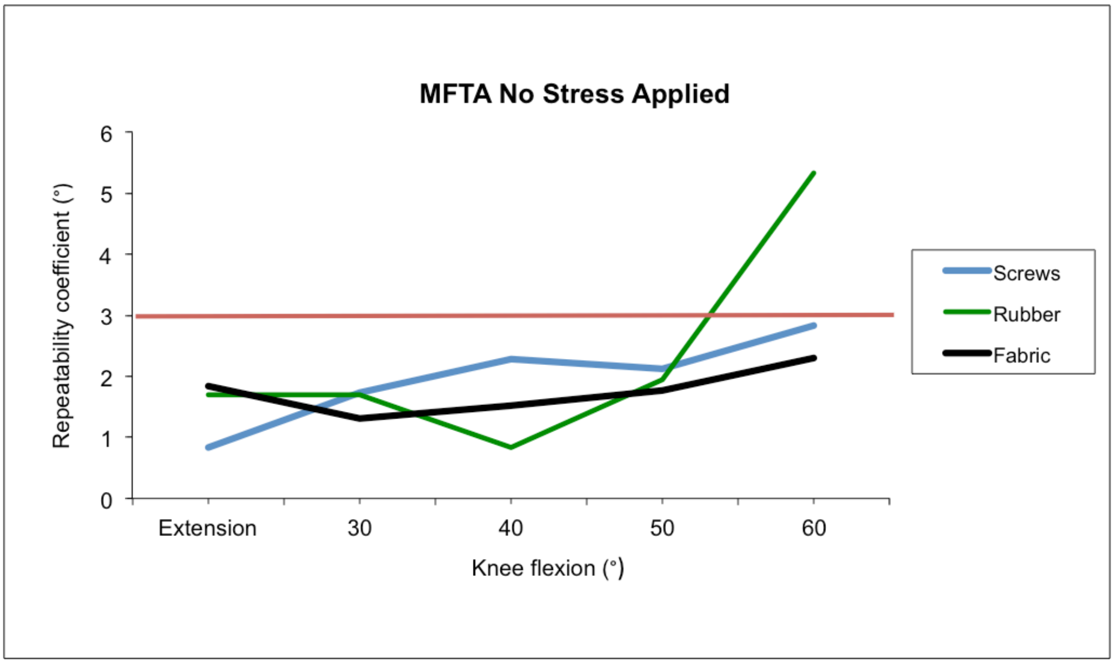

Figure 15 – Repeatability measuring MFTA with no stress (pilot study). Repeatability coefficient at each 10º interval of knee flexion for all three methods of tracker mounting (bone screws, rubber strapping and fabric strapping). Repeatability acceptable (<3º, indicated by red line) throughout flexion for bone screws and fabric strapping. Unacceptable for rubber strapping beyond 50º.

When measuring MFTA with no stresses applied to the limb, bone screw fixation and fabric strapping display very similar and satisfactory levels of repeatability throughout flexion, rubber strapping becomes unacceptable beyond 50˚ flexion (Fig.15).

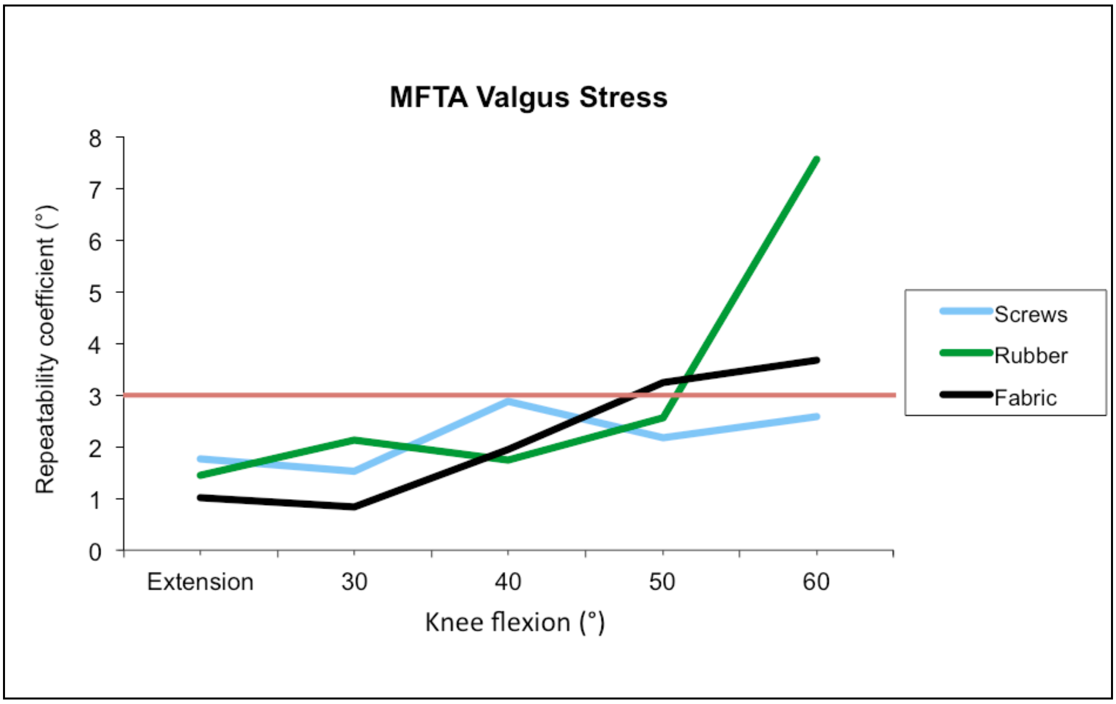

Figure 16 – Repeatability measuring MFTA with valgus stress (pilot study).
Repeatability measuring MFTA and applying valgus stress resulted in repeatability coefficient of >3º when flexing the knee beyond 40º when using fabric strapping and flexing beyond 50º when using rubber strapping. Bone screw fixation of trackers resulted in satisfactory repeatability throughout.

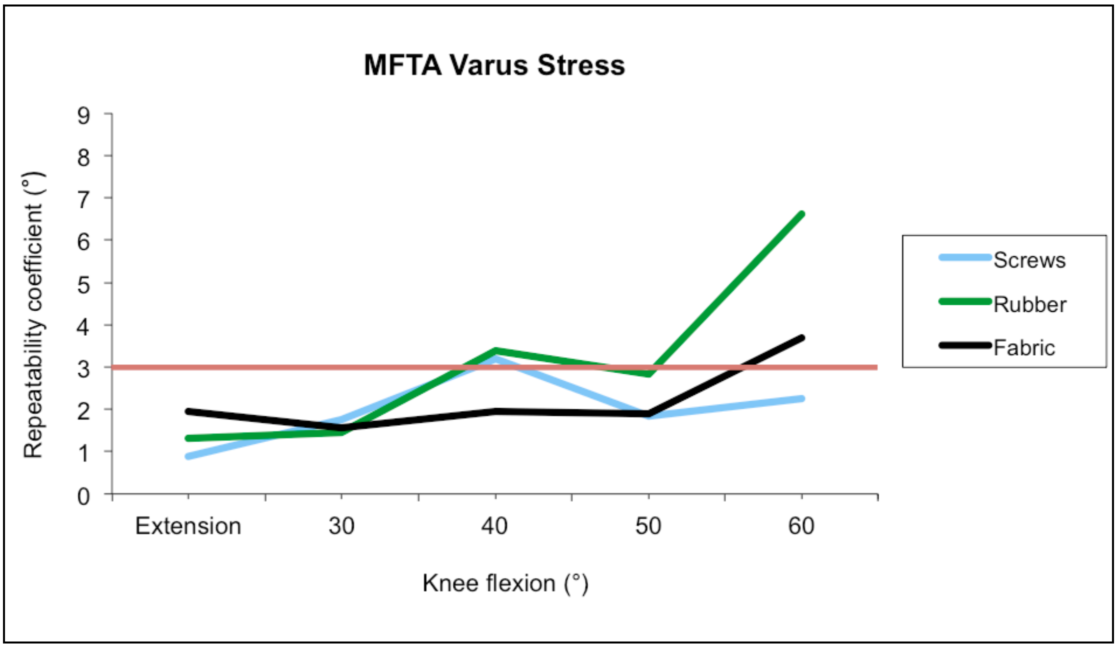

Figure 17 – Repeatability measuring MFTA with varus stress (pilot study).
Repeatability measuring MFTA and applying varus stress was again worsened by flexion. Fabric strapping remained acceptable until >50º knee flexion, rubber strapping until 30º knee flexion. Bone screw fixation gave a repeatability coefficient of 3.1º at 40º knee flexion, then remained acceptable.

When applying varus/valgus stress to the lower limb (Figs. 16 & 17), fabric strapping displays unacceptable repeatability beyond 50˚ flexion. Interestingly, bone screw fixation displayed borderline repeatability at 40˚ knee flexion. Rubber strapping performed generally worse, especially with varus stress and high flexion. Flexion appears to decrease repeatability of measurement of MFTA regardless of tracker fixation method and application of coronal stress (Figs 15-17). Bone screw fixation gives consistently repeatable measurements apart from the aforementioned episode at 40˚, which will be discussed.

2.10.3 Agreement measuring MFTA

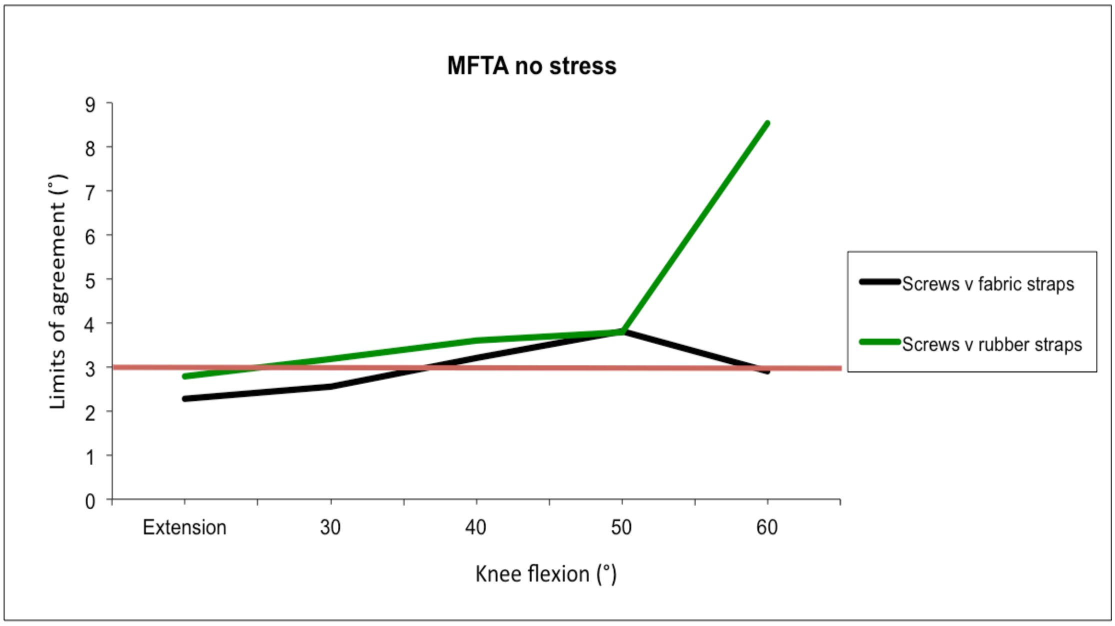

Figure 18 – Agreement measuring MFTA with no applied stress (pilot study).
Limits of agreement between screws and fabric (green) & screws and rubber strapping (black). Fabric strapping displays acceptable agreement from extension to 30˚ flexion, at which point rubber strapping displays unacceptable agreement.

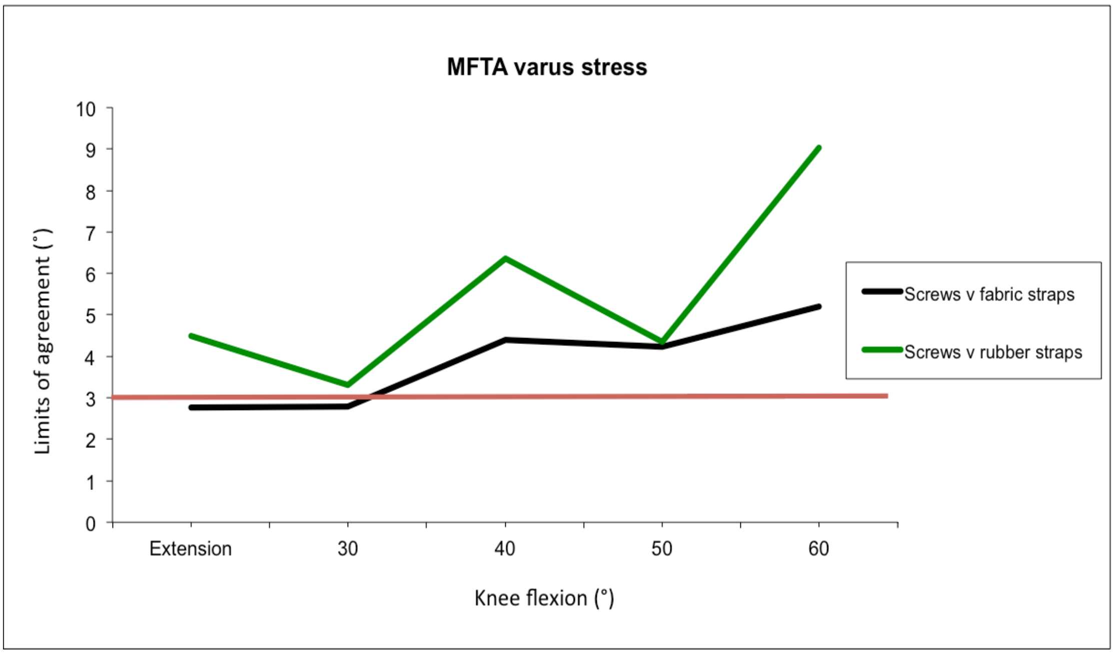

Figure 19 – Agreement measuring MFTA with varus stress (pilot study)
Limits of agreement when applying a varus stress; fabric straps display acceptable agreement from extension to 30˚ flexion. Rubber strapping is unacceptable throughout.

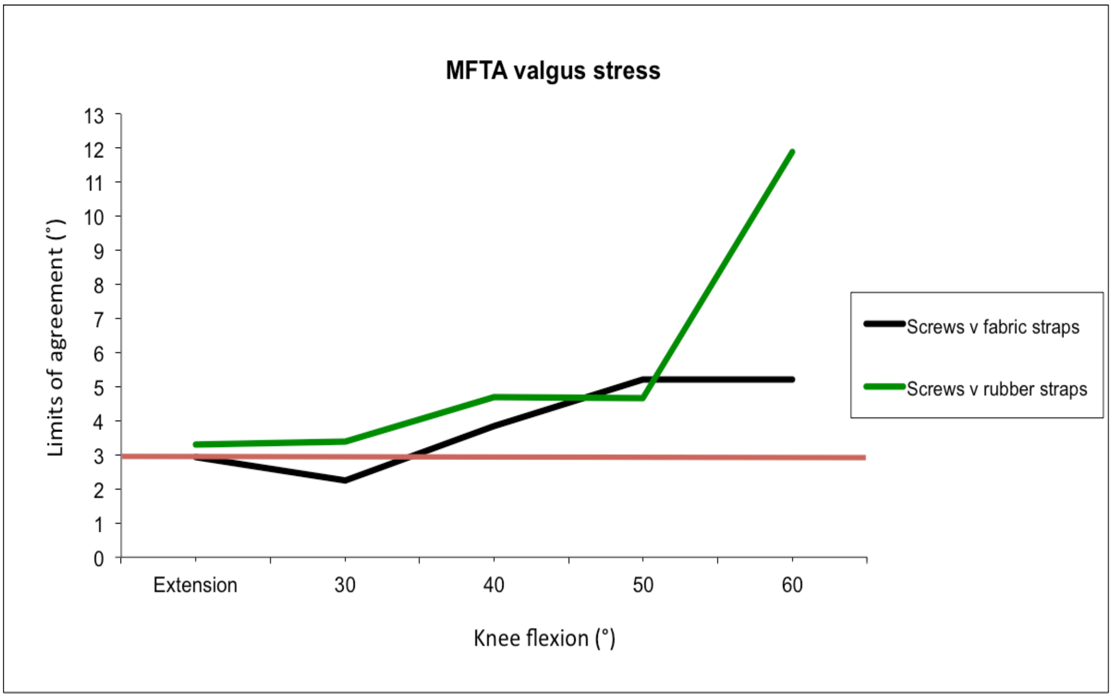

Figure 20 – agreement measuring MFTA with valgus stress (pilot study)
Limits of agreement applying a valgus stress; again fabric strapping displays acceptable agreement from extension to 30˚ flexion, rubber strapping is unacceptable throughout.

Agreement between invasive and non-invasive methods of tracker fixation, both fabric strapping and rubber strapping when measuring MFTA worsens with increasing knee flexion (Figs. 18-20). With no stress applied to the limb and both varus and valgus stress, fabric strapping agrees sufficiently with bone screw fixation in extension and 30˚ knee flexion (Figs. 18-20), beyond which agreement is unacceptable. Measurements taken using rubber strapping fixation do not sufficiently agree with invasive tracker fixation apart from in extension with no stress applied to the lower limb.

2.10.4 Reliability measuring anteroposterior translation

Table 3 – ICCs measuring anteroposterior translation (pilot study)

	Anteroposterior translation		
	ICC each method of tracker fixation		
	Bone screw	Fabric strap	Rubber strap
Mean	0.747	0.852	0.720
Range	0.435 - 0.966	0.633 - 1	0.566 - 0.943

It was noticed that anteroposterior translation stops being recorded beyond 50˚ of knee flexion. Results from extension to 40˚ will therefore be reported (Table 3). ICCs were acceptable when using optical trackers secured with bone screws and fabric strapping measuring AP translation in extension and at 30˚ of knee flexion (ICC >0.815). At 40˚ knee flexion, ICCs became unacceptable (<0.655). ICCs for measuring AP translation using rubber straps to secure the optical trackers were only acceptable in extension (ICC 0.943). At 30˚ knee flexion and beyond, ICCs became unacceptably low (<0.61). ICC mean with 95% confidence intervals is given in appendix 8.1.

2.10.5 Repeatability measuring anteroposterior translation

Lachman test was performed with the knee in slight flexion (mean 13.6°, range 5° – 21°).

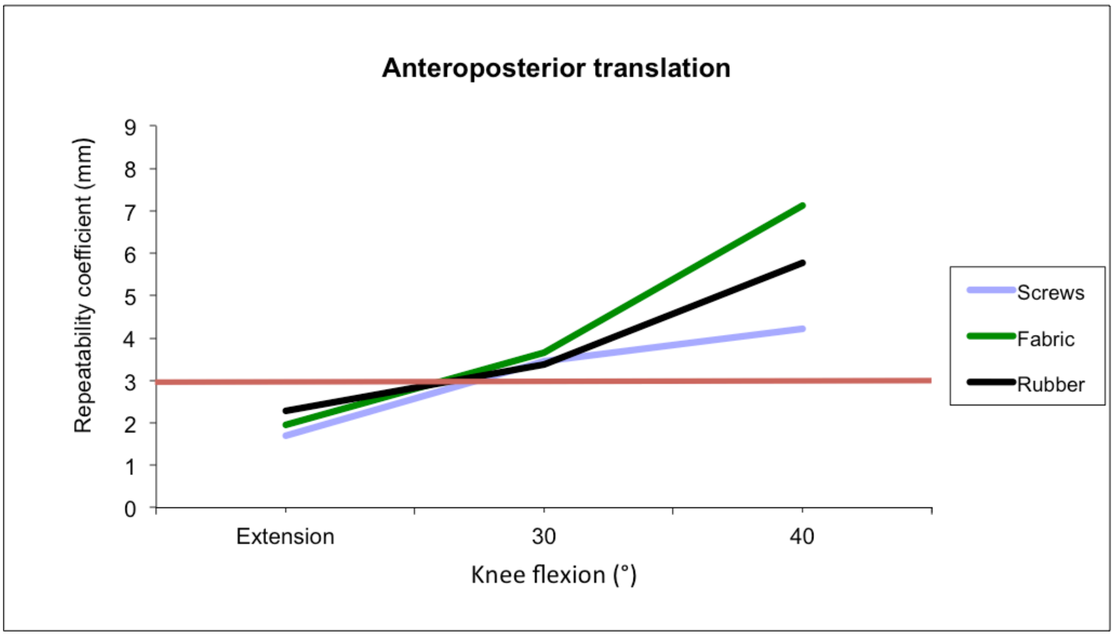

Figure 21 – Repeatability measuring AP translation (pilot study)
Repeatability coefficient at each 10º interval of knee flexion for all three methods of tracker mounting (bone screws, rubber strapping and fabric strapping) measuring anteroposterior tibial translation. Repeatability acceptable (<3mm, indicated by red line) using all methods of fixation in extension, becoming unacceptable ≥30˚ knee flexion. (NB sagittal alignment in extension from invasive measurement of all 6 specimens: mean 13.6°, range 5° – 21°).

