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Assessment of Coronal Mechanical Alignment with Applied Varus and Valgus Force Through the Range of Flexion Using Non-invasive Navigation

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This thesis is the result of the author’s original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.

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CONFLICT OF INTEREST STATEMENT

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ABSTRACT

Osteoarthritis of the knee is a highly prevalent disease, with total knee arthroplasty (TKA) a proven means of alleviating symptoms. In image-free knee navigation, infra-red markers are attached to bony landmarks to provide kinematic data during the TKA procedure, with the aim of improving the precision of implant placement. In non-invasive navigation, infra-red markers are attached to the skin surface; recent evidence suggests that this can give reliable measurements of lower limb mechanical alignment. The aim of this thesis was to evaluate the use of a non-invasive navigation system in the assessment of mechanical alignment with applied coronal force through the range of flexion.

A previously validated non-invasive system (Physiopilot) was tested on 23 volunteers with healthy knees. 2 users performed 2 registrations of the software workflow on each participant's right and left knees. A force was manually applied to the end-point of varus and valgus knee laxity and the measured change in mechanical alignment was recorded. Force was applied with the knee positioned in increments of flexion from 0°-90°.

In keeping with previous studies, satisfactory values of CR (Coefficient of Repeatability) of 1.55 and 1.33 were found for intra-observer repeatability in measurement of supine Mechanical Femoro-tibial Angle (MFTA) in extension, with a good inter-observer correlation of ICC (Intraclass Correlation Coefficient) 0.72. However, when flexion was introduced, intra-observer and inter-observer reliability fell outwith acceptable limits. The trial therefore did not support the Physiopilot system as a measure of MFTA when flexion is introduced. It was felt that learning-curve, soft tissue artefacts and lack of force standardisation equipment may have accounted for significant levels of error, with further studies required to address these issues.

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LIST OF ACRONYMS

ACL Anterior cruciate ligament
AKSS American Knee Society Score
AP Antero-posterior
ASTM American Society for Testing and Materials
BMI Body mass index
CAOS Computer assisted orthopaedic surgery
CI Confidence interval
CT Computed tomography
FAA Femoral anatomical axis
FAD Force application device
FMA Femoral mechanical angle
FMA angle Femoral mechanical anatomical angle
HTO High tibial osteotomy
IR Infrared
IM Intra-medullary
LCL Lateral collateral ligament (of the knee)
MCL Medial collateral ligament (of the knee)
MFTA Mechanical femoro-tibial angle
MRI Magnetic resonance imaging
NSAID Non-steroidal anti-inflammatory drug
OA Osteoathritis
OKS Oxford Knee Score
PCL Posterior cruciate ligament
SD Standard deviation
SF-36 Short form 36 (functional score)
TKA Total knee arthroplasty
TMA Tibial mechanical axis
UKA Unicompartmental knee arthroplasty
WOMAC Western Ontario and McMasters Universities Arthritis Index (functional score)

INTRODUCTION

Osteoarthritis of the knee presents as pain and loss of function; it is a highly prevalent disease and presents a significant demand to healthcare services. Surgical management in the form of total knee arthroplasty (total knee replacement) is an effective means of reducing pain and improving function.

In computer-assisted orthopaedic surgery (CAOS), knee navigation systems are used to give real-time kinematic data intra-operatively, with the aim of aligning implants with greater reliability and precision. The rationale for the research presented in this thesis was a requirement for further in-vivo testing of a non-invasive navigation system. A reliable system of this form could be clinically valuable in pre and post-operative biomechanical assessment of the knee.

The aim of this work was to evaluate the non-invasive Physiopilot knee navigation system in the measurement of mechanical lower limb alignment through the range of knee flexion, with manually applied varus and valgus force.

CHAPTER 1: LITERATURE REVIEW

1.1 Anatomy and function of the human knee

The knee joint consists of the articulation between the femur and tibia coupled with the articulation of the patella with the femur. The distal femur features 2 distinctive prominences, the medial and lateral condyles, which articulate with the medial and lateral condyles of the proximal tibia (the tibial plateau). These correspond to the medial and lateral compartments of the knee joint, separated by the inter-condylar fossa. The articular surfaces are covered with a layer of hyaline cartilage in the healthy knee. The medial and lateral menisci are additional C-shaped bodies of cartilage found on the tibial plateau. The joint is enclosed in an outer fibrous capsule, lined with synovium, a membrane which produces synovial fluid which lubricates the joint.