When performing manual anteroposterior translation (Fig. 21), all methods of tracker fixation were acceptable in extension giving similar values for repeatability. ≥30˚ knee flexion, all methods became unacceptable.

2.10.6 Agreement measuring anteroposterior translation

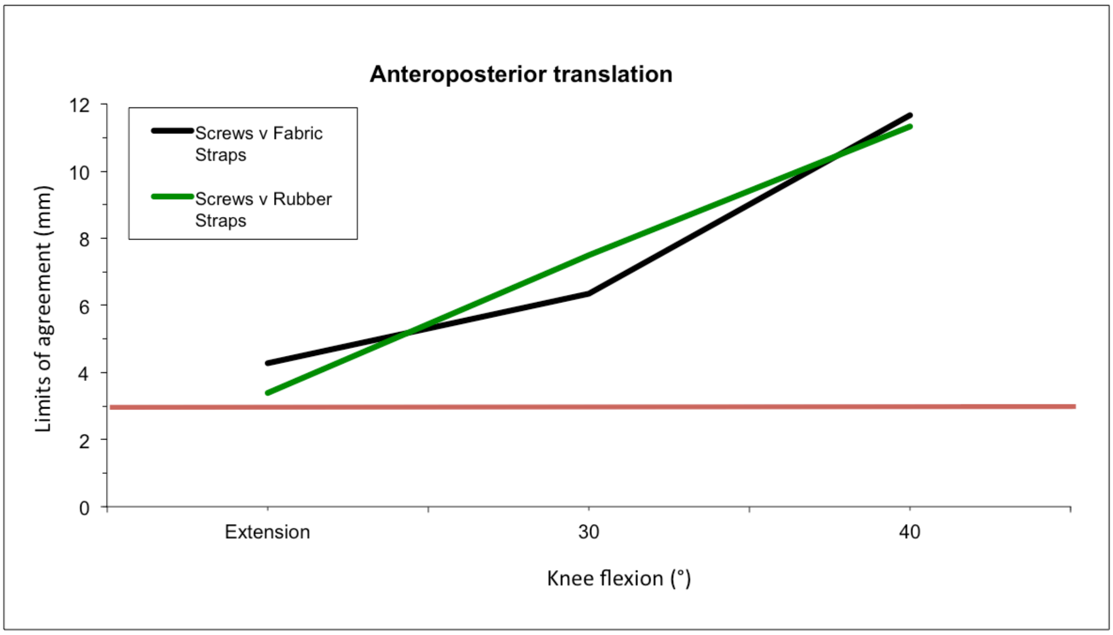

Figure 22 – Agreement measuring AP translation (pilot study)

Measuring anteroposterior translation, neither method of tracker fixation agrees consistently within 3mm with the invasive method (Fig. 22). Flexion worsens agreement from extension to 40˚.

2.10.7 Reliability measuring maximum extension and flexion

Table 4 – ICCs measuring maximum extension and maximum flexion (pilot study).

Measuring maximum extension					
Bone Screws		Fabric Strap		Rubber Strap	
ICC	Range	ICC	Range	ICC	Range
0.989	0.964 - 0.997	0.973	0.91 - 0.992	0.981	0.943 - 0.994
Measuring maximum flexion					
Bone Screws		Fabric Strap		Rubber Strap	
ICC	Range	ICC	Range	ICC	Range
0.994	0.98 - 0.998	0.995	0.981 - 0.998	0.993	0.977 - 0.998

Reliability measuring maximum extension and flexion was very good for all methods of optical tracker fixation (ICCs >0.9) (Table 4). ICC mean with 95% confidence intervals is given in appendix 8.1.

2.10.8 Repeatability measuring maximum flexion and extension

Table 5 - Repeatability coefficient measuring maximum knee extension and flexion (sagittal alignment) using all 3 methods of tracker fixation (pilot study).

Repeatability Coefficient (°)			
	Screws	Rubber	Fabric
Maximum extension	1.3	1.6	2.0
Maximum flexion	2.3	2.5	2.1

Repeatability is acceptable using all methods in measuring sagittal alignment (maximum extension and flexion) (Table 5).

2.10.9 Agreement measuring maximum extension & flexion

Table 6 – Agreement measuring sagittal alignment (pilot study)

Limits of agreement (˚)		
	Screws v fabric straps	Screws v rubber straps
Maximum extension	3.4	3.0
Maximum flexion	3.9	4.7

Agreement when measuring sagittal alignment (full extension and flexion) ranged from 3.0 – 4.7˚ (Table 6).

2.10.10 Reliability measuring internal and external rotation

Table 7 – ICCs measuring internal and external rotation (pilot study).

	Measuring internal rotation		
	ICC each method of tracker fixation		
	Bone screw	Fabric strap	Rubber strap
Mean	0.916	0.912	0.923
Range	0.843 - 0.974	0.865 - 0.962	0.826 - 0.974
	Measuring external rotation		
	ICC each method of tracker fixation		
	Bone screw	Fabric strap	Rubber strap
Mean	0.833	0.891	0.857
Range	0.681 - 0.991	0.679 - 0.981	0.673 - 0.935

Reliability measuring internal rotation was good throughout flexion for all methods of tracker fixation (ICCs > 0.826) (Table 7). Measuring external rotation, reliability was good (ICCs >0.855) from extension to 50˚ flexion apart from measurements taken using bone screw fixation at 30˚ knee flexion (ICC 0.715). At 60˚ knee flexion, ICCs were unacceptable using all methods of optical tracker fixation (ICCs <0.681). ICC mean and range given in appendix 8.1.

2.10.11 Repeatability measuring internal & external rotation

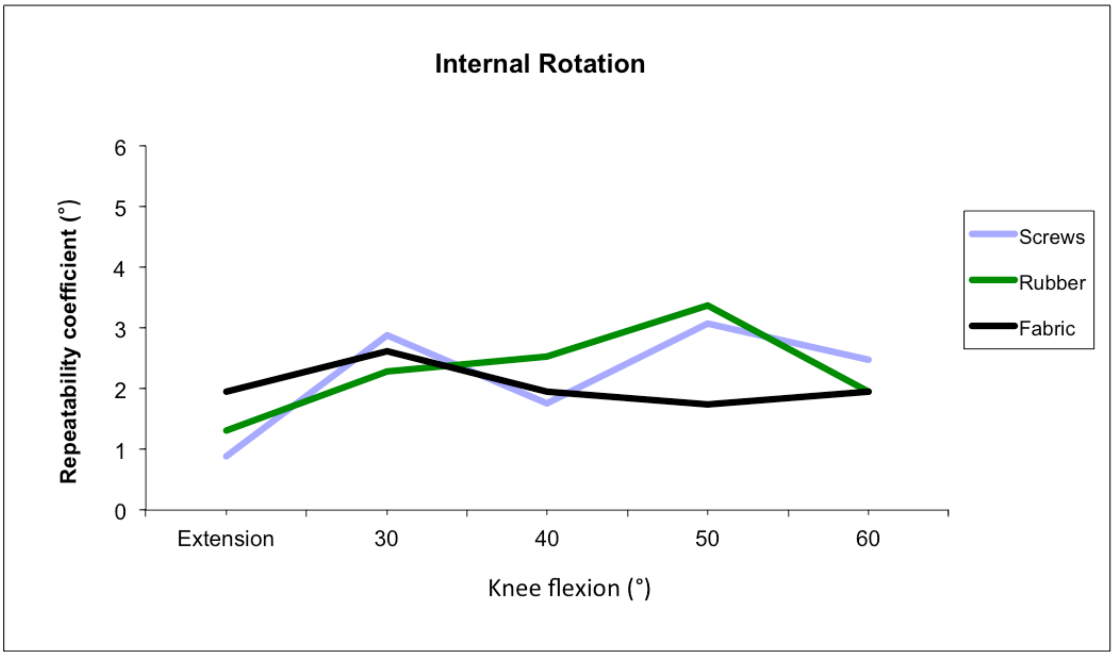

Figure 23 – Repeatability measuring internal rotation (pilot study)
Repeatability coefficient at each 10º interval of knee flexion for all three methods of tracker mounting (bone screws, rubber strapping and fabric strapping) measuring internal tibial rotation.

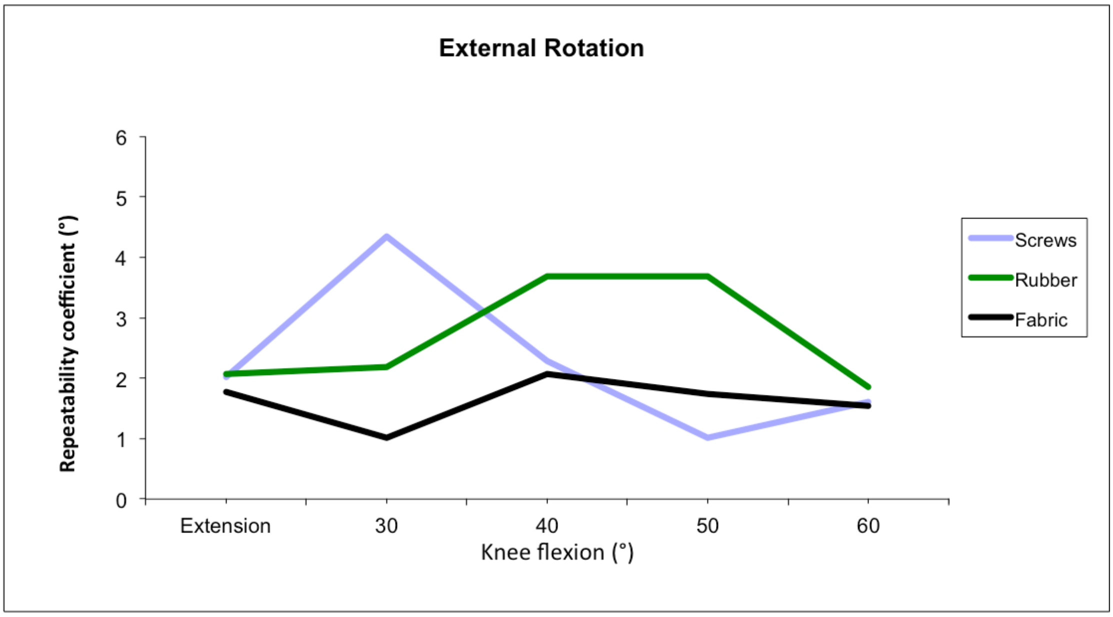

Figure 24 – Repeatability measuring external rotation (pilot study).
Repeatability coefficient at each 10º interval of knee flexion for all three methods of tracker mounting (bone screws, rubber strapping and fabric strapping) measuring external tibial rotation.

Regarding rotation (Figs. 23 & 24), no relationship is seen between knee flexion angle and repeatability using different methods of tracker fixation. Fabric strapping gives satisfactory repeatability throughout flexion with internal and external rotation. Although results are generally acceptable for internal rotation using bone screws and rubber strapping, both are unacceptable at 50˚. When measuring external rotation, screw fixation is unacceptable at 30˚ flexion, and rubber strapping at 40˚ & 50˚ knee flexion.

2.10.12 Agreement measuring internal & external rotation

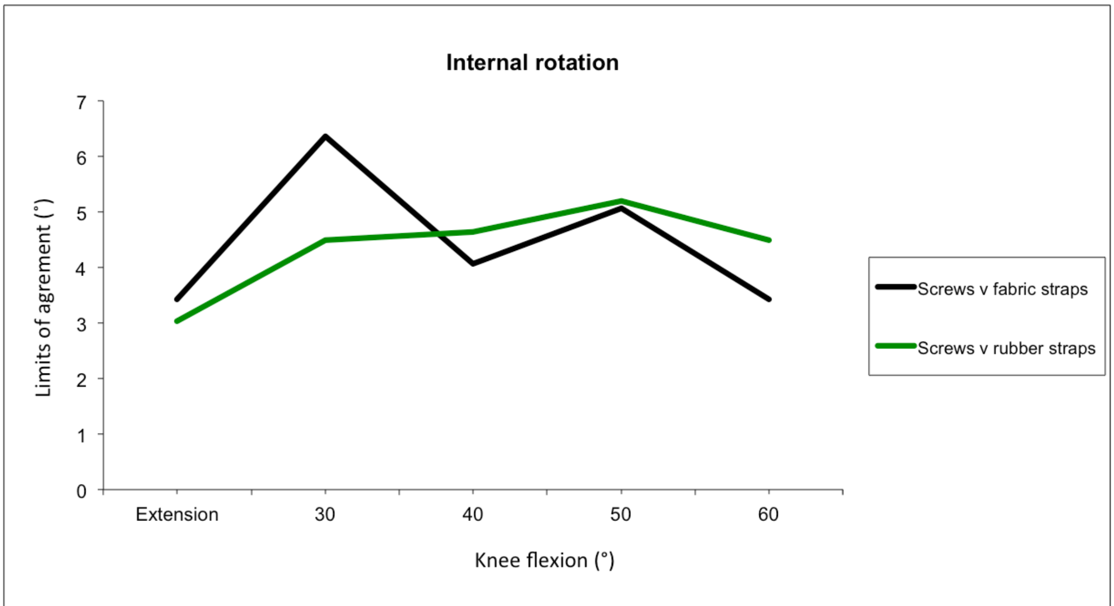

Figure 25 – Agreement measuring internal rotation (pilot study)
Agreement is insufficient between both non-invasive methods of tracker fixation and the invasive system when measuring internal rotation. Agreement does not appear to worsen with flexion of the knee.

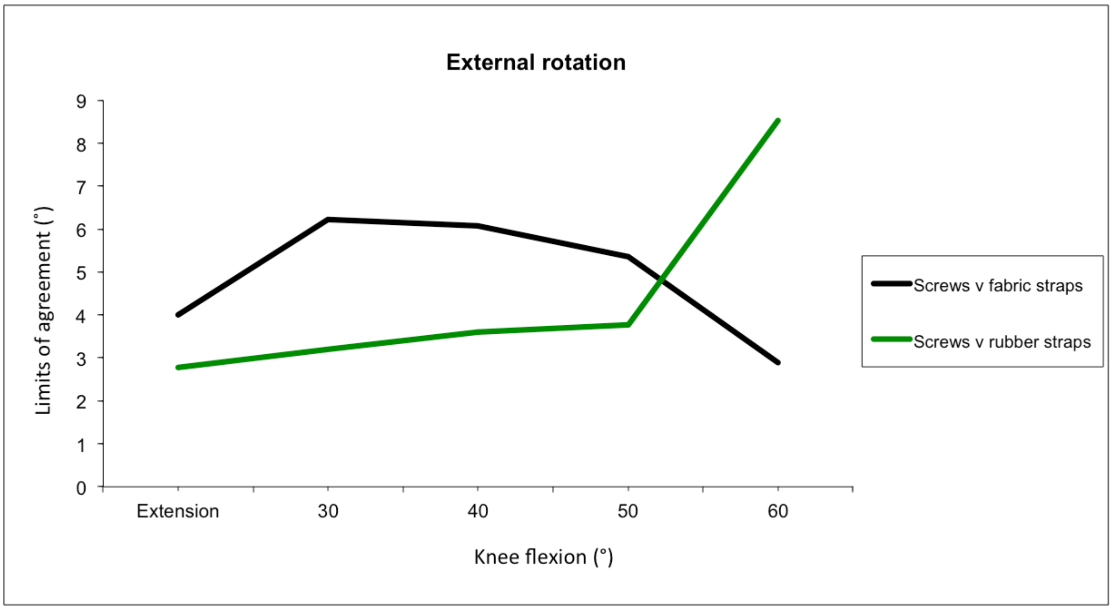

Figure 26 – Agreement measuring external rotation (pilot study)
Agreement is unacceptable using fabric strapping measuring external rotation throughout flexion. Using rubber strapping, agreement is acceptable in extension, but becomes markedly worse with flexion.

Agreement between the invasive and non-invasive methods of tracker fixation when measuring rotation is generally similar (Figs. 25 & 26). For fabric strapping measuring internal and external rotation, limits of agreement mean & range: 4.5 (3.4-6.4) & 3.5 (2.1 – 6.1) respectively. For rubber strapping measuring internal and external rotation: 4.4 (3.0 – 5.2) & 4.9 (2.9 – 6.2).

2.11 Discussion

Precision in measuring MFTA with no coronal stress applied to the leg was well within the limits of accepted repeatability throughout flexion using screw and fabric strap fixation. Repeatability and agreement was uniformly poorer using rubber strapping measuring each kinematic parameter compared with fabric strapping. Subjectively, movement of the trackers fixed with rubber strapping was observed during the experiment and we have demonstrated that passive trackers should not be secured with this material. Establishing a reliable method of tracker fixation is very important before moving forward with further laboratory based and in vivo testing of the device.

Applying varus and valgus stresses to the leg and flexing the knee reciprocally decreased repeatability when measuring MFTA for all methods of tracker fixation and reduced agreement between the invasive and non-invasive methods, particularly beyond 30° of knee flexion. This is most likely due to soft-tissue artefacts; however further laboratory-based work is required to quantitatively prove this statement. Precision and accuracy of the fabric strapping method is acceptable in extension and 30˚ flexion in measuring MFTA with stresses applied. Further study and consideration of a non-invasive method will focus on this material rather than the rubber strapping.

Measurement of anteroposterior tibial translation was carried out in extension (mean 12.8˚) and all methods of fixation demonstrated satisfactory precision however measurements taken with rubber and fabric strapping did not sufficiently agree with those using bone screws. A range of 10-30° for performing the Lachman test is quoted in the orthopaedic literature, particularly in laboratory studies, however an angle of 20° flexion is generally accepted (Logan et al., 2004; Christel et al., 2012). Further work is required to establish precision using standardised methods of force application at a flexion angle of 20°.

When measuring anteroposterior tibial translation in extension, either the non-invasive methods are precise but not accurate, or experimental error is present. The most obvious experimental variable, which is not accounted for in this pilot study, is force application during anteroposterior tibial translation. Evidence of this type of error is also present in measuring MFTA using bone screw fixation; despite the known validity of the invasive navigation device and consistent results in measuring MFTA using bone screws with and without coronal stress, at 40˚ flexion and application of varus stress, repeatability was unacceptable, and applying valgus stress, repeatability was borderline. It is most likely that this is again due to experimental error due to lack of standardised force application. Other factors may be involved and will be discussed. Presence of this uncontrolled variable reduces the ability to objectively validate the methods of non-invasive measurement.

With regard to rotation, precision using fabric throughout flexion measuring internal and external rotation was at worst 6.4˚ and 6.1˚ respectively. This compares very favourably to other non-invasive devices (section 2.5.7.2 (Almquist et al., 2002; Lorbach et al., 2009)). Again, this error may be due to a lack of standardised force application. A further source of error in all attempts to quantify tibial rotation highlighted by Branch et al (Branch et al., 2010) is that ankle joint excursion occurs during clinical testing of rotation, as the clinician/investigator uses the foot to apply torque, as was the case in this experiment. Estimation of flexion angle using the invasive and non-invasive methods displayed satisfactory precision. Agreement between invasive and non-invasive methods was better than visual estimation (Watkins et al., 1991) and hand-held goniometer (Edwards et al., 2004) and similar to electrogoniometers (Rowe et al., 2001). Again, force application, particularly when testing maximum flexion angle was arbitrary, however the non-invasive device displayed precision and accuracy similar to routinely used clinical and laboratory methods (Rowe et al., 2001; Edwards et al., 2004).

Limitations of this pilot study include the following which will be addressed in detail in chapter 3:

3.1 Use of embalmed cadaveric material

3.2 Limited number of specimens

3.3 Variable limb positioning during registration

3.4 Limb positioning during kinematic testing

3.5 Lack of blinding

3.6 Lack of standardised force application during varus / valgus stress testing and anteroposterior translation

3.7 Lack of force application during tibial rotation

2.12 Conclusion

Despite the limitations in the pilot study of using embalmed specimens, inconsistent limb positioning, low specimen number and lack of force application, the non-invasive fabric strap method of measuring knee kinematics displayed encouraging precision and accuracy; especially in measuring MFTA with and without coronal stress and anteroposterior translation in extension. It is very interesting to see that flexion consistently worsened precision and accuracy of MFTA and anteroposterior tibial translation measurement; this is likely due to soft tissue artefact and must be investigated further. The data confirms findings by Clarke (Clarke et al., 2012) that the device is precise and accurate measuring MFTA in extension, and adds to the literature to date an analysis of the effect of knee flexion on non-invasive measurement of MFTA, anteroposterior tibial translation, and tibial rotation. The data also reveals the importance of appropriate strapping for non-invasive optical trackers.

The pilot study firstly supports the rationale for further, more detailed validation in terms of resources and refinement of the experimental protocol purely for research into non-invasive methods of quantifying knee kinematics. The data also indicates that suitable refinement of the experiment methodology is required to validate this non-invasive method thoroughly in vitro in order to confirm or refute reliability for use in future in vivo testing and clinical practice.

3 Development of methodology

Limitations were identified following the pilot study, some of which were deliberate in limiting resource expenditure during preliminary testing. Carrying out a pilot study allowed assessment of the feasibility of experimental work of this nature, and allowed identification of areas of methodological development should further testing be appropriate. Results from the pilot study were encouraging and the following areas of experiment method were refined prior to further testing.

3.1 Use of embalmed cadaveric material

Embalmed cadaveric material was deliberately selected for the pilot study. The experiment protocol involved minimal dissection of cadaveric specimens, allowing future use of specimens. Embalmed cadaveric material differs markedly from in vivo material in terms of tissue hydration, mechanical properties especially in terms of stiffness and muscle tone. Fresh non-frozen cadaveric material better resembles in vivo limb mechanics, mainly due to hydration of tissues, but is limited compared to embalmed material due to expense and availability. Furthermore, the experiment protocol proposed requires long exposure times of the fresh specimens to room temperature, rendering them inappropriate for further use. Nonetheless this material was identified as more suitable for further work beyond the pilot study. It was thought that soft-tissue laxity and soft-tissue artefact would likely be increased using fresh cadaveric material and be more representative of the in vivo setting. It is important therefore that analysis of precision and accuracy of the non-invasive device in vitro must as fully as possible allow the impact of these variables to be quantified. Resources were secured to allow work on fresh cadaveric material.

3.2 Limited number of specimens

As explained in section 2.11, number of specimens was limited in the pilot study to allow a preliminary analysis of results prior to inappropriate consumption of resources. It was anticipated that limbs would be identified as unsuitable, and that duration of experiments would prohibit multiple experiment protocols being performed on each limb as the specimens degrade with prolonged exposure to room temperature. Obtaining results from at least 10 limbs would incorporate further specimen variability and allow for more robust analysis of precision and accuracy of the non-invasive method. Resources were secured to permit testing of at least 10 fresh non-frozen cadaveric lower limbs for each of the kinematic parameters being tested.

3.3 Variable limb positioning during registration

Subjectively, it was noticed that limb position, specifically knee flexion angle during acquisition and registration of bony landmarks of the knee (medial epicondyle, lateral epicondyle and midpoint between these landmarks) influenced agreement between values of MFTA when using the non-invasive method of tracker fixation. An experiment was undertaken to analyse this.

3.3.1 Method

Three fresh non-frozen cadaveric lower limbs were used. Two female limbs and one male limb; mean age 75.6y (range 65-85). Registration was carried out using the invasive method of tracker mounting registering the bony landmarks with the knee in extension. Measurement of MFTA was recorded at 10˚, 20˚, 30˚ & 40˚ flexion. This was repeated. The same procedure was then followed but registering the bony landmarks with the knee held at 40 - 45˚ flexion. These experiment steps were then performed using non-invasive tracker mounting. Results at each flexion interval were compared using limits of agreement. Limits of agreement ≤3˚ are acceptable (Mahaluxmivala et al., 2001; Bathis et al., 2004). A six-way comparison was made across the across the two pairs of variables i.e. invasive and non-invasive tracker fixation, and landmark registration in extension and landmark registration at 45˚ (Fig. 27).

	Invasive	Non-invasive
Registration in extension	*a*	*b*
Registration at 45˚	*c*	*d*

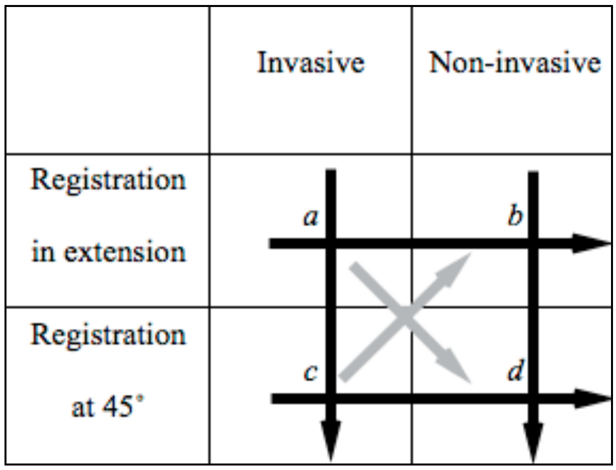

Figure 27 – Comparison of paired variables.

3.3.2 Results

Table 8 - Limits of agreement measuring MFTA between different methods of registration described above.

	Limits of agreement MFTA no stress from extension to 40˚ flexion	
Registration positions	Mean	Range
Invasive in ext vs invasive 45˚	1.64	1.08 - 2.06
Non-invasive in extension vs non-invasive 45˚	**4.1**	**3.07 - 5.35**
Invasive in extension vs non-invasive in extension	**4.29**	**3.45 - 5.15**
Invasive 45˚ vs non-invasive 45˚	2.04	1.68 - 2.94
Invasive in extension vs non-invasive 45˚	2.31	1.74 - 2.91
Invasive 45˚ vs non-invasive in extension	**4.42**	**3.51 - 5.55**

3.3.3 Discussion

Knee flexion angle does not influence agreement between registrations using the invasive method (Table 8). Examining the 'gold-standard' i.e. invasive method of tracker fixation first of all, measurements taken using invasive tracker mounting with the knee registered in extension agree sufficiently with invasive measurements taken following registration with the knee at 45˚, indeed comparison of registration positions using the invasive method of tracker fixation gave very good agreement, superior to all other comparisons made. Therefore, position of the knee whether in extension or mid flexion during landmark registration does not appear to affect measurement of MFTA. Invasive registration in extension also agrees with non-invasive registration at 45˚, but does not agree with non-invasive registration in extension. Indeed values of MFTA obtained using the non-invasive method of tracker fixation and knee placed in extension during registration did not agree sufficiently with any measurements taken using the invasive method of tracker fixation, or with measurements taken from non-invasive registration with the knee placed at 45˚. Despite the fact that measurements of MFTA taken following non-invasive registration in extension and invasive measurements both with the knee in full extension and at 10˚ flexion were all within 3˚, the data did not stand up to the robust method of statistical testing used to demonstrate limits of agreement. Furthermore, MFTA values obtained using both methods at higher flexion angles were clearly disparate leading to larger limits of agreement.

The best agreement between invasive and non-invasive methods of tracker fixation registrations was seen from registration of the knee using the invasive method of tracker fixation at 45˚, and the non-invasive method of tracker fixation at 45. Acquiring the medial and lateral epicondyles with the knee at 45˚ improves agreement between the invasive and non-invasive methods. This may be due to more accurate acquisition of the epicondyles, particularly the lateral epicondyle as the soft-tissues may obscure this landmark in extension. Flexing the knee slightly stretches the soft-tissues making the epicondyles easier to identify.

3.3.4 Conclusion

Possible causes have been identified for poor agreement between registrations. Further in vitro testing will incorporate registration of the medial and lateral epicondyles with the knee at 45˚ flexion.

3.4 Limb positioning during kinematic testing

Limb position during the pilot study was not constant. Between tests, the limb was placed on the laboratory table, and then picked up again in a manner consistent with clinical examination. Using the non-invasive method of tracker fixation, there was a concern that placing the limb on the work surface may induce movement or sliding of the fabric strap on the skin. However, this was not observed at any point in the pilot study. Several solutions were sought, including use of an assistant, however availability could not be guaranteed during the extended period of testing. An experiment set up allowing a single investigator to perform all tests was sought. This set up had to allow consistent limb positioning and maximise freedom of the investigator to apply controlled manual stress. Initially, the limb was left hanging over the end of the laboratory table to maintain a consistent position of the thigh and allow flexion and extension of the knee. Whilst preliminary testing using invasive tracker fixation was satisfactory, non-invasive strapping of the distal thigh moved along with the thigh soft-tissues which 'spread-out' as the dependent limb rested on the work surface; this resulted in large movements of the femoral tracker and erroneous output of MFTA.

The method of limb positioning must therefore:

- Maintain consistent limb position between tests to minimise confounding variables
- Free the investigator sufficiently to allow consistent force application
- Minimise soft-tissue artefacts from work surfaces

A sling suspended from a laboratory stand was used to suspend the thigh from the work surface. This again caused displacement of the soft tissues and therefore gross movement of the fabric strap and optical tracker. To resolve this, a single bicortical eyelet screw (length 20mm, width 75mm, manufacturer part no. N330, B&Q, U.K.) was inserted into the anterior femur approximately at the junction of the proximal third and distal two-thirds of the thigh (Fig. 28). Strong cord was looped through the eyelet screw and attached to a laboratory stand to maintain the hip at a flexion angle of 20°. No obvious movement of the fabric strapping or optical tracker was observed and the limb position was controlled in the position required for testing independent of the investigator.

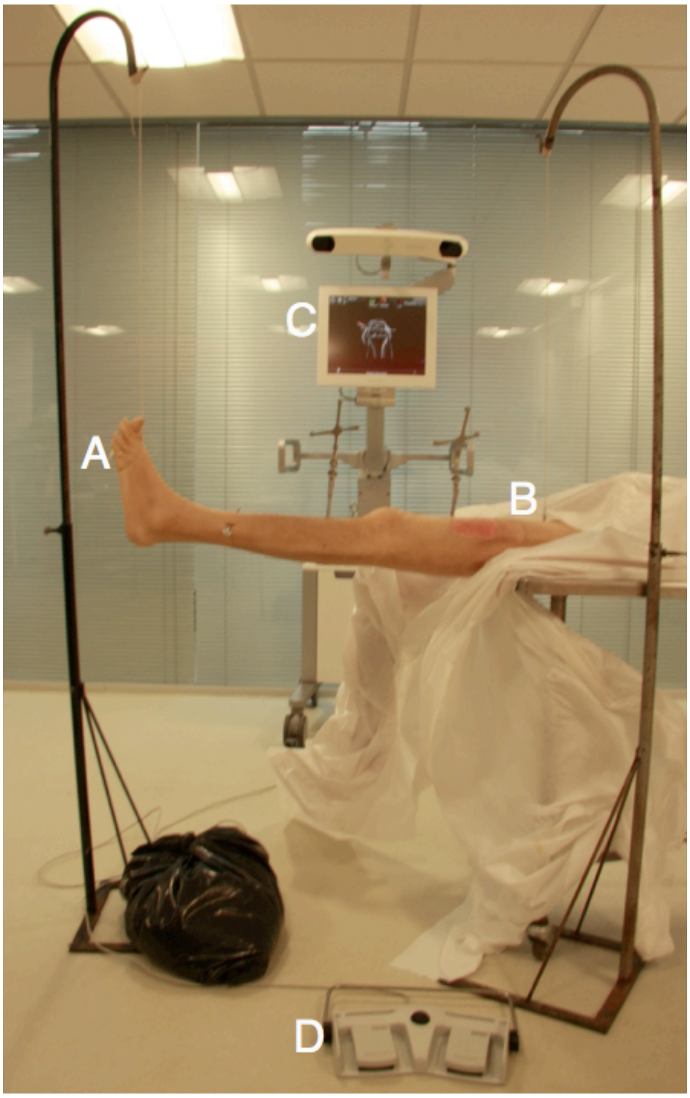

Figure 28 – Limb support construct.
A – Foot support suspended rom laboratory stand. B – Thigh eyelet screw suspended from laboratory stand. C – OrthoPilot device. D – Footpedal.

To further secure the limb position in terms of knee flexion angle, the foot was suspended again using strong cord from a laboratory stand. A spool of excess cord was created on this laboratory stand to allow adjustment of the height of the foot and thus, knee flexion angle. Using these two methods proved highly satisfactory in maintaining a consistent limb position and allowing the investigator to concentrate on force application. It also minimised the previously uncontrolled variables of limb position and soft tissue artefacts. To further stabilise the thigh, metal side supports secured by large clamps were placed either side of the proximal thigh. These did not create soft-tissue artefact concerning the distal thigh strap, and provided some opposition to varus and valgus forces applied to the leg (Fig 29).

Figure 29 - Side supports helping to stabilise the thigh during varus / valgus testing

3.5 Lack of blinding

Blinding to readings of MFTA was not a feature of the pilot study. This could lead to bias during testing. In order to maximise the quality of data obtained, readings of MFTA were blinded for further experiments by simply placing an opaque black card over the screen area displaying MFTA following satisfactory registration.

This was not possible during testing of anteroposterior translation and rotation. Both of these measures are displayed following an initial screen to set knee flexion angle. The knee flexion angle reading on the first screen would be obscured by an opaque card to blind readings of anteroposterior translation and rotation. Furthermore, readings of anteroposterior translation and tibia rotation were recorded by the system as the maximum excursion which occurred during testing, i.e., following removal of the displacing force, the value on screen did not change. Considering this, and the fact that the investigator's attention would be focused on the force application device and not the screen during testing, it was felt that investigator influence on the result would be minimal.

3.6 Lack of standardised force application during varus / valgus stress testing and anteroposterior translation

Review of the literature regarding validation of devices used to quantify kinematics of the lower limb revealed the importance of quantification of displacing force applied in order to minimise variation. Ideally, this should be a controlled variable in both the laboratory and clinical setting, seeking to standardise methodology during clinical examination, as discussed previously.

A transducer was purchased which permitted digital readout of force applied in grams. The transducer had a hook to allow attachment. Initially, Velcro strapping with a plastic loop was used to transfer force to the limb both in an anteroposterior, and varus/valgus direction (Fig. 30).

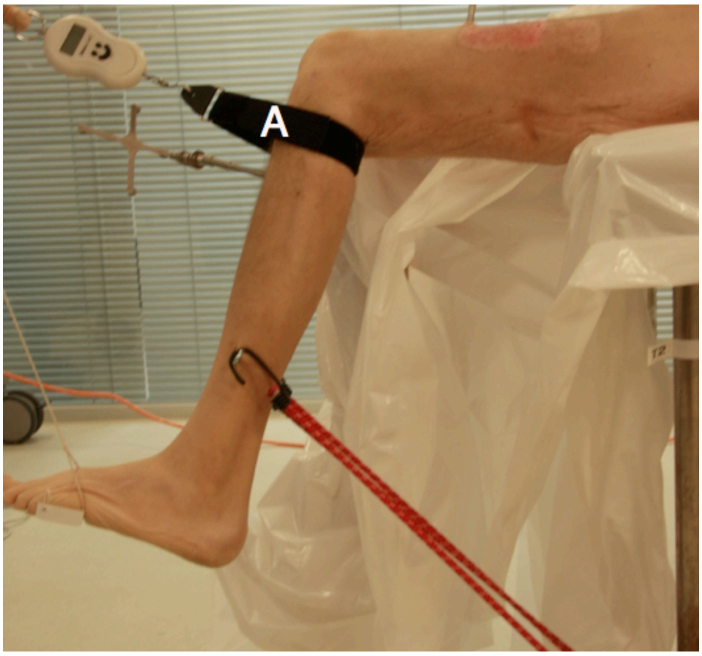

Figure 30 - Demonstration of strapping used to apply load.
'A' – Velcro strapping.

This method resulted in several problems, firstly, position of the strap between tests could not be made completely consistent as the strap was not tightly fixed to the limb to minimise soft-tissue artefact. This would result in different moments being applied, furthermore, direction of force application may not be consistent between tests. Secondly, some soft-tissue artefact occurred when applying anteroposterior force if the investigator was not careful to place the Velcro strap away from the tibial tracker strapping. Thirdly, force applied was dispersed by the soft-tissues. Ideally, force should be applied to the bony anatomy directly. All of these problems were overcome by the insertion of a bicortical eyelet screw (length 20mm, width 75mm, manufacturer part no. N330, B&Q, U.K.) in the tibial tuberosity, in a manner similar to that described by Christel et al. (2012) to allow application of anterior distraction of the tibia (Fig 31).

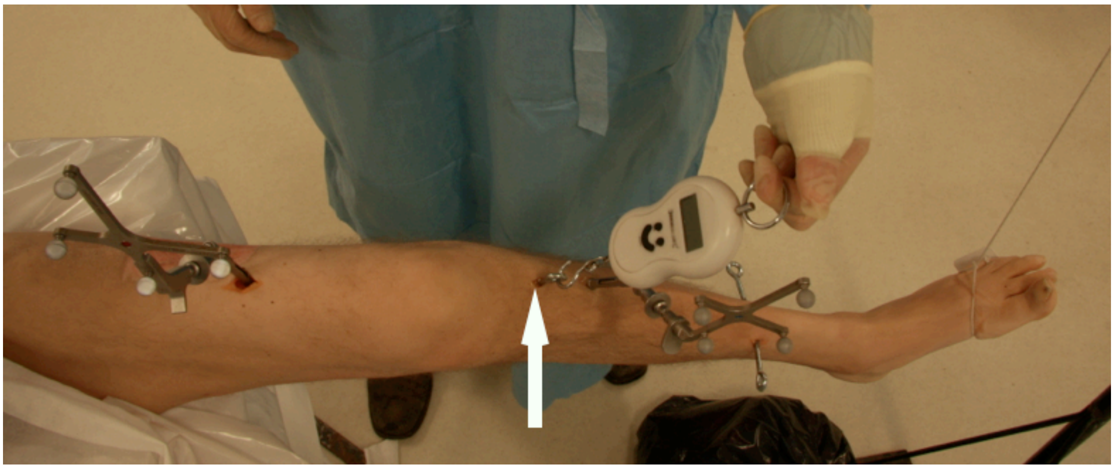

Figure 31- Tibial tuberosity screw.
White arrow indicates tibial tuberosity eyelet screw with the transducer held in position for demonstration.

To allow application of varus/valgus force, unicortical eyelet screws (manufacturer part no. N330, B&Q, U.K) were inserted in the coronal plane of the distal tibia at a set distance from the joint line, depending on the length of the lower limb (Fig. 32). Using this distance, the force required to create a moment of 15Nm could be calculated. This force is similar to that exerted during clinical examination of coronal knee ligamentous laxity (Grood et al., 1981; Stahelin et al., 2003; Wilson et al., 2012). Using screws allowed more uniform direction of force application as the transducer could be lined up with the longitudinal axis of the screw for each test. No cut out occurred during preliminary testing.

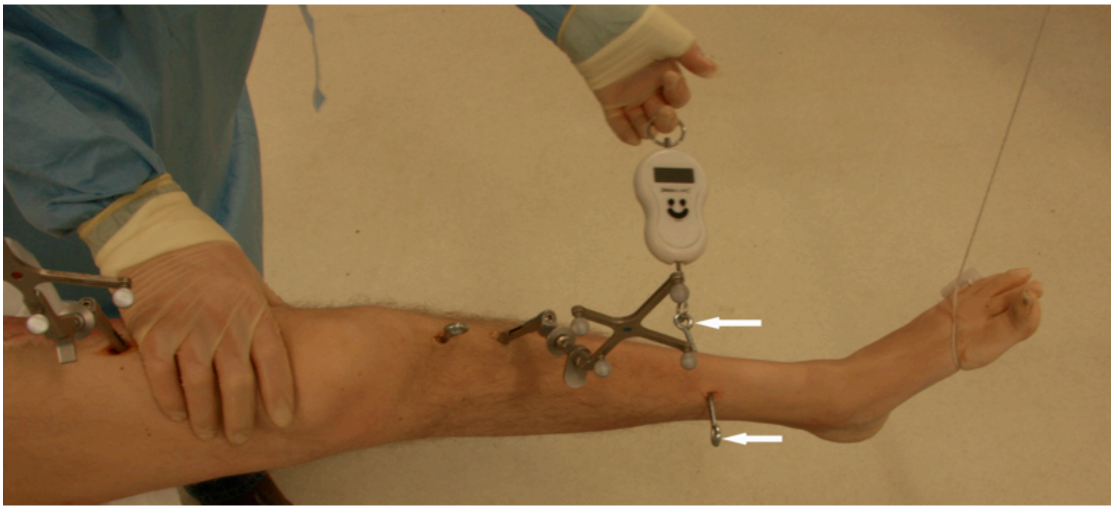

Figure 32 - Unicortical dstal tibial screws.
Indicated by white arrows allowing force application with the hand-held transducer.

3.7 Lack of force application during tibial rotation

The issue of standardising torque applied during tibial rotation is difficult and has not been satisfactorily addressed in the literature to minimise or remove excursion of the ankle soft-tissues. Only by implanting a device directly into the tibia can one ensure that the force applied will directly influence rotation of the tibia. This was not possible using the specimen mounting required for this study. As was noted in the review of the literature, excursion of ankle soft-tissues would have be accepted for any method of force application. A variety of methods to standardise applied torque were attempted, this proved quite difficult. The most successful method involved creating an adjustable footplate, which was to be strapped to the foot and ankle (Fig. 33).

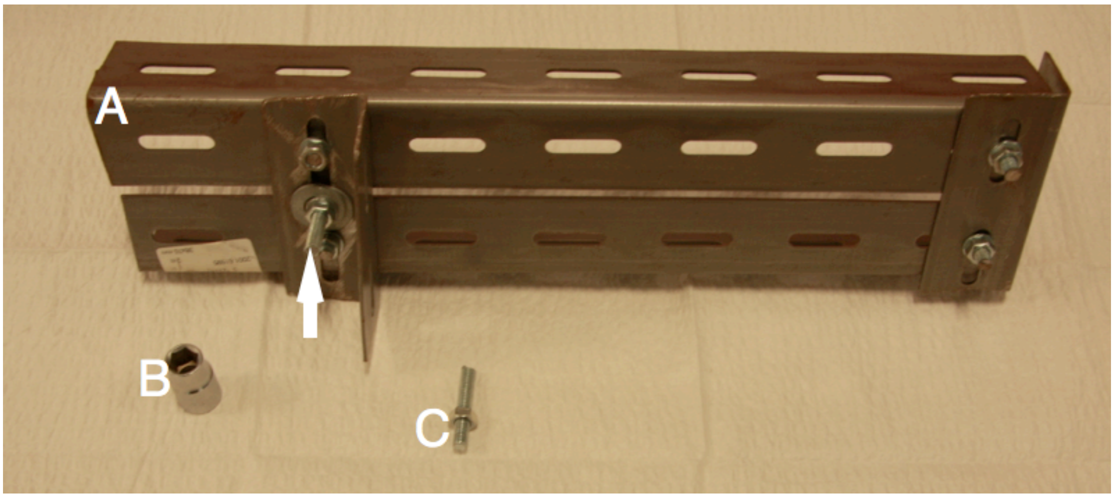

Figure 33 – Foot support for force application.
Footplate (A) with drive bit (B) and sheared bolt (C), originally attached to point marked by the white arrow.