Movements of the knee are essential to human locomotion and function. The greatest range of motion is exhibited in the sagittal anatomical plane - flexion and extension. The former is under the action of the musculature of the posterior compartment of the thigh (*biceps femoris, semimembranosus, semitendinosus*) and the latter due to action of the muscles of the anterior compartment of the thigh (*rectus femoris, vastus medialis, vastus intermedius, vastus lateralis*, which together form the *quadriceps tendon*). The range of movement in the sagittal plane in the healthy human knee has been reported as -10° (10° hyperextension) to 135° [American Academy of Orthopaedic Surgeons, 1991].

The research presented in this thesis focuses on the range of movement in the coronal plane. When the joint is at its limit of extension, it is described anatomically as 'locked' and thus exhibits its least laxity in the coronal plane. At full extension the tibia externally rotates relative to the femur in the axial plane, tightening the cruciate ligaments and ‘screwing-home’ the knee into the locked position. The principal structure restraining against varus force is the lateral collateral ligament, running from the lateral epicondyle of the femur to the head of the fibula. The medial collateral ligament, running from the medial epicondyle of the femur to the medial surface of the proximal tibia, is the primary restraint to valgus force. The collateral ligaments are described as exhibiting greatest laxity at 30° of flexion. An applied varus or valgus force at 30° will therefore result in the greatest degree of joint distraction, or opening, on the medial or lateral side.

Additional structures which are thought to have a role in the coronal stability of the knee include the tissues of its posterior aspect. The posteromedial capsule of the knee joint has been described by some authors as fibres continuous with the superficial part of the posteromedial collateral ligament

[Williams et al, 1995]. Other authors have described a discrete structure separate from the MCL, named the posterior-oblique ligament [Neilsen et al, 1984]. In conjunction with the attachment of the semitendinosus tendon, these structures act as a passive valgus restraint with the knee in extension [Robinson et al, 2004]. Posterolaterally, structures consist of the iliotibial band, biceps femoris tenson and LCL more superficially, with the posterolateral capsule, popliteal tendon and popliteofibular ligament deep to these; the deep structures also act as restraints to varus force [Shahane et al, 1999]. Alignment of the lower limb in the coronal plane is discussed in more detail below.

The knee joint can undergo antero-posterior translation - the tibia moving anteriorly and posteriorly with respect to the femur. The principal structures restraining against AP translation are the anterior and posterior cruciate ligaments, the former passing from the anterior tibial plateau to insert on the lateral wall of the intercondylar fossa, and the latter passing from the posterior tibial plateau to insert on the medial wall of the intercondylar fossa. As with the medial and lateral collateral ligaments, the cruciate ligaments are thought to have greatest laxity at 30° of flexion, and hence at this point the AP laxity is at its greatest.

Movement of the knee joint as a facet of normal locomotion and function of the lower limb involves a combination of rotations around the axes described above, a detailed description of which is beyond the scope of this thesis. This complexity leads to difficulty in quantifying and assessing a single plane in kinematic measurement.

1.2 Alignment of the Lower Limb

Varus and valgus kinematics form the basis of the research presented here, with range of knee motion in the sagittal (flexion and extension) and axial (anterior-posterior laxity) planes already defined. A number of terms are applied to the mechanics of the lower limb in the coronal plane. Defining the axes of the lower limb in the coronal plane necessitates delineating anatomical landmarks in the hip, knee and ankle. These have largely been described in studies of lower limb radiographs, as illustrated in Figure 1.1.

Lower limb axes are described as *mechanical* and *anatomical*. The femoral and tibial anatomical axes are visualised as straight lines passing through the mid-shaft (diaphysis) of the bone. Mechanically, the centre of the hip joint is taken as the centre of the femoral head. The mechanical axis of the femur is visualised as a straight line from the centre of the femoral head to the mid-point of the femoral condyles, between the insertions of the anterior and posterior cruciate ligaments in the sagittal plane. The tibial mechanical axis is the straight line from the midpoint of the tibial plateau proximally to the midpoint of the distal tibia at the centre of the ankle joint. These axes represent the direction of the action of the reactive ground force on the weight-bearing lower limb [Cooke et al, 2007].

As discussed below, the currently accepted best practice in total knee arthroplasty is to place implants such that the mechanical axis of the lower limb is 0°, that is, a straight line from hip to knee to ankle centres. Femoral and tibial implants are therefore placed at 90° to the respective femoral and tibial mechanical axes. The femoral mechanical anatomical (FMA) angle is formed between the anatomical (i.e. mid-shaft) and mechanical axes of the femur. The corresponding femoral mechanical (FM) angle lies between the mechanical axis of the femur and a straight line along the articulating surfaces of the femoral condyles. Mean FMA angle in the population of healthy knees has been described in a number of studies, including 5.1° valgus in a recent study of 199 Chinese adults [Wang et al, 2010], and 5.8° valgus in a sample of 120 Western adults [Hsu et al, 1990].