A torque wrench was the used to apply rotatory torque (Torque Wrench, product ID 24677, Park Tools, Minnesota , USA) (fig. 34).

Figure 34 - Torque wrench

Unfortunately, during the first experiment, the axle between the wrench and footplate sheared and failed. This was repaired only for the same problem to recur. Owing to time constraints involved in using fresh cadaveric material, this method was abandoned and manual force to end of range used. This method has been shown to be reproducible (Almquist et al., 2011), as discussed in section 2.5.7.2.

4 Fresh Cadaver Study: Non-invasive measurement of mechanical alignment in early flexion

4.1 Introduction

Results of the pilot study in non-invasive measurement of all kinematic parameters was encouraging despite limitations in methodology. Addressing limitations of the pilot study (chapter 3) improved test conditions, especially control over dependent variables influencing reliability, precision and accuracy of the non-invasive system in testing coronal and sagittal mechanical alignment of the lower limb allowing comparison with a validated, commercially available image-free navigation device.

4.2 Method

16 limbs from 8 completely intact fresh, non-frozen cadavers were available for inclusion in the study. Mean age 80.5y (range 65-91y), 5 were female, 3 were male. 4 of the 16 limbs were excluded from the study; 3 due to previous knee surgery and 1 limb could not be registered with the non-invasive system due to oedema and poor hip registration. A single investigator carried out all testing on the 12 suitable cadaveric lower limbs.

As in section 2.8, the image-free OrthoPilot navigation system (B. Braun Aesculap, Tuttlingen, Germany) was used with passive optical trackers. Experimental software PhysioPilot v1.0 based on algorithms from 'KneeSuite High Tibial Osteotomy' and 'KneeSuite ACL' was used for the experiments. Again the software 'PhysioPilot v1.0' was used.

Between sessions, the cadavers were placed in a refrigerator overnight. The morning of the experimental work the specimens were left for 1 hour at room temperature. The specimen number, date of testing, which side of the body was being tested and sex of the specimen were recorded. The optical camera was positioned 1.9m meters from the specimen. This could be measured using a setup screen at the beginning of testing. The specimen table and Orthopilot wheels were locked. Temperature of the laboratory was consistent throughout the testing process. The specimens were not used for any other purpose between testing sessions. The experiment limb was put through a series of manipulations to minimise soft tissue creep throughout the experiment (Shin et al., 2007). This included:

- 24 hip circumductions
- 24 full flexion and extensions of the limb
- 24 varus / valgus stresses at 20˚, 40˚ and 90˚.
- 24 anteroposterior translations at 20˚, 40˚ and 90˚
- 24 internal and external rotations at 20˚, 40˚ and 90˚

Despite these efforts, it is recognised that the specimen tissue temperature would elevate through the day and that a degree of tissue creep will occur with any experiment involving repeated joint manipulation (Shin et al., 2007).

Cadavers remained grossly intact throughout the experiment and supine. The limb was set up as described in section 3.4 (fig. 23) with distal tibial pins inserted as described in section 3.6. Depending on the length of the tibia, a force was selected in order to apply 15Nm torque in the coronal plane when applying varus or valgus stresses to the limb. All bar one limb could accommodate distal tibial screws 30cm from the medial and lateral joint lines. A force of 50N was applied to these limbs. A force of 60N was applied to the short specimen 25cm from the joint line.

Registration was carried out using invasively mounted optical trackers. Trackers were placed exactly as described in section 2.8. Mechanical femorotibial alignment in the coronal plane (MFTA) from the first registration was noted. A second registration was then carried out to ensure MFTA in extension was within 2˚ of the first attempt. If not, registration was repeated. This was a precaution against proceeding to testing using an erroneous registration. Measurement of maximum extension and flexion angle was recorded during each registration. To obtain the extension angle, the limb was supported at the heel only. To obtain the maximum flexion angle, a manual force was applied to flex the knee to end of range. The investigator was not blinded to measurement of maximum flexion or extension angle. The MFTA in extension was noted. Once these angles were recorded, the MFTA display was covered to blind the investigator leaving the knee flexion angle visible on the monitor. MFTA was recorded using no stress at 10˚ intervals from full extension to 90˚ flexion. A further registration was then performed and MFTA in extension noted. Providing the second registration was within 2˚ of the first, the MFTA display on the OrthoPilot monitor was covered once again and MFTA recorded using no stress applied to the leg again at 10˚ intervals. At the end of recording, side supports were fitted to the table. MFTA was measured at each 10˚ interval with varus and valgus stress of 15Nm applied. These measurements were repeated. The limb was then registered using the non-invasive method of tracker fixation and the same process carried out as that used for the invasive experiment. The only difference when using the non-invasive method was that the trackers and fabric strapping were removed and replaced between registrations. On nine knees, measurement of MFTA with no stress applied to the leg was repeated during one of the registrations. This was not part of the original protocol but introduced in order to ascertain any difference in precision of the invasive and non-invasive systems within a single registration.

As in the pilot study (section 2.9), ICCs were calculated to convey reliability of measurements. Repeatability coefficient were calculated for the invasive and non-invasive systems separately using repeated measurements at each 10˚ flexion interval and each condition of stress (i.e. no stress applied, 15Nm varus stress, 15Nm valgus stress). Limits of agreement were calculated to compare data obtained from the invasive and non-invasive systems regarding measurements of MFTA recorded at each 10˚ flexion interval in each condition of stress. ICC, repeatability coefficient and limits of agreement were also applied to measurement of maximum extension and flexion.

4.3 Results

4.3.1 Measuring MFTA within a single registration

The nine limbs where MFTA was repeated with no stress applied to the lower limb had a mean age of 78.3y (range 65 – 86), three were female, five right and four left limbs were tested. Flexion contracture mean and range for these limbs was 7.3˚ (1˚ – 14˚) Reliability of measurement measuring MFTA from a single registration using invasively placed optical trackers and a single registration using non-invasively placed optical trackers was acceptable throughout the range of flexion tested. Mean and range ICCs throughout flexion: invasive; 0.995 (0.982 – 1), non-invasive; 0.972 (0.936 – 0.99). Throughout the remaining sections, where ICCs are summarised, 95% confidence limits are not given in order to keep the results clear and concise. Individual ICCs for each repeated measurement are given in the appendices along with individual 95% confidence intervals. Unless stated, the 95% confidence intervals have not altered the conclusions given, but have been examined and made available nonetheless (Appendix 8.2). Repeatability was acceptable throughout the range of flexion tested using both invasive and non-invasive optical tracker placement (Fig. 35).

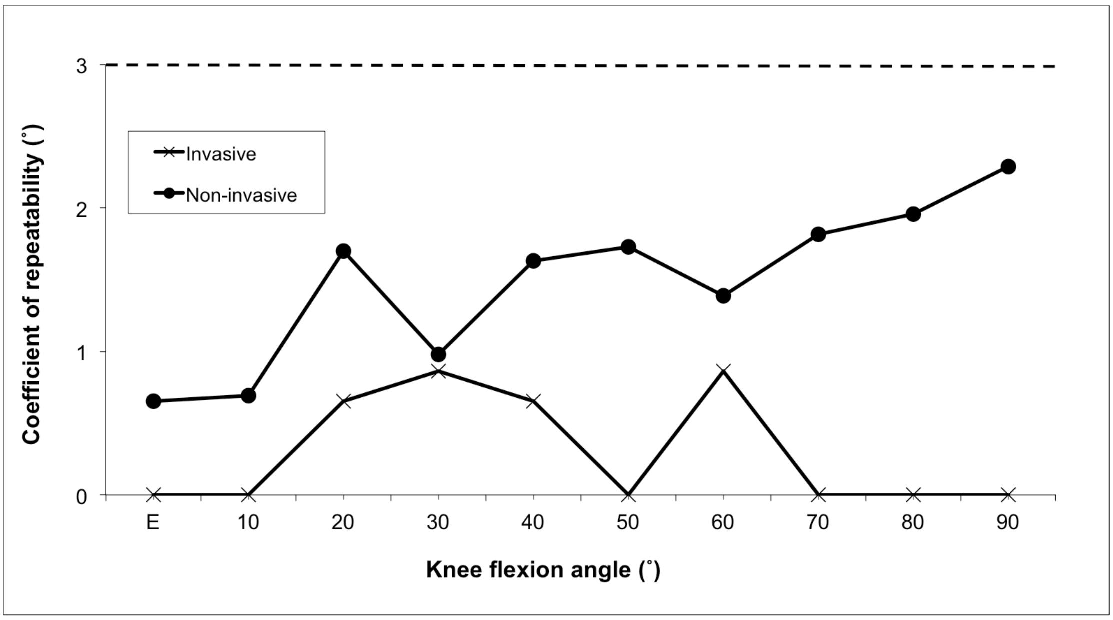

Figure 35 - Repeatability coefficient measuring MFTA with no stress applied, measurements taken from a single registration.

Agreement between these two methods of optical tracker fixation however was only acceptable from extension to 40˚ of knee flexion (Fig. 36).

Figure 36 - Agreement between the invasive and non-invasive methods measuring MFTA with no stress applied to the lower limb. Measurements are taken from a single registration.

4.3.2 Measuring MFTA with two separate registrations

Mean fixed flexion contracture for the 12 limbs was 5.8˚ (range of full extension values; -6˚ – 15˚)

Mean and range ICCs throughout the range of flexion tested measuring MFTA with no stress applied using two separate registrations during testing with invasively mounted optical trackers and two separate registrations with non-invasively mounted optical trackers; 0.976 (range 0.957 – 0.988) for invasive measurement and 0.917 (range 0.785 – 0.988) for non-invasive measurement (Appendix 8.2).

Repeatability measuring MFTA using the invasive method of optical tracker fixation was acceptable throughout the range of flexion tested (Fig. 37). Repeatability using the non-invasive method of optical tracker fixation was acceptable from extension to 50˚ knee flexion, with increasing knee flexion resulting in poorer repeatability.

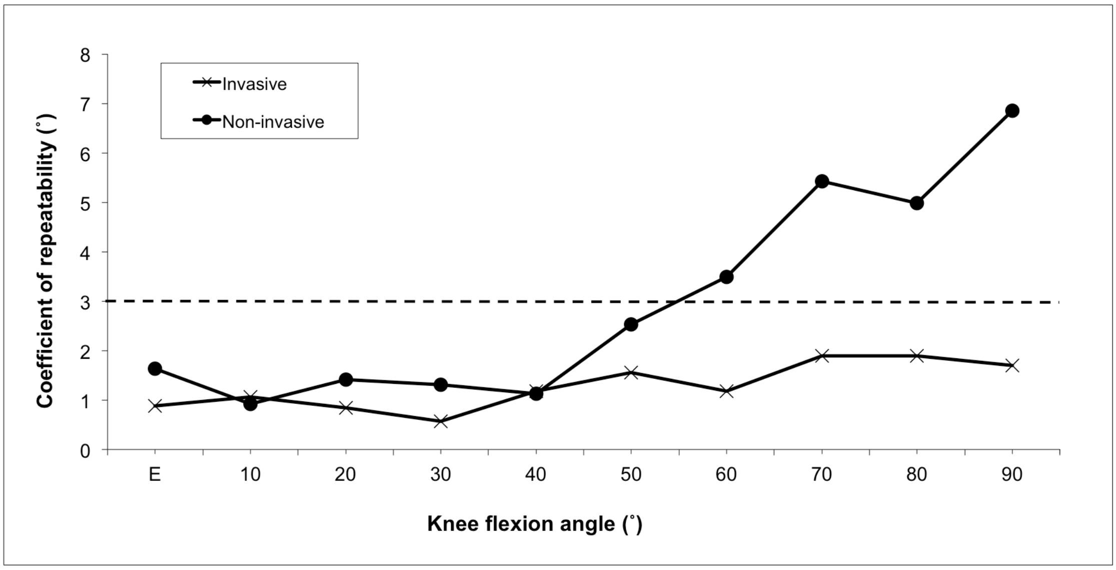

Figure 37 - Repeatability of the invasive and non-invasive methods throughout flexion measuring MFTA with no stress applied to the lower limb. Repeated measurements for each method of tracker fixation taken from a separate registration of the limb.

Agreement between invasive and non-invasive methods of optical tracker fixation was acceptable from full extension to 40˚ flexion (Fig. 38). Beyond 40˚ knee flexion, increasing knee flexion resulted in poorer agreement.

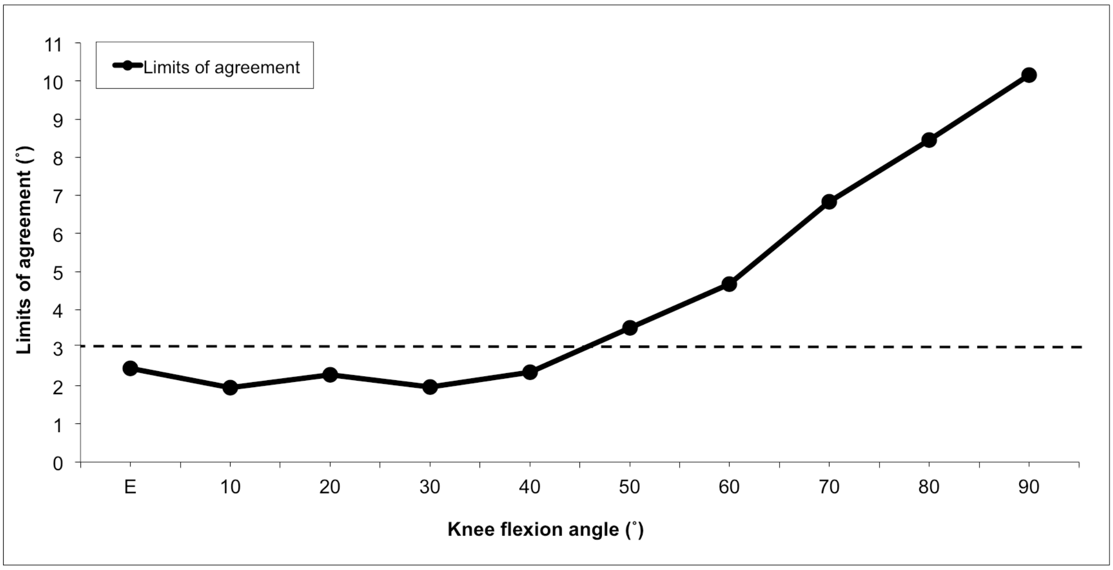

Figure 38 - Agreement between the invasive and non-invasive methods measuring MFTA.

Mean and range ICCs throughout the range of flexion tested measuring MFTA whilst applying 15Nm of valgus moment were acceptable throughout the range of knee flexion; 0.995 (range 0.988 – 1.0) for invasive measurement and 0.98 (0.95 – 0.995) for non-invasive (Appendix 8.2).

Repeatability was also acceptable throughout flexion using both methods of optical tracker fixation whilst applying 15Nm valgus moment (Fig. 39).

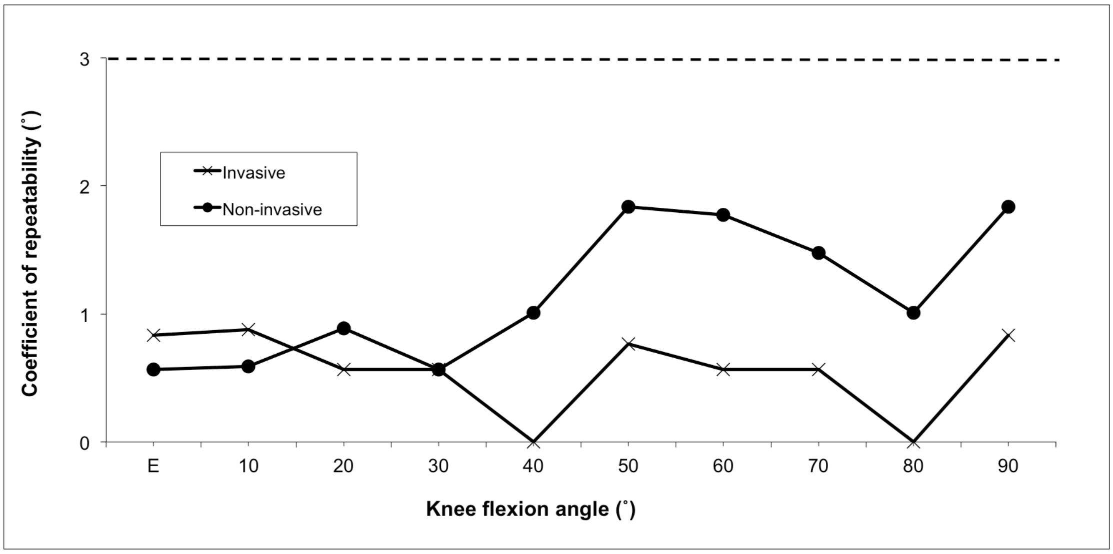

Figure 39 - Repeatability coefficient measuring MFTA whilst applying 15Nm valgus stress throughout flexion.

Mean and range ICCs throughout the range of flexion tested were acceptable using both methods of optical tracker fixation when measuring MFTA and applying 15Nm of varus torque; 0.998 (range 0.992 – 1.0) for invasive measurement and 0.989 (0.959 – 0.997) for non-invasive (Appendix 8.2).

Repeatability was also acceptable for both methods of optical tracker fixation throughout flexion when measuring MFTA and applying 15Nm varus moment (Fig. 40)

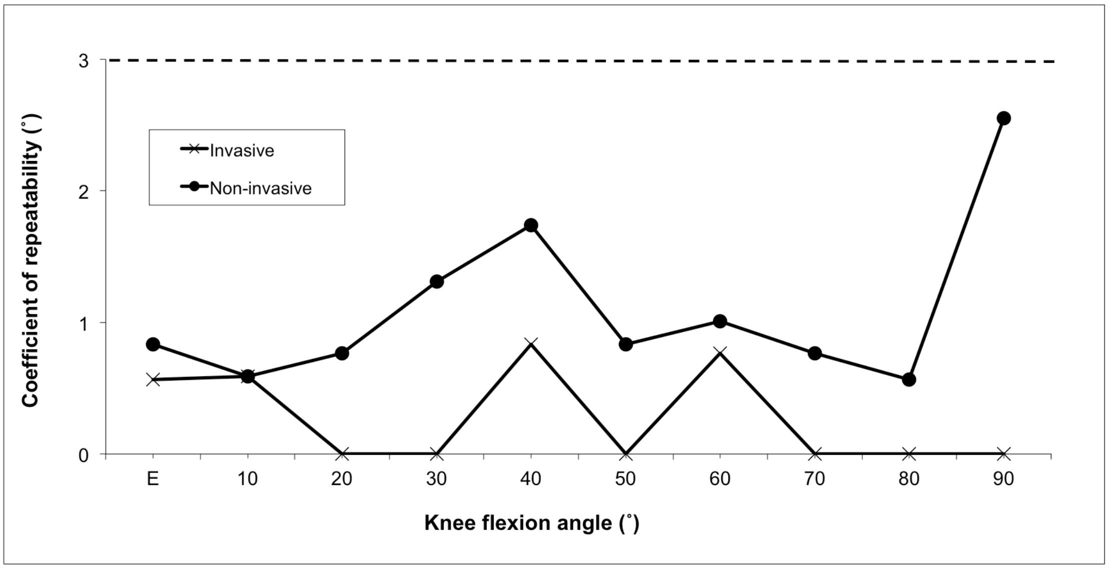

Figure 40 - Repeatability coefficient measuring MFTA whilst applying 15Nm varus stress throughout flexion.

Agreement between measurements of MFTA taken using the invasive and non-invasive methods of optical tracker fixation whilst applying 15Nm varus or valgus torque was acceptable from extension to 30˚ knee flexion, with agreement worsening in both conditions as knee flexion increased (Fig. 41). Applying varus or valgus moment to the limb during testing resulted in unacceptable agreement at 40˚ knee flexion where agreement between the methods of optical tracker fixation had been acceptable when no stress was applied to the lower limb (Figs. 38 & 41).

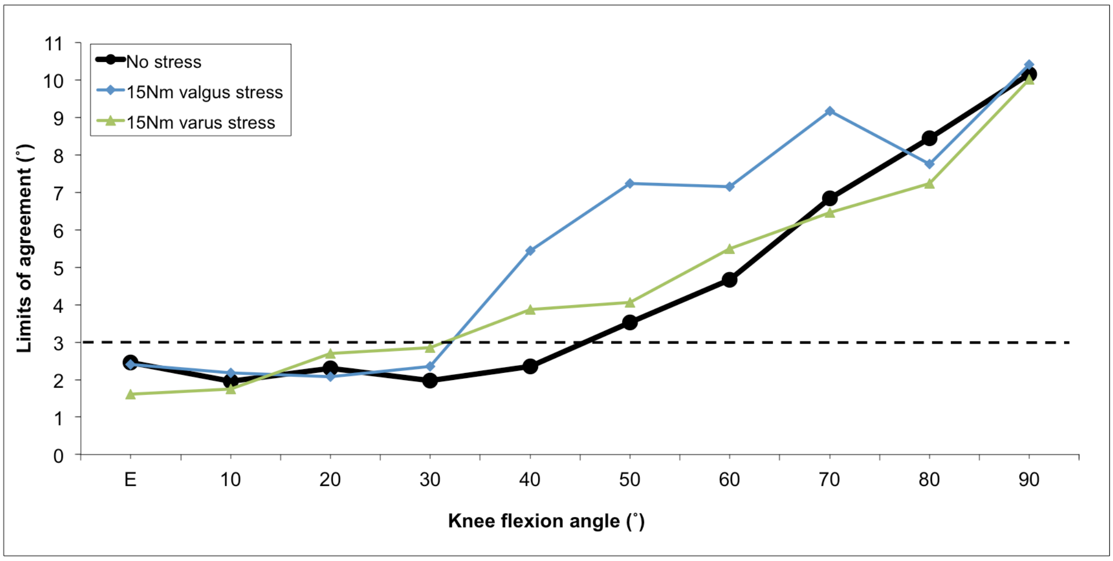

Figure 41 - Agreement between the invasive and non-invasive methods in all 3 conditions of coronal stress.

4.3.3 Measuring sagittal alignment

ICCs were very good measuring maximum extension and flexion (sagittal alignment) both by invasive and non-invasive means (Table 9 & appendix 8.2).

Table 9 – ICC measuring maximum extension and flexion.

	Invasive		Non-invasive	
	ICC	Range	ICC	Range
Full extension	0.93	0.78 - 0.98	0.94	0.8 - 0.98
Full flexion	1.00	1.00 - 1.00	1.00	0.99 - 1.00

Repeatability coefficient measuring maximum extension and flexion (sagittal alignment) were acceptable for both the invasive and non-invasive system except measurement of extension using the invasive system (Table 10). This may be due to one difference between invasive measurements of extension which differ by 5˚. Excluding this result, repeatability of the invasive method measuring maximum extension was 2.1˚. Agreement was adversely affecting regarding extension, and excepting this erroneous result LOA remains unacceptable at 4.6˚ instead of 5.1˚ (Table 10). Agreement between invasive and non-invasive methods of optical tracker fixation measuring maximum flexion was borderline (LOA 3.4˚, Table 10).

Table 10 – Repeatability and agreement measuring sagittal alignment.

	Repeatability coefficient (˚)		Limits of agreement (˚)
	Invasive	Non-invasive	
Extension	3.3	2.6	5.1
Flexion	1.5	2.4	3.4

4.4 Discussion

Reliability and repeatability of measuring MFTA in conditions of no stress and varus / valgus stress is acceptable throughout flexion using the invasive method (Figs. 35, 37, 39, & 40). In all conditions the invasive system is superior to the non-invasive system.

It is interesting to note that while repeatability of the non-invasive method is acceptable measuring MFTA throughout flexion with no stress applied (Fig.35), repeatability of the same measurement across two registrations becomes unacceptable after 50˚ of knee flexion (fig. 32). Using the same non-invasive method, Clarke (Clarke et al., 2012b) demonstrated superior agreement between two limb registrations using 30 volunteers measuring MFTA in extension (LOA 0.8˚). It should be noted that Clarke used non-corrected standard deviation of the differences between repeated measurements per registration, however 1.96 x standard deviation of the differences between measurements can be referred to as limits of agreement or repeatability coefficient (Bland et al., 1986). Details of the more robust method of calculating limits of agreement using a correction for repeated measures used in this cadaveric study have been discussed (section 2.9). It must also be noted that during volunteer testing, Clarke used the median of five measurements from each registration. This would definitively reduce variability in measurement following analysis. In this cadaveric study, using the non-invasive system between two separate episodes of registration to measure MFTA in extension gave a repeatability coefficient of 1.55˚. Clarke also looked at repeatability within a single registration using the non-invasive method of optical tracker fixation, this experiment was repeated, the repeatability coefficients in experiments one and two were 1.2˚ and 1.1˚ respectively when measuring MFTA in extension. In this cadaveric study, comparing non-invasive measurements of MFTA obtained within a single registration, gave a repeatability coefficient of 0.65˚. These results are comparable in terms of mean difference and repeatability both within one limb registration and two limb registrations. Clarke also analysed 30 patients with end stage osteoarthritis of the knee using the non-invasive method of tracker fixation before and after total knee arthroplasty using the median of three measurements from each registration compared to median of five in volunteer testing (Clarke 2012). Intra-operative alignment data was also collected before and after implantation of total knee arthroplasty. Before and after total knee arthroplasty, limits of agreement within registrations were 1.8˚ and 1.2˚ respectively; between registration limits of agreement were 1.8˚ and 1.6˚ respectively. Again, these results are similar to those reported in the cadaveric study. Limits of agreement measuring MFTA with no stress applied to the lower limb in this cadaveric study were 2.5˚. Clarke did compare out-patient pre and postoperative non-invasive data with intra-operative data, specifically MFTA with no stress, varus and valgus stress and sagittal alignment, however these data are not a suitable invasive vs. non-invasive comparison owing to differences in measurement setting. The most significant of these differences include influence of anaesthesia, arthrotomy and limb positioning. Unfortunately, data does not exist in the literature analysing agreement in measuring any kinematic parameters between invasive and non-invasive optical tracker fixation, or use of the the non-invasive method of optical tracker fixation analysing the effect of flexion on repeatability *in-vivo*. The effect of multiple registrations on precision and accuracy of measurement of non-invasive quantification of MFTA is negligible in extension and early flexion, as demonstrated by results discussed above from work by Clarke (Clarke 2012). The fact that similar repeatability was observed between extension and 50˚ to that displayed by the invasive method (Figs. 35 & 37), and agreement with the invasive system between extension and 40˚ using either single or consecutive registrations (Figs. 36 & 38) again highlights that multiple registrations do not affect precision of measurement. It is therefore likely that the decrease in repeatability examining measurements from two separate registrations using the non-invasive method to when flexing the knee beyond 50˚ is the result of soft-tissue artefact. Repeated registration does not affect the invasive method in terms of repeatability (Fig. 37). However using the non-invasive method, relocating the optical trackers does not affect measurement repeatability, or agreement with the invasive system from extension to 50˚, but in higher flexion, differences in soft-tissue location and therefore differences in movement of the soft-tissues relative to the optical tracker and baseplate between experiments may cause disparate measurements. Using repeated measures from a single registration, the effect of coronal stress was analysed on the invasive and non-invasive methods. Repeatability for each method throughout flexion was acceptable with the invasive system displaying superior precision (Figs. 39 & 40). Clarke et al (2012a) also reported satisfactory repeatability between 3 clinicans performing six varus / valgus stress tests with the knee in extension on a single volunteer: range of repeatability coefficient for varus stress testing 0.6˚ - 2.2˚, and 0.4˚ to 1.4˚ for valgus stress testing. Similar repeatability is reported in the patient cohort. Repeatability coefficients using the non-invasive method of optical tracker fixation in the cadaver study during varus and valgus stress testing were 0.8˚ and 0.6˚ respectively, these results are similar to those reported by Clarke. Agreement between the systems (Fig. 41) when 15Nm varus or valgus stress was applied became unacceptable beyond 30˚ knee flexion, compared to being acceptable until 40˚ knee flexion when no stress is applied to the limb. Again, no data is available for comparison in the medical literature and it is likely that soft-tissue movement differs from bony movement especially during the application of coronal stress. It is also worth noting the as yet un-quantified influence of soft-tissue artefacts on non-invasive measurement reliability, precision and accuracy measuring any kinematic parameter. The invasive method of tracker fixation provides rigid tracker body position in a constant relationship to the bony anatomy, whereas the non-invasively placed trackers are not rigidly fixed and movement artefacts are also likely to influence measurement. In early flexion, stabilising the knee and applying a varus or valgus stress causes minimal rotatory moment on the femur. Subjectively, it was observed during the testing process that in higher flexion, application of varus or valgus stress to the tibia caused larger excursion of the invasive compared with non-invasive femoral tracker in the axial plane. This however, could not be quantified using the methodology described for this experiment save for the phenomenon being represented by the effect of flexion angle on agreement.

Limitations of this methodology include use of cadaveric specimens, as mentioned previously. Tissue quality, tone and artefacts will differ from the in-vivo setting. Use of fresh cadaveric material is expensive and limits time available prior to degradation of the material when used for extensive testing at room temperature. It is reassuring to note similar repeatability to previously published work in-vivo in extension (Clarke 2012). Given the likely soft-tissue artefact in higher flexion, it will be important to analyse the effect of flexion on measurement repeatability in-vivo. This will require use of a force application device suitable for in-vivo use as the method used in this study is invasive.

4.4.1 Relevance of this data in determining ‘normal’ mechanical alignment and variation in subpopulations

Establishing the ‘normal’ static and dynamic alignment of the lower limb is an area of ongoing research (Tang et al., 2000; Bellemans et al., 2012; Nicolella et al., 2012; Orishimo et al., 2012; Whatman et al., 2012) and questions still exist as to what is ‘normal’ dynamic mechanical alignment (Bellemans et al., 2012). Bellemans et al. (2012) revealed that 32% of males and 17% of females from a cohort of 250 young adults had varus alignment of ≥3˚ measured on long-leg standing radiographs. Non-invasive, non-radiological methods of determining MFTA both in supine and weight-bearing conditions (Clarke 2012) may help determine variation in 'normal' alignment, and whether variation in alignment influences the development of osteoarthritis (Hunter et al., 2007). The non-invasive device described in this study represents an efficient method with minimal consequence to the patient of determining mechanical alignment and laxity and can be used weight bearing and during dynamic movements in early flexion. A method allowing dynamic assessment of MFTA in the early functional range may help in establishing influence of age, gender, laxity and ethnicity on kinematic characteristics and their influence on development of osteoarthritis.

4.4.2 Relevance to arthroplasty

As discussed (section 2.3), the medical evidence to date remains in favour of achieving 'neutral' component alignment (Jeffery et al., 1991; D'Lima et al., 2001; Green et al., 2002; Werner et al., 2005), and 'neutral' overall mechanical alignment (Jeffery et al., 1991; Ritter et al., 1994; Berend et al., 2004) however most major studies supporting this view have used short-leg radiographs to assess alignment (Lotke et al., 1977; Bargren et al., 1983; Hvid et al., 1984; Rand et al., 1988; Ritter et al., 1994). Biomechanical and clinical studies suggest that varus mal-alignment may be more problematic than valgus (Lotke et al., 1977; Bargren et al., 1983; Hvid et al., 1984; Jeffery et al., 1991; Ritter et al., 1994; D'Lima et al., 2001; Green et al., 2002; Berend et al., 2004; Werner et al., 2005). Further research is needed in evaluating current aims in restoring neutral versus 'constitutional' alignment in total knee arthroplasty (Mahaluxmivala et al., 2001; Bathis et al., 2004; Bellemans 2011; Lombardi et al., 2011), any effect on clinical outcome

(Matziolis et al., 2010) or survivorship (Parratte et al., 2010); all of these studies are based on static measurements of MFTA.

Difficulty lies in estimating the mechanical femorotibial axis in the coronal plane (MFTA), especially how this changes with weight bearing and in early flexion. Current methods used in examination before, during and following surgery are subjective and prone to variation both in technique and especially when using visual interpretation of coronal and sagittal alignment (Shetty et al., 2011). Methods to standardise examination, provide descriptions or classification of laxity have been proposed, however it is difficult to communicate findings from examination which is not standardised, far less to make recommendations based on this as to how to proceed with management of soft-tissues during total knee replacement (Krackow 1990; Engh 2003; Ries et al., 2003). Short leg radiographs are inadequate and can even cause clinicians to completely misinterpret alignment (van Raaij et al., 2009). Many clinicians nonetheless still rely primarily on physical examination and short-leg radiographs. Long leg radiographs are superior in determining lower limb mechanical alignment however they are prone to rotational error (Krackow et al., 1990; Mahaluxmivala et al., 2001; Hunt et al., 2006; Yaffe et al., 2008), do not allow dynamic assessment, and expose the patient to radiation. Goniometers and other surface landmark based methods may be able to give information on disease progression or diagnose deformity but do not provide accurate assessment within the required limits of $\pm$ 1.5° (Hinman et al., 2006; McDaniel et al., 2010; Navali et al., 2012). Comparison between long-leg radiograph and a unique upright MRI scanning device has demonstrated agreement within the required limits (Liodakis et al., 2011) however conventional MRI is limited in terms of dynamic assessment. In the UK, current clinical department resources are usually limited to CT scanning in terms of the best method of three-dimensional imaging of bony anatomy, and component orientation following arthroplasty (Jakob et al., 1980; Kim et al., 2012); again dynamic assessment is not possible using this method and it exposes the patient to significantly more ionising radiation than that used to obtain a standard radiograph. It may be possible to overcome the rotational problems associated with long leg radiographs using low radiation dose CT scanogram, however, using current techniques this again presents a static, non-weight-bearing evaluation (Henckel, Richards et al. 2006; Mohanlal and Jain 2009).

Ideally, the clinicians would have access to a relatively inexpensive, reliable, precise and accurate method of assessing dynamic, weight-bearing mechanical alignment and knee joint laxity in extension and early flexion before and after total knee arthroplasty, ideally with a similar frame of reference to any computer assisted system used during surgery. Following surgery, such a device would be ideal for audit and research as described above, as well as assessing problematic knees such as those describing flexion instability which accounts for a significant proportion of revision surgery (Fowler 1980; Fehring, Odum et al. 2001). Prior to surgery, this would allow detailed assessment of kinematics and planning of tissue release & resection. Achieving a satisfactory surgical outcome depends on understanding the degree of deformity present prior to surgery, whether or not this can be corrected on manipulation or whether the only means to correct deformity is soft tissue resection with or without bony resection. Following surgery, such a device would be ideal for audit and research as described above, as well as assessing problematic knees such as those describing flexion instability which accounts for a significant proportion of revision surgery (Fowler 1980; Fehring et al., 2001). The ability to quantify alignment intra-operatively in a consistent and reliable manner has led surgeons to develop algorithms guiding decision making regarding balancing the knee to achieve neutral alignment without sacrificing stability (Picard et al., 2007; Unitt et al., 2008; Hakki et al., 2009; Jenny 2010; Lehnen et al., 2011; Aunan et al., 2012; Moon et al., 2013). Rate of intra-operative collateral ligament release vary in these studies between 11-25%. At time of writing, major limitations to intra-operative assessment are present in terms of relating intra-operative findings to weight-bearing biomechanics following surgery and complete healing of the soft-tissues. Factors such as the influence of anaesthesia, incision, supine position, lack of joint capsule tension from fluid and scar tissue are unlikely to be accounted for intra-operatively until such times as we better understand alignment and how laxity characteristics change from the intra-operative to post-operative setting, and how healing and scar formation further change joint kinematics. Factors such as the lack of standardised force application during manual stress applied by the surgeon intraoperatively may be remedied by use of a force application device (Wilson, Deakin et al. 2011; Clarke, Riches et al. 2012; Siston, Maack et al. 2012), which would aid transmission of findings between surgeons and aid surgical training. Again, this technology would have to be available in the clinical setting to minimise confounding variables between settings. At present, non-invasive devices are means by which comparative kinematic testing is possible. The current study provides a reassuring in-vitro validation of this non-invasive device in terms of its ability to estimate mechanical alignment and coronal laxity of the knee using a similar frame of reference to established image-free navigation technology within ± 1.5˚ from extension to 40˚ when no stress is applied. When simulating laxity testing, the device was acceptably precise an accurate from extension to 30˚. This is within the range relevant to laxity testing such as that used in soft-tissue algorithms (Picard et al., 2007; Unitt et al., 2008; Hakki et al., 2009; Jenny 2010; Lehnen et al., 2011; Aunan et al., 2012; Moon et al., 2013). This non-invasive device would be useful for assessing pre-operative deformity and laxity characteristics, and assessment of postoperative alignment and laxity.

Future augmentation of non-invasive navigation technology with ultrasound detection of bony landmarks would improve accuracy of registration (Masson-Sibut et al., 2012) and eventually may allow real-time three-dimensional imaging if multiple landmark locations can be relayed to a localiser, eliminating soft-tissue artefact.

4.4.3 Relevance to collateral ligament injury assessment

Collateral ligament laxity testing following trauma is currently limited in terms of using devices to quantify coronal laxity to examination of joint space opening (LaPrade et al., 2008; Laprade et al., 2010; LaPrade et al., 2010; Gwathmey et al., 2012). At present no clinical scenario exists using change in mechanical alignment properties to quantify or grade collateral ligament injury in a consistent manner. The non-invasive method described in this study is reliable, precise and accurate within the early flexion range used for clinical testing in the out-patient clinic, and under anaesthesia. Should the method prove reliable in-vivo, concomitant use of a validated force application device could allow standardisation of clinical examination and potentially a grading system based on this method to quantify collateral ligament laxity. This may also include dichotomous comparison with the non-injured knee.

4.4.4 Quantifying sagittal alignment

Measurement of maximum extension and flexion using both the invasive and non-invasive devices was highly reliable (table 9), however as discussed, despite satisfactory repeatability measuring maximum flexion using both invasive and non-invasive methods, agreement was borderline. Measurement of maximum extension gave repeatability just outside the accepted limit for the invasive system, yet acceptable for the non-invasive system. As discussed, this is likely due to an erroneous measurement in one specimen, with a difference between repeated invasive measurements of 5˚. Thus limits of agreement were 5.1˚.

Measuring extension, repeatability is inferior to that reported by Clarke (2012) who reported repeated measurements of sagittal alignment on 30 volunteers giving a within registration repeatability coefficient of 2.1˚. Between or intra-registration repeatability coefficients were 1.2˚ supine and 5˚ standing. Clarke also analysed 30 patients before and after total knee arthroplasty using the non-invasive method of optical tracker fixation, in this study, the median of three measurements from each registration was used for comparison. Within registration repeatability coefficient for the pre-operative and post-operative groups was 6.9˚ and 3.8˚ respectively, between registration repeatability was 4.4˚ and 3.3˚ respectively. Larger variation compared to the healthy volunteer results may be attributable to using median of three instead of five measurements per registration, and may also be due to the presence of flexion contracture in the pre and postoperative groups: mean 7.7˚ and 6.7˚ respectively compared to mean of -1.7˚ in the healthy volunteer group. In this cadaveric study, the invasive system gave a repeatability coefficient of 3.3˚ and the non-invasive system: 2.8˚. These results are slightly less repeatable than those from the pilot study (repeatability coefficient 1.3˚, non-invasive 1.6˚ (section 2.10)).

Superior repeatability in the embalmed cadaver experiment may be the result of less laxity in the embalmed cadaveric specimens. Nonetheless, reliability and repeatability of the no-invasive system measuring maximum extension is acceptable and similar to previously reported results discussed above.

The validated gold-standard of invasive image-free navigation gave borderline repeatability despite demonstrating excellent reliability and repeatability measuring coronal alignment (sections 4.3.1 & 4.3.2). The image-free concept has been validated thoroughly and has an accuracy of <1˚ (Wiles et al., 2004; Pearle et al., 2007; Picard 2007; Rudolph et al., 2010), leading to the conclusion that experimental error must be present. This may have occurred during registration, (Amanatullah et al., 2013). The increased variability may also be accounted for by differences in tissue laxity between embalmed and fresh cadaveric material. Another possibility is difference in limb positioning setup between the two experiments. In comparison to the study by Clarke (2012), obvious differences in the *in-vitro* and *in-vivo* settings include absence of muscle tone and control, as well as differing tissue characteristics. Furthermore, the limbs used in the cadaveric study had significant flexion contracture. Inability to fully extend may reduce stability and reproducibility of full extension the knee due to reduced tension across the posterior capsule and a lack of a functioning 'screw home' mechanism in the cadaveric specimens (Croce et al., 2006; Sheehan 2007), this may add to inconsistency in limb positioning during testing. Unfortunately, regardless of the cause of error in invasive measurement, comparison between invasive and non-invasive measurement is less relevant. These factors will have had a negative impact on limits of agreement between the two methods in measuring maximum extension; LOA of 5.1˚ are greater than expected.

Repeated measures of maximum flexion angle using the invasive system gave a mean repeatability coefficient of 1.53˚, whilst the non-invasive method gave repeatability coefficient of 2.4˚. Again variability is slightly increased in the fresh cadaveric setting compared to the embalmed where repeated measures of maximum flexion gave repeatability of 2.3˚ and 2.1˚ using the non-invasive method. Limits of agreement in measuring maximum flexion between the two systems were 3.4˚. In the embalmed cadaveric study these 3.9˚. Clarke also compared knee flexion angle measured using the non-invasive method of tracker fixation and an electrogoniometer on a single volunteer demonstrating limits of agreement of 3.2˚ measuring at 10˚ intervals from extension to 130˚ (Clarke et al., 2012a). These results are similar to the cadaveric study. Force application in positioning the limbs in maximum flexion was not used in either the embalmed or fresh cadaver study. Lack of control of this dependent variable is highly likely to increase variability in maximum flexion angle achieved.

Repeatability and agreement is superior to visual assessment which has been shown to be very unreliable (± 10˚, i.e. agreement ≥20˚ (Shetty et al., 2011)). Despite this fact, most surgeons continue to rely on visual assessment (Watkins et al., 1991). The non-invasive device is also superior to goniometry which has a margin of error of at least ±5˚. As discussed in section 2.4, radiological methods are limited to static assessment only apart from fluoroscopy which is not used in clinical practice to determine knee flexion.

As discussed in section 2.4, the majority of knee movement occurs in the sagittal plane. Achieving full extension is vital to normal biomechanics of the knee, if this is not achieved, excessive loading of the quadriceps and the joint itself occurs (Perry et al., 1975; Su 2012). The ability to achieve at least 105˚ flexion following total knee arthroplasty is important for allowing most activities of daily living common to western culture in individuals falling within the typical age group requiring total knee arthroplasty (Mulholland et al., 2001; Gonzalez Della Valle et al., 2007; van der Linden et al., 2008). The importance of quantifying patient's range of motion pre-operatively as a predictor of postoperative range of motion has been dicussed (Nelson et al., 2005; Ritter et al., 2007; Su 2012) (section 2.4.2), and should form part of pre-operative assessment to help the surgeon plan to achieve a satisfactory post-operative range of motion.

The non-invasive device demonstrated similar precision to the invasive device, however agreement between the two devices was >3˚ in measuring both extension and flexion. It is likely that limb positioning and lack of muscle tone could account for some of this variability in measuring both extension and flexion, and a lack of force application will have influenced variability in flexion angle. Nonetheless, it is likely that this non-invasive device could be useful for assessing pre-operative deformity and the progression of post-operative deformity.

4.5 Conclusion

The non-invasive method demonstrates satisfactory reliability, precision and accuracy in-vitro measuring MFTA with no stress applied to the lower limb between extension and 40˚ knee flexion when compared to a commercially available system for surgical navigation. Flexion has a consistent negative effect on precision and accuracy of the non-invasive device, whilst the invasive device remains precise throughout flexion.

Application of quantified coronal stresses has a negative impact on accuracy of the non-invasive system beyond 30˚ knee flexion.

5 Non-invasive quantification of anteroposterior laxity of the knee

5.1 Introduction

Results from the pilot study (section 2.10) indicated satisfactory precision using bone screws and fabric strapping whilst measuring anteroposterior translation. Agreement was unsatisfactory however (>3mm) between these 2 methods throughout knee flexion.

One of the main points noted in critiquing the methodology used in the pilot study was a lack of measurement and / or standardisation of force application. Limb positioning, cadaveric material and number of specimens was also not optimal in providing an in vitro test environment as close to in vivo as possible, whilst minimising the influence of variables. The following experiment aimed to address these limitations.

5.2 Aims

The primary aim of this experiment was to determine the precision and accuracy of a non-invasive method of optical tracker fixation compared to a known validated method of measuring anteroposterior translation of the tibia. An image-free navigation system using conventional bone screw mounted optical trackers was the 'gold-standard' method of measurement.

5.3 Materials and methods

6 male and 6 female cadaver lower limbs were used. Average age 80.5y (65 – 96y).

General specimen testing conditions and pre-conditioning was identical to that described in section 4.2.

The specimens were mounted with the limb suspended in a manner similar to that described in section 3.4, however the ankle was restrained during testing of anteroposterior tibial translation. The foot was supported in the same manner as that previously described in section 3.4 to limit knee flexion. In order to limit knee extension, 4 separate bungee cords were attached to the distal tibial screws and secured to points at the base of the laboratory table. Various lengths were available and changed to adapt to various positions of knee flexion, keeping the bungee cords as tight as possible according to position of the foot throughout range of knee flexion. The pull of the bungee cord was counteracted by the foot support resulting in no excursion of the knee during anteroposterior tibial stress testing (Fig. 42).

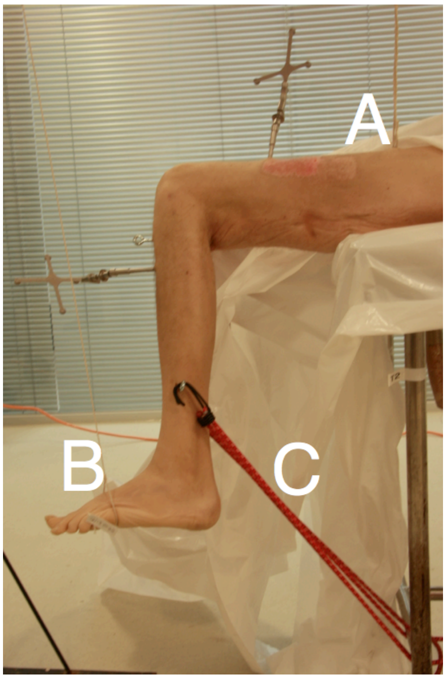

Figure 42 - Limb setup for testing anteroposterior translation.
A: femoral suspension screw, B: foot support to restrict knee flexion, C: 4 separate taught bungees to restrict knee extension.

In order to allow attachment of a transducer to the anterior tibia to allow application of a moment perpendicular to the coronal plane of the tibia, a screw with eyelet was inserted into the tibial tuberosity (Fig. 43). This method has been described in a previous cadaveric study during which it was necessary to apply anterior force to the tibia to stress the anterior cruciate ligament (Christel et al., 2012). A 3cm incision was made over the most prominent point of the tibial tuberosity and soft-tissues cleared down to bone. A drill hole was made through both cortices and an eyelet screw inserted. The eyelet screws have a very prominent thread, which prevented cut out.

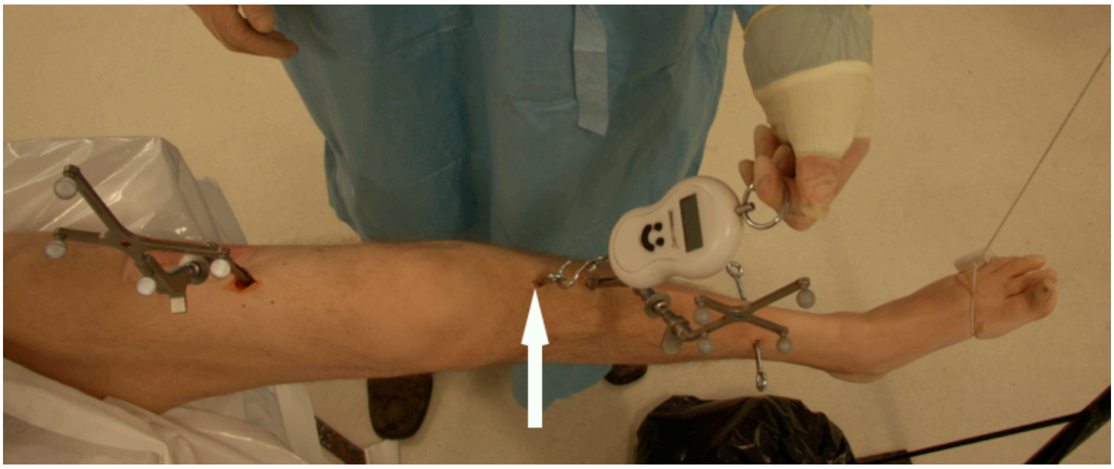

Figure 43 – AP force application.
White arrow indicates position of tibial tuberosity screw. In this photograph the transducer is in position however no force is being applied.

Distal tibial screws, invasive and non-invasive optical trackers were mounted during this experiment in the same manner as described previously (section 3).

In order to apply a standardised quantifiable force to the tibial tuberosity, a hand held static dynamometer was used (Model 251066, Silverline, Somerset, UK, CE Certified). This was zeroed before every use and could be attached directly to the eyelet screws.

The following steps were performed firstly with the invasive bone screw method of tracker fixation, then with the non-invasive method using fabric strapping.

Registration was carried out using the OrthoPilot® device and PhysioPilot v1.0 software as in section 2.8 & 4.2. The lower limb was then fixed in extension using the foot strap and bungee cords. The 'AP Shift / Rotation Range' display was selected (Fig. 44).

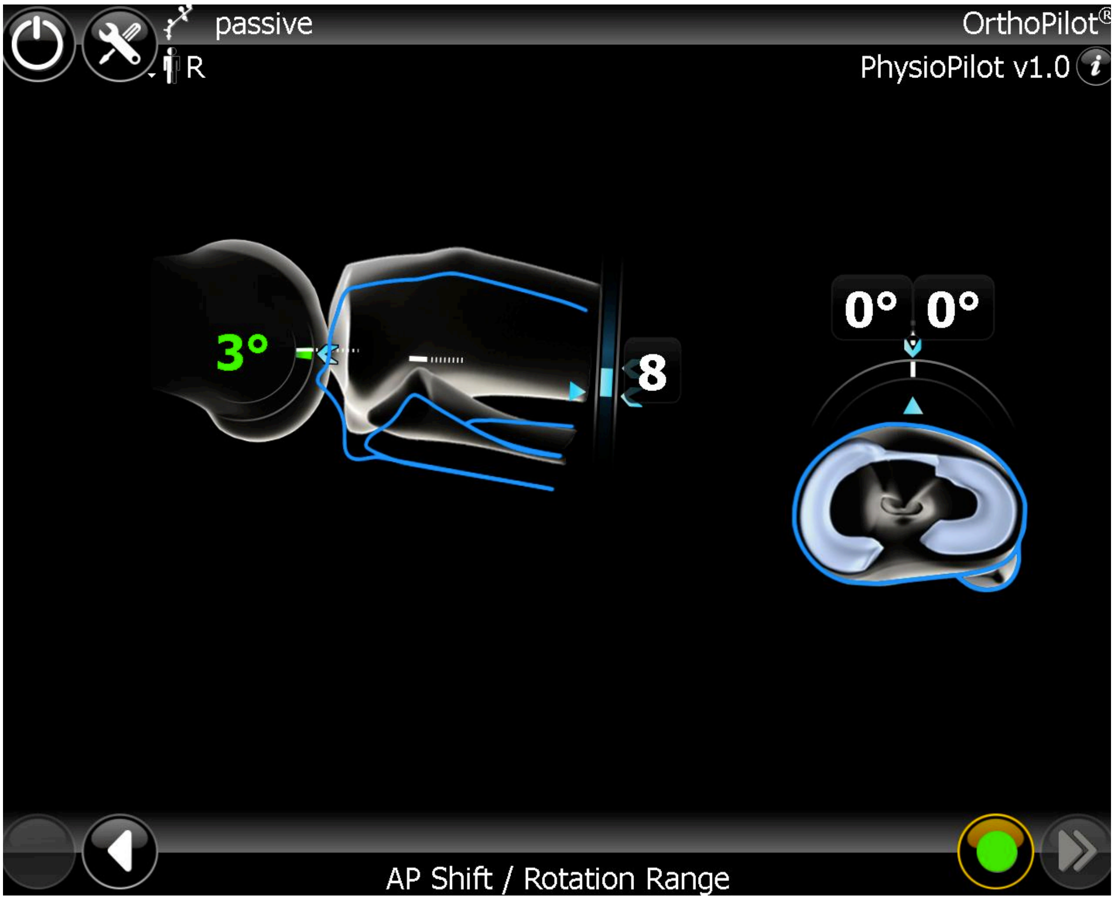

Figure 44 - 'AP Shift / Rotation Range' display screen.
From left to right, knee flexion angle (˚), anteroposterior tibial translation (mm), internal rotation (˚) and external rotation (˚) of the tibia are displayed.

It was not possible to remain blind to measurements of anteroposterior translation during this experiment. The knee flexion angle setup screen placed the flexion value in the space where the subsequent screen placed the anteroposterior tibial translation measurement. This would have required moving from the specimen to the screen to and obscuring the reading between each measurement. This was neither practical nor safe as it presented a contamination risk. Nonetheless the measurement was recorded on screen automatically as the maximum displacement that occurred during force application i.e. once force application ceased, the maximum displacement remained on screen. Furthermore, application of force involved stabilising the knee with one hand and applying a slow linear force perpendicular to the longitudinal axis of the tibia until a value of 100N was reached. During this time, the investigator was facing the transducer, not the screen. Once the prescribed force was reached, the transducer was removed and the displacement recorded.

It must be acknowledged that despite the lack of ability to control final measurement, complete blinding was not featured in this method.

Force application was carried out at 10˚ intervals from extension to 40˚; this was performed twice using the invasive method. Measurements were not performed beyond 40˚ owing to findings from the pilot study (section 2.10), which revealed that the system did not record anteroposterior translation beyond this angle of knee flexion. The limb was then re-registered using trackers mounted by fabric strapping followed and an identical protocol followed.

5.3.1 Statistical tests

ICC was used to test reliability. Repeatability coefficient was calculated to reflect precision of the invasive method and non-invasive method of tracker fixation separately. Values of anteroposterior translation at each flexion interval were compared between repeated runs of the protocol. Limits of agreement were calculated using the mean of repeated tests from each method of tracker fixation to analyse agreement between the methods. Details of these statistical methods are given in section 2.9.

5.4 Results

Reliability and precision within the individual invasive and non-invasive systems was acceptable throughout the range of flexion tested (mean ICC invasive 0.936, range 0.903 – 0.994, non-invasive 0.94, range 0.882 – 0.971). (Appendix 8.3)

Repeatability for both methods of tracker fixation were similar and within the acceptable limit of 3mm (Fig. 45).

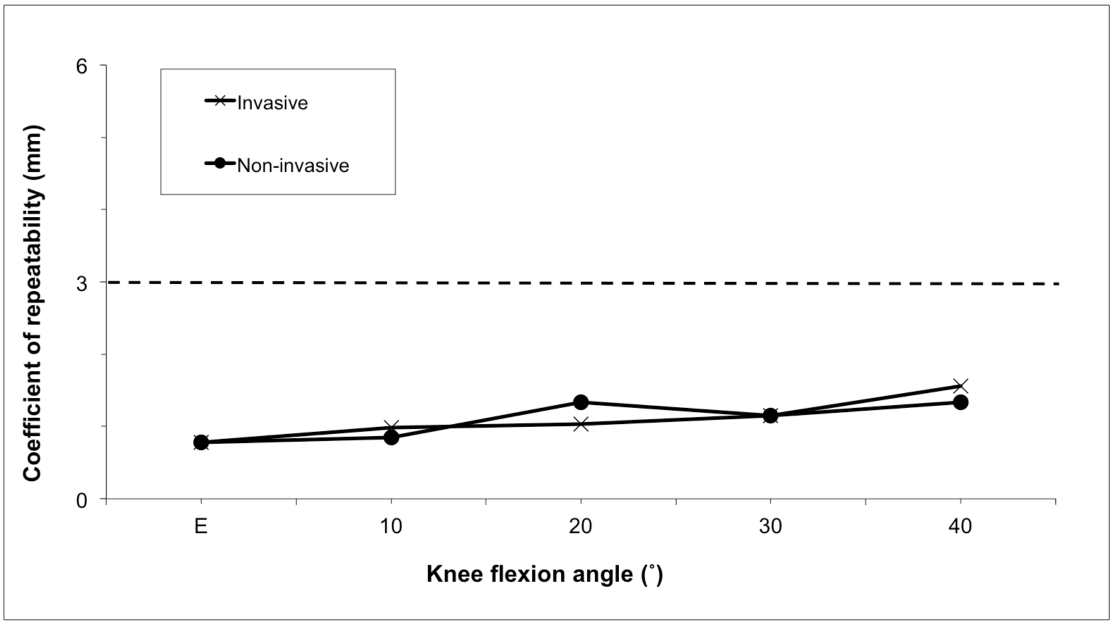

Figure 45 – Repeatability measuring AP translation

Agreement between the invasive and non-invasive methods of optical tracker fixation were acceptable throughout the range of flexion tested (Fig. 46).

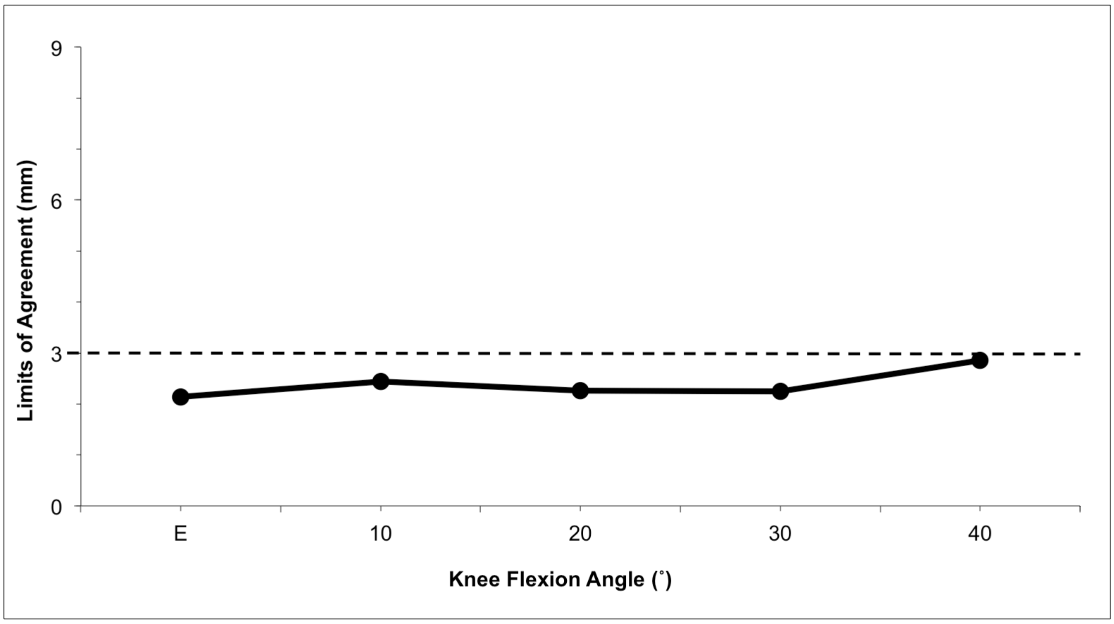

Figure 46 - Limits of agreement between invasive and non-invasive methods of tracker fixation when measuring anteroposterior tibial translation throughout knee flexion.

5.5 Discussion

From extension to 40˚ knee flexion, both devices display similarly good reliability and precision. From extension to 40˚, agreement between the devices is also acceptable. The validity of the non-invasive device has been demonstrated in the in vitro setting as it has demonstrated acceptable reliability, precision and accuracy between extension and 40˚. Further in vivo work should be carried out to further validate the device, as this range of knee flexion is highly relevant to a number of clinical tests including the Lachman test, and is a useful range for demonstrating dynamic weight bearing stability in early flexion such as squatting, ascending or descending a step when patients with anterior cruciate insufficiency often report feelings of 'giving way'.

Limitations of this experiment include use of cadaveric tissue which lacks muscle tone, and has different tissue properties to the in vivo setting. This may be particularly important in determining the influence of soft tissue artefacts. The experiment setup in terms of limb suspension and securing knee flexion angle will alter kinematics of the lower limb although this was necessary to allow a single investigator to perform testing. It was also not possible to simulate a weight bearing or load-bearing scenario using this setup. Nonetheless, these limitations are characteristic to in-vitro validation of devices and such experimental work is very important before progressing to reliability testing in vivo, where comparison of kinematic measurement is either not attempted, or involves consequential intervention such as invasive placement of markers, or ionising radiation. There is also potential for bias owing to lack of complete blinding during this experiment. Reasons to justify this are given in section 5.3. It was felt that during the experiment, as the investigator could only observe readings from the hand-held dynamometer, and because the device records maximum anteroposterior tibial displacement; that opportunity to influence the results was minimal.

From extension to 40˚, the results of reliability, precision and agreement are favourable for the non-invasive method of tracker fixation compared to the non-invasive devices summarised in sections 2.5.5 and 2.5.6. Generally these devices provide a reliability (ICC) of 0.6 (Branch et al., 2010; Kuroda et al., 2012). Concerns have been raised over accuracy of the most popular clinical devices such as the KT-1000 (Daniel et al., 1985; Forster et al., 1989; Graham et al., 1991; Wiertsema et al., 2008).

Anteroposterior laxity rather than rotatory laxity is the most reliable kinematic indicator of cruciate ligament integrity. Despite this, recent studies focus on non-invasive quantification of rotatory laxity as a means of diagnosing cruciate pathology (Almquist et al., 2002; Lorbach et al., 2009; Branch et al., 2010; Alam et al., 2011; Almquist et al., 2011; Lorbach et al., 2012; Alam et al., 2013). Increase in anteroposterior laxity in the presence of cruciate pathology may represent a more measurable parameter, both in terms of the change in sagittal vs. axial laxity, and in ability of non-invasive devices to detect displacement. Increase in anterior translation following sectioning of the cruciate ranges in the literature from 2-14.4mm using various methods of force application and measurement (Noyes et al., 1991; Isberg et al., 2006; Oh et al., 2011; Christel et al., 2012). Difference between normal and knees with anterior cruciate rupture measured using radiostereometric analysis were 7.4mm (2.2-17.4) in a study of 22 patients by Isberg et al. (2006), whereas sectioning of the anterior cruciate has been shown in biomechanical studies to increase internal rotation only between only 2-4˚ with the knee in early flexion (20˚ - 30˚) (Lipke et al., 1981; Nielsen et al., 1984; McQuade et al., 1989; Lane et al., 1994; Andersen et al., 1997; Diermann et al., 2009). The posterior cruciate ligament is even less involved in rotatory stability, only demonstrating significant effect at 90˚ knee flexion (Gollehon et al., 1987; Grood et al., 1988). Furthermore, reconstruction of the anterior cruciate ligament may not restore rotational kinematics (Georgoulis et al., 2007). Non-invasive devices assessing tibial rotation with an aim of detecting cruciate ligament pathology or dysfunction would have to be very sensitive compared to those detecting anteroposterior instability. Reliability of current devices used to quantify rotational laxity is relatively low and such devices are not routinely used in clinical practice, with the vast majority still in pre-clinical development (Branch et al., 2010). Until more sensitive means of analysing tibial rotation are available, it may be more useful to detect anteroposterior instability for diagnosis of cruciate pathology and develop means of assessing rotatory stability in a dichotomous manner to evaluate surgical reconstruction of the cruciate ligaments. The pivot shift phenomenon has been mapped and characterised using invasive navigation based technology allowing comparison of anterior cruciate reconstruction techniques (Lane et al., 2008; Pearle et al., 2009; Bedi et al., 2010; Musahl et al., 2011; Suero et al., 2011), however a non-invasive adaptation of this has not yet tested in the clinical setting. The pivot shift is a more dynamic test representing functional stability, and should this non-invasive means of optical tracker fixation prove reliable and accurate, it may be possible to 'map' the pivot shift in an out-patient setting, in a similar manner to that discussed (section 2.5.8.7).

The data in this study suggests that further in vivo validation be carried out as this method of quantifying anteroposterior translation may represent a reliable adjunct to clinical examination both in diagnosis of cruciate injury, and when following up patients. The Lachman test remains one of the most sensitive tests for cruciate insufficiency (Torg et al., 1976; Daniel et al., 1985; Donaldson et al., 1985; Zarins et al., 1986; Mitsou et al., 1988), yet it cannot be used to evaluate anteroposterior translation of the tibia as a continuous variable. Should the non-invasive method of tracker fixation method prove valid in vivo, it would provide a useful adjunct to clinical examination aiding diagnosis of cruciate pathology. A method of quantifying the forces applied during examination would increase knowledge of 'normal' laxity, allow standardisation of examination technique and permit comparison of surgical results between practitioners.

5.6 Conclusion

In the in vitro setting, the non-invasive method of tracker fixation proved as reliable and precise as the invasive method in measuring anteroposterior tibial translation, and demonstrated acceptable agreement within diagnostically applicable limits from knee extension to 40˚ knee flexion.

6 Non-invasive measurement of tibial rotation

6.1 Introduction

Assessment of rotational laxity conveys information about the integrity of both the capsular and cruciate ligaments, as outlined in section 2.5.7. At present, devices quantifying rotational laxity are limited in terms of reliability and accuracy, as discussed in section 2.5.7.2. Image-free navigation technology used during surgery can quantify tibial rotation, however this cannot be used in the out-patient setting owing to the invasive nature of tracker fixation.

The primary aim of this experiment was to determine the reliability and repeatability of both the invasive and non-invasive methods of tracker fixation in quantifying tibial rotation, and determine agreement between these two methods.

6.2 Materials and methods

6 male and 6 female cadaver lower limbs were used. Average age 80.5y (65 – 96y).

As discussed in section 3.7, the proposed method for quantifying rotational force was not possible due to equipment failure. The experiment was carried out using manual stress to end of range.

General specimen testing conditions and pre-conditioning was identical to that described in section 4.2. The specimens were mounted with the femur suspended in a manner similar to that described in section 3.4. The foot however was not secured but supported manually to allow rotation of the tibia.

The following experiment was carried out firstly using invasively mounted trackers, then non-invasive mounted of trackers. Trackers were mounted in the exact same manner as that described in the previous experiments (section 2.8.1). Following registration, the following tests were performed at 10° intervals from extension to 90°. Full internal

rotation to end of range was performed, with care to maintain the flexion angle, then external rotation. During testing, the investigator used one hand to support the knee, whilst the other hand exerted rotatory force to end of range in the same manner as clinical testing of rotational laxity. On performing tests with the knee at 90˚, the protocol was repeated a second time using the same method of tracker fixation, and the experiment repeated.
As in previous chapters, reliability and repeatability of results from each method of tracker fixation were tested using ICCs and repeatability coefficient respectively (section 2.9). LOA were calculated to assess agreement of results between the two methods of tracker fixation.

6.3 Results

ICC were acceptable measuring internal rotation using both the invasive and non-invasive methods of optical tracker fixation, mean & range ICCs 0.929 (0.86 – 0.99) for invasive fixation, 0.94 (0.9 – 0.99) for non-invasive fixation. ICCs were acceptable measuring external rotation using the invasive method of optical tracker fixation: 0.94 (0.86 – 0.99). All but one set of repeated measurements using the non-invasive method to measure external rotation were acceptable, this measurement was taken at 90˚ knee flexion (ICC 0.7). Measurements of external rotation taken using the non-invasive method from extension to 80˚ knee flexion were acceptable. Overall, from extension to 90˚ knee flexion measuring external rotation using the non-invasive method, ICC mean and range: 0.9 (0.7 – 0.98). 95% confidence intervals and individual ICC values for each repeated measurement are included in the appendices (Appendix 8.4). Repeatability coefficients for measuring internal and external rotation were similar throughout the range of knee flexion for both the invasive and non-invasive methods of tracker fixation and did not appear to worsen significantly with increasing knee flexion (Figs. 47 & 48). Invasive optical tracker fixation was superior to non-invasive in repeatability measuring both internal and external rotation by an order of approximately 1˚ in terms of mean repeatability coefficient (Table 11).

Table 11 – Repeatability coefficient measuring internal and external rotation

		Repeatability Coefficient (˚)	
		Invasive	Non-invasive
External Rotation	Mean Range	2.3 1.3 - 4.8	3.5 1.8 - 6.6
Internal Rotation	Mean Range	2.4 1.3 - 3.7	3.4 2.1 - 4.6

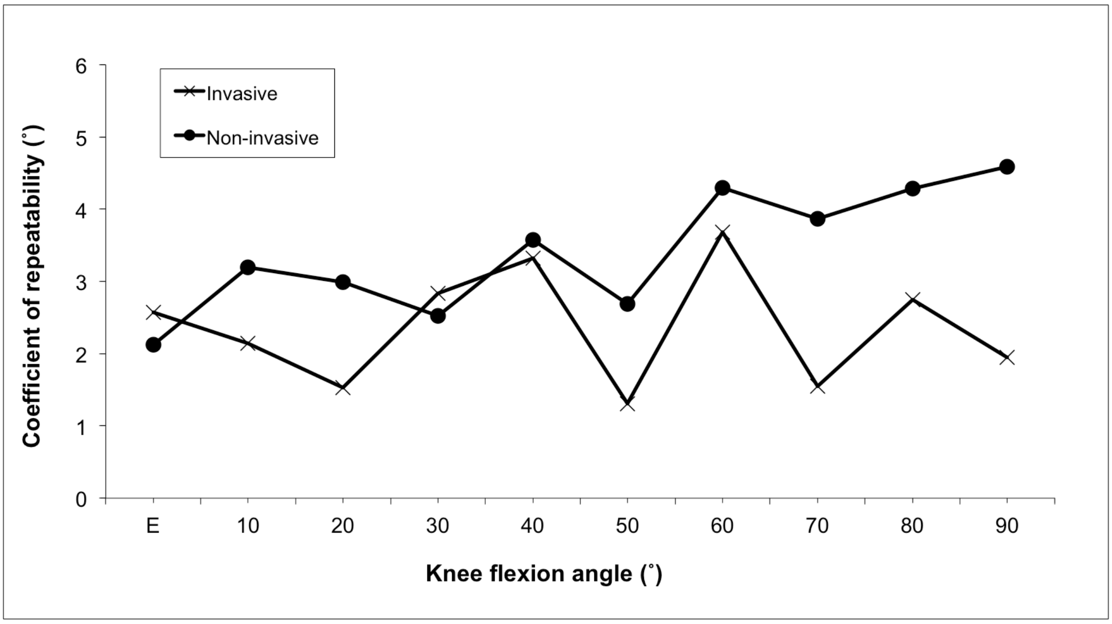

Figure 47 – Graph illustrating repeatability coefficients measuring internal rotation throughout flexion.

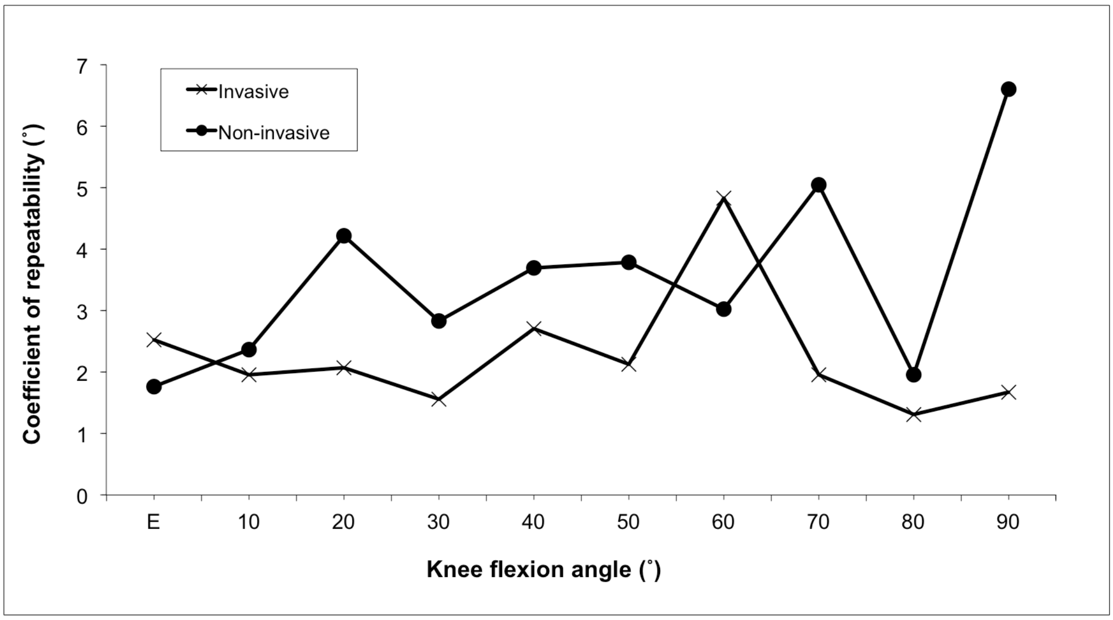

Figure 48 – Graph illustrating repeatability coefficients measuring external rotation throughout flexion

Agreement was slightly better measuring external rotation rather than internal rotation (Table 12, Fig. 49). Whilst agreement between the invasive and non-invasive methods of optical tracker fixation measuring external rotation were similar throughout the range of flexion, agreement measuring internal rotation was poor from extension to 30˚ knee flexion, and improved during flexion of the knee to similar levels seen measuring external rotation (Fig. 49).

Table 12 – Limits of agreement mean and range measuring internal and external rotation

		Limits of agreement (˚)
External Rotation	Mean	7.4
	Range	4.3 - 9.4
Internal Rotation	Mean	9.0
	Range	6.1 - 13.5

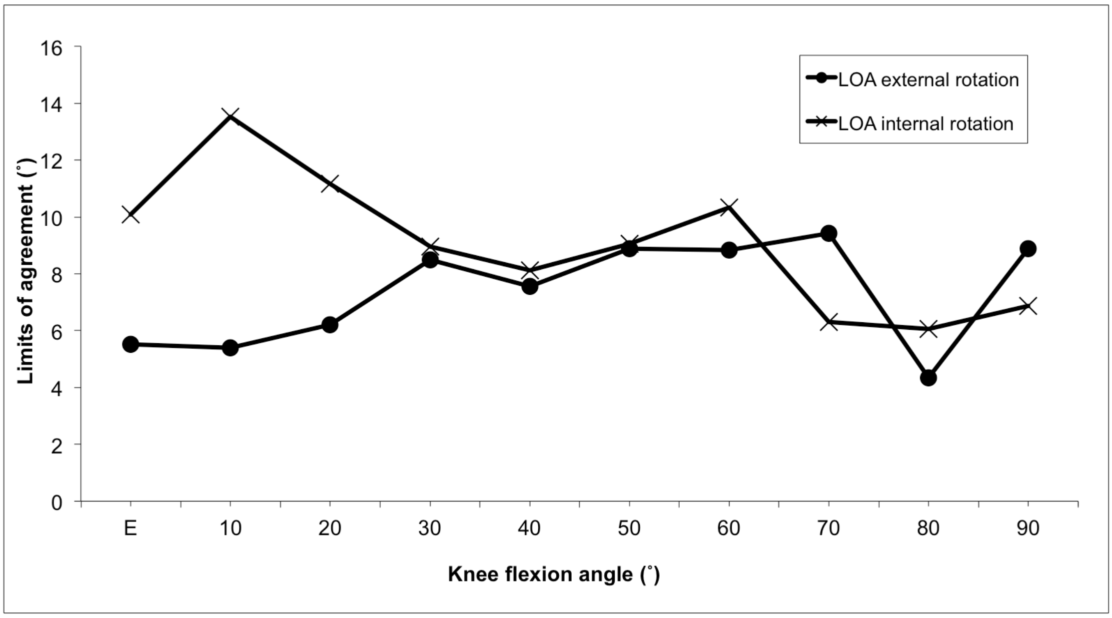

Figure 49 – Graph illustrating limits of agreement measuring internal and external rotation during flexion

6.4 Discussion

Reliability of measurement was acceptable for both methods of tracker fixation measuring internal rotation and external rotation, with one exception being non-invasive measurement of external rotation at 90˚, which gave borderline reliability (ICC 0.7).

Limitations of our methodology include use of cadaveric specimens; use of fresh cadavers is expensive and limits time available prior to irreversible degradation of the material when used for extensive testing at room temperature. However efforts were made to keep testing conditions consistent regarding tissue characteristics, specifically keeping temperature constant and use of a motion protocol to minimise soft-tissue creep during testing. The major limitation to this experiment is a lack of standardised force application despite attempts made to implement this (section 3.7). However, use of 'end of range feel' on manual testing, as is used in clinical practice has proven to be reliable when testing rotational laxity of the knee; Almquist et al (2011) used 'end feel', one week apart to measure internal and external tibial rotation at 30˚, 60˚ & 90˚ of knee flexion. Reliability of measurement was (ICCs) 0.82, 0.76 & 0.65, conveying reasonable reliability without standardising torque application at 30˚ and 60˚. In this cadaver experiment, the lack of standardised force application affects both invasive and non-invasive measurement of tibial rotation. Despite this, slightly superior repeatability is observed using the invasive system, implying that movement artefacts may be further decreasing repeatability when using the non-invasive system (Table 11, Fig. 47 & 48). These movement artefacts may come from the soft-tissue, they may also be simply due to the non-rigid fixation of optical trackers when using non-invasive attachment compared to optical trackers being secured using bone screws. Unlike invasive and non-invasive measurement of MFTA, the trend of poorer repeatability with increasing knee flexion is not as apparent. That mean precision of the invasive system in terms of repeatability was acceptable is reassuring given the presence of experimental error in terms of limited control of force application during testing. Agreement is uniformly unacceptable between the methods of tracker fixation when measuring both internal and external rotation throughout the range of knee flexion. Mean limits of agreement including internal and external rotation together were 8.2˚ (range 4.3˚ – 13.5˚). Progression of flexion did not appear to improve or reduce agreement significantly. The limits of agreement are more than twice the repeatability coefficients for each method of tracker fixation (Table 11) demonstrating the importance of quantifying accuracy despite satisfactory reliability and repeatability in measurement.

Reliability, repeatability and agreement are favourable compared to non-invasive devices reported in the literature, many of which measure foot angle to represent rotation at the knee and therefore overestimate total tibial rotation by 20 – 30˚, in some cases recording 200% of the actual range of motion depending on the amount of torque used as a result of excursion of the foot and ankle during testing (Almquist et al., 2002; Lorbach et al., 2009; Alam et al., 2011; Almquist et al., 2011; Lorbach et al., 2012; Alam et al., 2013; Almquist et al., 2013). Reliability of such devices is summarised as 'moderate' (ICC 0.6) in a comprehensive review by Branch et al of recent clinical and biomechanical research systems (Branch et al., 2010). One of the major advantages of the invasive and non-invasive methods of optical tracker fixation is that they measure tibial rotation alone, and do not measure position of the foot as a surrogate of tibial rotation. A further advantage is simultaneous quantification of knee flexion, a feature which is missing from other devices, requiring use of a handheld goniometer to determine knee flexion angle (Musahl et al., 2007; Tsai et al., 2008). Robotic systems have been shown to be very reliable in terms of inter-tester and between test reliability, however validation details are not given in the literature and these devices may be best suited to dichotomous comparison at present (Park et al., 2008; Branch et al., 2010). Furthermore, these devices are not suitable for clinical use due to expense, lack of accuracy and expertise required.

The 'Vermont knee laxity device' was initially presented as a method of measuring anteroposterior displacement, however this remained laboratory based (Uh et al., 2001).

No literature was available validating the device for discrete measurement of internal and external tibial rotation. Reliability of the device ranged from (ICC) -0.28 to 0.92.

The methodology described by Lorbach et al (Lorbach et al., 2009) in validating the 'Rotameter' is interesting as simultaneous use of invasive navigation as the gold-standard comparison permitted use of manual, un-quantified rotational torque. This method allowed detection of gross over-estimation of tibial rotation by the 'Rotameter' of up to 42˚ in combined internal and external rotation, despite correlation coefficients of 0.9 – 0.95 between results from the two systems. These results are inferior to the non-invasive method of tracker fixation used in this study in terms of accuracy. The method is interesting, however it would require the use of two OrthoPilot systems simultaneously analysing the invasive and non-invasively mounted trackers; one using passive optical trackers, the other using active. Indeed, this method could be applied to validation of the non-invasive method in measuring MFTA, AP translation and tibial rotation. The poor reliability demonstrated in validating the ' Rotameter', and in further clinical testing (Lorbach et al., 2009), limits use of the system as a means of dichotomous comparison of rotatory laxity in an individual. More recently however, Alam et al (2013) report very encouraging agreement of a non-invasive device measuring tibial rotation at 30˚ & 90˚ to within 2˚ when compared to measurements taken using electromagnetic, non-invasive 'nest of birds' sensors. This device includes a femoral clamp, tibial splint with paired inclinometers, and a boot used to apply standardised torque.

One significant advantage of the non-invasive method of optical tracker fixation over previously reported devices (Almquist et al., 2002; Lorbach et al., 2009; Alam et al., 2011; Almquist et al., 2011; Lorbach et al., 2012; Alam et al., 2013; Almquist et al., 2013) is the lack of equipment attached to the patient, allowing full weight bearing in extension and early flexion (Clarke 2012; Clarke et al., 2012; Clarke et al., 2012). Patients often describe symptomatic rotatory laxity in this range on weight bearing when stepping off a kerbside for example (Carson 1988; Engle et al., 1989) yet most devices measuring laxity require the patient to be seated and / or have not been validated in the range of 0° - 30° knee flexion.

Although standardisation of torque during testing of rotational laxity has been widely reported in scientific literature (Almquist et al., 2002; Park et al., 2008; Lorbach et al., 2009; Branch et al., 2010; Alam et al., 2013) it is rarely used in current clinical practice. Should 'end of range feel' prove reliable (Almquist et al., 2011), it would minimise equipment cost. Furthermore, functional testing on weight bearing and quantifying bony displacement of the bony anatomy during manoeuvres such as the pivot shift may be more clinically relevant than simply reporting range of rotatory motion (Kocher et al., 2004; Lane et al., 2008).

Standardisation of torque applied during testing of rotational laxity is desirable to help create grading of rotational laxity and ease communication of examination findings between clinicians (Branch et al., 2010). It would also allow direct comparison of surgical reconstruction methods used to re-create rotational stability, including cruciate and capsular ligament reconstruction. Further blinded, multiple investigator studies must be performed in-vivo to analyse reliability of this non-invasive device using both clinical 'end range feel' and standardised torque application.

A question remains over the diagnostic role of simply testing rotation to detect cruciate ligament pathology. Detection of rotational laxity is relied upon in diagnosis of posterior cruciate and posterolateral capsular injury. A further feature of posterior cruciate ligament injury is posterior 'sag' of the tibial tuberosity when compared to the contralateral limb. It is much easier to observe differences between limbs in terms of rotational laxity using manually applied torque on simultaneous dichotomous testing such as the dial test, as the direction of the feet indicates disparity in a manner that is easy to appreciate. No such visual cues help in diagnosis of anterior cruciate pathology, and no tests of pure tibial rotation are used to diagnose anterior cruciate pathology in clinical practice. The pivot shift test depends partly on rotational laxity present with anterior cruciate injury, however the diagnostic ‘clunk’ depends on reduction of the tibiofemoral articulation (Liu et al., 1995). Biomechanical studies indicate that the cruciate ligaments are not the dominant determinant of rotational laxity; the structures responsible for limiting rotation of the tibia in the axial plane include the lateral, posterolateral, medial, posteromedial capsule, cruciate ligaments and the menisci with dynamic/active restraint provided by the muscles crossing the knee (Markolf et al., 1976; Lipke et al., 1981; Shoemaker et al., 1985; Gollehon et al., 1987; Louie et al., 1987; Grood et al., 1988; More et al., 1993; Fu et al., 1994; Bodor 2001; Amis et al., 2003; Robinson et al., 2004). Sectioning of the medial collateral ligament increases internal rotational laxity much more dramatically than sectioning of the anterior cruciate (Lipke et al., 1981; Fu et al., 1994). The posterolateral capsular structures slant posteriorly as they pass distally, internal rotation slackens them whereas external rotation tightens them (Amis et al., 2003); biomechanical studies have shown that these capsular elements are the major restraint to external rotation of the tibia and sectioning the posterior cruciate ligament has little effect on external rotatory laxity at low flexion angles (Gollehon et al., 1987; Grood et al., 1988; Veltri et al., 1995; Veltri et al., 1996).

Recent attempts have been made to relate the use of rotational laxity testing devices to cruciate ligament status (Almquist et al., 2002; Lorbach et al., 2009; Branch et al., 2010; Alam et al., 2011; Almquist et al., 2011; Lorbach et al., 2012; Alam et al., 2013). Where methods of examination used routinely in clinical practice give a sensitivity of 95% in detecting anterior cruciate pathology (Torg et al., 1976; Donaldson et al., 1985; Zarins et al., 1986; Mitsou et al., 1988; Liu et al., 1995), the role of establishing rotatory laxity using specialised devices for diagnostic purposes is unclear. Such devices would be of use to those specialising in reconstruction of capsular injuries such as injury to the posterolateral corner. Furthermore, rotational laxity is an important prognostic parameter following treatment of cruciate injury. Kocher et al (2004) examined 202 patients undergoing anterior cruciate ligament reconstruction 2 years following surgery; anteroposterior laxity was not associated with any symptom reporting or poor function ($p>0.05$), however pivot shift, which may be a more functional representation of stability, was associated with poor satisfaction, giving way and limitation of activities, including sports ($p<0.05$). Following cruciate injury with or without reconstruction, rotational laxity, not anteroposterior laxity alone may be responsible for accelerated joint destruction and symptomatic instability (Stergiou et al., 2007; Branch et al., 2010). Rotational stability is therefore very important in terms of prognosis and deciding if further intervention is needed following operative or non-operative treatment of cruciate injury to be able to assess the ability of the knee soft-tissues to resist rotational moments in a quantitative manner with minimal consequence to the patient. The ability to quantify rotational laxity could help surgeons determine which methods of soft-tissue reconstruction confer optimum functional biomechanics in the long-term. Further development of non-invasive systems may allow mapping of the pivot shift test such as that reported using invasive intra-operative navigation systems (Lane et al., 2008), this may be able to more closely represent functional integrity of the cruciate ligaments (Kocher et al., 2004) and prove a more relevant tool for prognostic and post-operative evaluation purposes.

6.5 Conclusion

This non-invasive adaptation of image-free navigation technology can quantify rotational laxity of the knee with similar and in some cases superior accuracy to other devices reported in the literature. Advantages include use of a system most specialists are familiar with without the need for extra equipment which may allow weight bearing assessment of knee kinematics, direct measurement of tibial rotation and knee flexion angle. Further study is required to assess the reliability of this device between users, including in-vivo validation during passive examination and weight bearing.

7 Overall discussion

Determination of lower limb kinematics relevant to clinical practice covers a wide area of ongoing research. Accurately establishing lower limb alignment parameters and displacement of the bony anatomy is currently limited to imaging techniques, most of which are static, and non-invasive techniques are currently limited in terms of accuracy required for surgical planning. Adaptation of optical tracker technology used in computer aided surgery aims to overcome these problems. Clarke (2012) has reported development and initial validation of this technology, and demonstrated satisfactory repeatability in measuring lower limb alignment in extension, both supine, standing and under stress testing however no data exists validating this technique in early flexion of the knee. Furthermore, this technology can be used to quantify anteroposterior tibial displacement and tibial rotation. No data exists in the literature to date validating these uses. During review of the literature, validation studies were appraised regarding strengths and weaknesses in testing procedure and analysis. One such study by Lorbach et al. (2009) used a commercially available computer assisted surgery system as the ‘gold-standard’. A pilot study was then developed to evaluate reliability, repeatability and agreement of the non-invasive method with commercial navigation.

7.1 Pilot Study

The pilot study used purposefully limited resources in terms of cadaveric material, using embalmed cadavers only. Due to the minimally invasive nature of dissection required and ability to perform prolonged experiments without detrimental degradation of the specimens, the experiments could be performed yet the specimens would remain suitable for further use. One of the aims of this study was to determine whether strapping material affected measurement precision and accuracy. Throughout the pilot study, fabric rather

than rubber strapping provided superior reliability, precision and accuracy in measuring kinematic parameters. Rubber strapping was abandoned for subsequent experiments.
The non-invasive method of optical tracker fixation proved to be reliable and repeatable measuring mechanical femorotibial alignment in the coronal plane (MFTA) with and without stress from extension to 50˚ knee flexion, however agreement with the invasive CAS system was only acceptable in extension and 30˚ with and without coronal stress testing. Repeatability during anteroposterior stress testing was satisfactory in extension only for the non-invasive fabric strap method, however agreement with the invasive method was unacceptable throughout flexion. The non-invasive method gave acceptable repeatability but borderline agreement measuring sagittal alignment, and promising repeatability and agreement measuring internal and external rotation of the tibia.
The pilot study demonstrated promising results despite major methodological flaws. It was therefore feasible to progress to a more intensive study requiring much more time and more resources.

7.2 Methodology development

The major methodological weaknesses were identified and corrected where possible. Resources were secured to allow testing of 12 fresh limbs. Experiment set up and registration was optimized from a series of small trial experiments leading to improved, more consistent limb positioning and registration protocol. It was found that registering the epicondyles with the knee at 45˚ flexion conveyed the best agreement between the invasive and non-invasive methods of tracker fixation.
Further protocols were developed successfully to incorporate force application for any stress maneuvers, however the method developed for standardising rotational laxity could not be employed due to repeated failure of the device designed to support the foot;

rotational torque on the tibia could therefore not be standardized, however ‘end of range feel’ has been shown to be reliable between tests (Almquist et al., 2011).

7.3 Non-invasive measurement of coronal mechanical alignment in early flexion

Repeatability of the non-invasive method of optical tracker fixation has been demonstrated to be satisfactory measuring MFTA in extension with and without stress. This experiment confirmed that conclusion, and added validation in early flexion. The non-invasive method was reliable, precise and accurate measuring MFTA from extension to 40˚ with no coronal stress applied to the lower limb, and from extension to 30˚ when 15Nm varus or valgus moment was applied to the lower limb. This technology has significant potential in determining ‘normal’ static and dynamic lower limb mechanical alignment in population subgroups, identifying those at risk of developing osteoarthritis (section 4.4.1), assessing and planning in total knee arthroplasty (section 4.4.2), and capsular injury of the knee including assessment of collateral ligament injury (section 4.4.3). Non-invasive measurement of sagittal alignment did not quite meet the criteria set of LOA <3˚, but remained far superior to visual and handheld goniometer assessment. Determining flexion contracture of the knee, and range of motion before surgery is vital to planning and can influence decision between unicompartmental and bicompartmental total knee arthroplasty, as well as being the best predictor of post-operative range of motion (Nelson et al., 2005; Ritter et al., 2007; Su 2012).

7.4 Non-invasive quantification of anteroposterior laxity of the knee

Using standardised force application, the non-invasive method of optical tracker fixation provided acceptable reliability, precision and accuracy in measuring anteroposterior translation from extension to 40˚ knee flexion. This has important clinical uses including diagnosis of cruciate pathology, follow-up and evaluation of different surgical repair techniques, and potential for allowing non-invasive assessment of more functionally representative kinematic parameters such as the pivot shift test, and displacement in the sagittal plane on weight bearing and early flexion. Further in-vivo reliability testing is required, however these data add for the first time an assessment of the reliability, precision and accuracy of the non-invasive method in assessing anteroposterior laxity of the knee.

7.5 Non-invasive quantification of tibial rotatory laxity

The non-invasive method of tracker fixation demonstrated superior reliability, precision and agreement to many devices reported in the literature (Almquist et al., 2002; Lorbach et al., 2009; Branch et al., 2010; Alam et al., 2011; Almquist et al., 2011; Lorbach et al., 2012; Alam et al., 2013; Almquist et al., 2013). This experiment was limited by a lack of standardised force application, however results were encouraging. Advantages of the non-invasive method of optical tracker fixation in measuring tibial rotation include measurement of the tibial rotation as many devices measure excursion of the foot, and the ability to simultaneously measure knee flexion angle as some devices require concomitant use of a handheld goniometer. Tibial rotatory laxity has been studied in depth recently with suggestions that non-invasive devices able to quantify this parameter may be able to convey information regarding cruciate ligament integrity (Almquist et al., 2002; Park et al., 2008; Lorbach et al., 2009; Branch et al., 2010; Alam et al., 2013). A further and possibly more direct use of such devices would be assessment of capsular integrity in the knee, particularly assessment of posteromedial and posterolateral corner injury, and evaluation following surgery. The ability to accurately quantify tibial rotation in a non-invasive manner is crucial in development of non-invasive quantification of pivot shift as discussed above (sections 5.5 & 6.4).

7.6 Final conclusion

Developers of image-free navigation technology have from the outset sought to marry pre-operative examination and planning to intra-operative processes (Picard 2007). Currently, during the patient journey through knee reconstruction, especially in conventional arthroplasty the intra-operative plan is usually based on subjective examination, short or long-leg radiographs and knowledge of intra-operative ‘targets’ such as neutral mechanical alignment of the lower limb. When using CAS, intra-operative data is available to confirm acquisition of the alignment targets based on surgical planning, however deficiencies still exist in pre-operative determination of lower limb alignment.

Non-invasive navigation-based technology may offer a means to pre-operatively acquire discrete parameters used during computer–assisted and conventional arthroplasty, ligament reconstruction and osteotomy. By using a similar frame of reference to that used during computer-assisted surgery, and with standardisation of forces applied during examination and surgery, the potential exists to minimize subjectivity and increase communicability in every kinematic aspect of pre, and post-operative assessment and intra-operative intervention. The data presented in this thesis is the first to date to examine the reliability, precision and accuracy of the non-invasive method of optical tracker fixation by direct comparison with an invasive method of optical tracker fixation such as is used in commercial navigation in measuring coronal and sagittal mechanical alignment of the lower limb with and without stress, anteroposterior laxity and rotatory laxity during early knee flexion. The ability to quantify these parameters non-invasively has many important applications especially at a time when patient expectation in all areas of knee reconstruction is increasing, greater understanding of normal and pathological knee kinematics is crucial to developing surgical method.

8 Appendix

8.1 Pilot study intraclass correlation coefficients (chapter 2)

Measuring MFTA no applied stress

	Bone Screws			Fabric Strap			Rubber Strap		
	ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper		Lower	Upper
Extension	0.991	0.97	0.997	0.961	0.871	0.989	0.982	0.94	0.995
30	0.831	0.514	0.948	0.891	0.665	0.967	0.982	0.94	0.995
40	0.801	0.445	0.938	0.928	0.771	0.979	0.978	0.925	0.994
50	0.914	0.731	0.975	0.963	0.977	0.989	0.948	0.83	0.985
60	0.846	0.498	0.959	0.897	0.641	0.973	0.166	-0.485	0.698

Valgus stress

	Bone Screws			Fabric Strap			Rubber Strap		
	ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper		Lower	Upper
Extension	0.963	0.96	0.989	0.988	0.96	0.997	0.995	0.983	0.999
30	0.926	0.766	0.978	0.967	0.889	0.99	0.788	0.416	0.934
40	0.784	0.408	0.933	0.888	0.659	0.966	0.908	0.714	0.973
50	0.926	0.794	0.978	0.919	0.745	0.976	0.918	0.74	0.976
60	0.916	0.72	0.977	0.839	0.479	0.958	-0.456	-0.83	0.201

Varus stress

	Bone Screws			Fabric Strap			Rubber Strap		
	ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper		Lower	Upper
Extension	0.957	0.857	0.987	0.98	0.932	0.994	0.858	0.581	0.957
30	0.771	0.38	0.928	0.83	0.511	0.948	0.917	0.739	0.975
40	0.757	0.35	0.923	0.898	0.684	0.969	0.689	0.22	0.899
50	0.908	0.713	0.973	0.961	0.871	0.989	0.907	0.709	0.972
60	0.868	0.557	0.965	0.822	0.435	0.953	-0.218	-0.725	0.442

Anteroposterior translation

	Bone Screws			Fabric Strap			Rubber Strap		
	ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper		Lower	Upper
Extension	0.966	0.888	0.99	0.949	0.834	0.985	0.943	0.815	0.983
30	0.815	0.478	0.943	0.888	0.659	0.967	0.61	0.087	0.87
40	0.655	0.16	0.887	0.633	0.123	0.878	0.566	0.19	0.852

Measuring internal rotation

	Bone Screws			Fabric Strap			Rubber Strap		
	ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper		Lower	Upper
Extension	0.954	0.849	0.987	0.868	0.605	0.96	0.897	0.684	0.969
30	0.884	0.646	0.965	0.947	0.827	0.984	0.948	0.831	0.985
40	0.974	0.912	0.992	0.962	0.875	0.989	0.974	0.912	0.992
50	0.923	0.755	0.977	0.918	0.742	0.976	0.971	0.902	0.991
60	0.843	0.544	0.952	0.865	0.599	0.959	0.826	0.502	0.947

Measuring external rotation

	Bone Screws			Fabric Strap			Rubber Strap		
	ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper		Lower	Upper
Extension	0.876	0.626	0.963	0.875	0.625	0.962	0.934	0.788	0.981
30	0.715	0.268	0.909	0.981	0.936	0.995	0.886	0.652	0.966
40	0.904	0.701	0.971	0.946	0.823	0.984	0.855	0.573	0.956
50	0.991	0.97	0.997	0.975	0.916	0.993	0.935	0.791	0.981
60	0.681	0.205	0.896	0.679	0.202	0.896	0.673	0.192	0.894

Measuring maximum extension

Bone Screws			Fabric Strap			Rubber Strap		
ICC	95% confidence limits		ICC	95% confidence limits		ICC	95% confidence limits	
	Lower	Upper		Lower	Upper		Lower	Upper
0.989	0.964	0.997	0.973	0.91	0.992	0.981	0.934	0.994

Measuring maximum flexion

Bone Screws			Fabric Strap			Rubber Strap		
ICC	Range		ICC	Range		ICC	Range	
	Lower	Upper		Lower	Upper		Lower	Upper
0.994	0.98	0.998	0.995	0.981	0.998	0.993	0.977	0.998

Measuring maximum extension

Bone Screws		Fabric Strap		Rubber Strap	
ICC	Range	ICC	Range	ICC	Range
0.989	0.964 - 0.997	0.973	0.91 - 0.992	0.981	0.943 - 0.994

Measuring maximum flexion

Bone Screws		Fabric Strap		Rubber Strap	
ICC	Range	ICC	Range	ICC	Range
0.994	0.98 - 0.998	0.995	0.981 - 0.998	0.993	0.977 - 0.998

8.2 Intraclass correlation coefficients for fresh cadaver Study: Non-invasive measurement of mechanical alignment in early flexion (chapter 4)

MFTA no stress, same registration

	Invasive			Non-invasive		
	ICC	95% C.I.		ICC	95% C.I.	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	1.000	1.000	1.000	0.990	0.955	0.998
10	1.000	1.000	1.000	0.989	0.947	0.998
20	0.992	0.964	0.998	0.936	0.746	0.985
30	0.982	0.924	0.996	0.979	0.909	0.995
40	0.991	0.959	0.998	0.955	0.814	0.990
50	1.000	1.000	1.000	0.966	0.858	0.992
60	0.987	0.945	0.997	0.984	0.933	0.996
70	1.000	1.000	1.000	0.981	0.917	0.996
80	1.000	1.000	1.000	0.978	0.907	0.995
90	1.000	1.000	1.000	0.965	0.855	0.992

MFTA no stress applied, 2 registrations

	Invasive			Non-invasive		
	ICC	95% C.I.		ICC	Range	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	0.988	0.958	0.996	0.950	0.838	0.985
10	0.984	0.941	0.996	0.988	0.955	0.997
20	0.987	0.957	0.996	0.971	0.904	0.992
30	0.987	0.955	0.996	0.971	0.903	0.992
40	0.980	0.933	0.994	0.983	0.941	0.995
50	0.967	0.889	0.990	0.935	0.791	0.981
60	0.982	0.937	0.995	0.902	0.696	0.971
70	0.964	0.880	0.989	0.796	0.435	0.937
80	0.957	0.858	0.987	0.885	0.651	0.966
90	0.967	0.888	0.990	0.785	0.409	0.933

MFTA 15Nm valgus stress

	Invasive			Non-invasive		
	ICC	95% C.I.		ICC	Range	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	0.989	0.962	0.997	0.995	0.983	0.999
10	0.988	0.957	0.997	0.995	0.982	0.999
20	0.996	0.986	0.999	0.988	0.958	0.996
30	0.996	0.988	0.999	0.994	0.980	0.998
40	1.000	1.000	1.000	0.984	0.947	0.995
50	0.993	0.977	0.998	0.950	0.837	0.985
60	0.997	0.989	0.999	0.957	0.858	0.987
70	0.997	0.988	0.999	0.979	0.930	0.994
80	1.000	1.000	1.000	0.989	0.962	0.997
90	0.995	0.984	0.999	0.964	0.879	0.989

MFTA 15Nm varus stress

	Invasive			Non-invasive		
	ICC	95% C.I.		ICC	Range	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	0.996	0.987	0.999	0.991	0.970	0.997
10	0.997	0.988	0.999	0.996	0.984	0.999
20	1.000	1.000	1.000	0.994	0.978	0.998
30	1.000	1.000	1.000	0.974	0.913	0.992
40	0.992	0.971	0.998	0.959	0.865	0.988
50	1.000	1.000	1.000	0.993	0.976	0.998
60	0.992	0.973	0.998	0.991	0.970	0.997
70	1.000	1.000	1.000	0.996	0.985	0.999
80	1.000	1.000	1.000	0.997	0.991	0.999
90	1.000	1.000	1.000	0.997	0.991	0.999

Measuring sagittal alignment

	Invasive		Non-invasive	
	ICC	95% CI	ICC	95% CI
Full extension	0.93	0.78 - 0.98	0.94	0.8 - 0.98
Full flexion	1.00	1.00 - 1.00	1.00	0.99 - 1.00

8.3 Intraclass correlation coefficients measuring anteroposterior translation (chapter 5)

Measuring anteroposterior translation

	Invasive			Non-invasive		
	ICC	95% confidence limits		ICC	95% confidence limits	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	0.958	0.862	0.988	0.96	0.868	0.988
10	0.918	0.726	0.977	0.971	0.898	0.992
20	0.919	0.744	0.976	0.882	0.642	0.964
30	0.957	0.859	0.987	0.948	0.832	0.985
40	0.903	0.699	0.971	0.941	0.808	0.983

8.4 Intraclass correlation coefficients measuring internal and external tibial rotation (chapter 6)

Internal Rotation

	Invasive			Non-invasive		
	ICC	Range		ICC	Range	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	0.892	0.670	0.968	0.985	0.946	0.996
10	0.888	0.630	0.969	0.979	0.922	0.994
20	0.982	0.940	0.995	0.966	0.885	0.990
30	0.889	0.660	0.967	0.966	0.888	0.990
40	0.872	0.617	0.961	0.935	0.791	0.981
50	0.982	0.940	0.995	0.954	0.849	0.987
60	0.862	0.590	0.958	0.905	0.705	0.972
70	0.988	0.958	0.996	0.907	0.711	0.972
80	0.962	0.873	0.989	0.908	0.713	0.973
90	0.970	0.899	0.991	0.898	0.685	0.969

External Rotation

	Invasive			Non-invasive		
	ICC	Range		ICC	Range	
Flexion (˚)		Lower	Upper		Lower	Upper
Extension	0.863	0.594	0.959	0.973	0.909	0.992
10	0.917	0.723	0.977	0.932	0.768	0.981
20	0.952	0.841	0.986	0.853	0.568	0.955
30	0.980	0.932	0.994	0.896	0.681	0.969
40	0.948	0.830	0.985	0.907	0.711	0.972
50	0.942	0.813	0.983	0.928	0.769	0.979
60	0.867	0.603	0.960	0.954	0.848	0.986
70	0.972	0.906	0.992	0.915	0.734	0.975
80	0.991	0.970	0.997	0.980	0.931	0.994
90	0.990	0.964	0.997	0.703	0.245	0.904

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