In an uncomplicated primary knee arthroplasty (that is, without significant incorrectible deformity on examination), a *distal valgus cut* is therefore made to compensate for the intrinsic valgus FMA angle. In conventional total knee arthroplasty with intramedullary instrumentation (described in more detail in Chapter 1.4), it is common practice to select a cut of 5° or 6° [Kharwadkar et al, 2006]. Routine selection of a fixed 5° or 6° distal valgus cut has been challenged in a number of studies, with a recommendation that the angle of femoral resection should be adjusted specifically to each patient. In a study of 174 patients with osteoarthritis awaiting TKA, Deakin et al found a mean FMA angle of 5.7° on long-leg radiographs with standard deviation 1.2° and range 2°-9° [Deakin et al, 2012]. In a subsequent study by the same authors, 124 TKAs performed using a fixed valgus angle of 7° were compared with a group of 87 TKAs where the distal cut was adjusted to FMA angle on pre-operative long-leg radiographs. Distal cut angles ranging from 4°-8° were used in this group. There was a statistically significantly higher proportion of patients found to have a satisfactory knee alignment (within 3° of neutral) when the valgus cut was adjusted [Deakin and Sarungi, 2014]. However, in a study by McGrory et al published in 2001, 124 TKAs in 94 patients were randomised to either undergo or not undergo a long-leg radiograph pre-operatively. In the former, distal cut was adjusted to FMA angle measured on long-leg radiograph, with a fixed valgus cut of 5° taken in the latter group [McGrory et al, 2002]. No significant difference in restoration of a neutral mechanical axis of post-operative long-leg radiographs was found between the 2 groups.

The mechanical femoro-tibial angle (MFTA), of particular relevance to this project, is the angle formed between the intersection of the femoral mechanical axis and tibial mechanical axis. The reactive ground force passing through the knee joint is distributed between the medial compartment (corresponding to the medial femoral condyle) and the lateral compartment (corresponding to the lateral femoral condyle) [Cooke et al, 2007]. Taken as a measure of the mechanical alignment of the lower limb in the coronal plane, the MFTA has been studied as a biomechanical parameter following arthroplasty and is thought to be of significance in clinical outcome. Further discussion is found in Chapter 1.7.

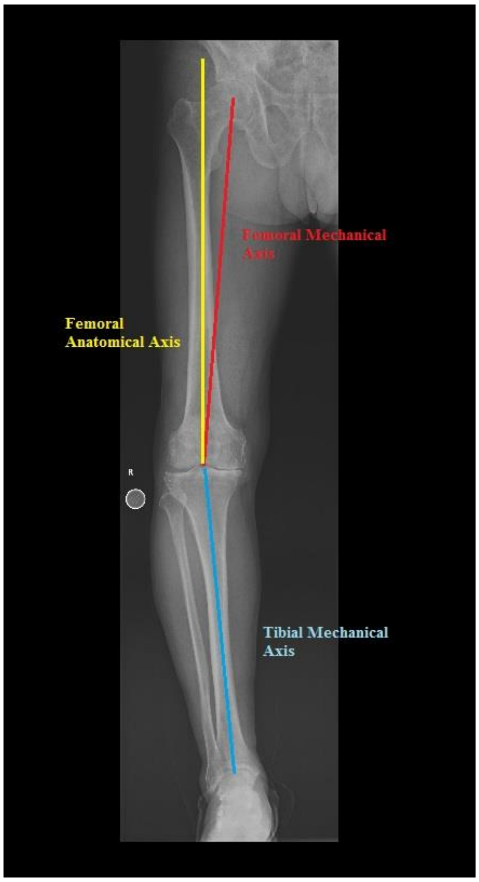

Figure 1.1: Illustration of relevant anatomical and mechanical lower limb axes. The femoral mechanical anatomical angle is found between the yellow and red lines. The mechanical femoro-tibial angle is found between the red and blue lines.

Biomechanical definition of the MFTA leads us to a discussion of how this parameter can be measured clinically. There is little evidence to support the use of visual estimation of limb alignment, or measurement manually with goniometers. Radiologically, plain radiographs, computed tomography (CT) [Chauhen et al, 2004] and magnetic resonance imaging (MRI) [White and Buckwalter, 2002] have all been proposed in the assessment of alignment. In addition, navigation systems can give real-time measurement of MFTA, as discussed in Chapter 1.5. Clinical studies advocate the use of a standing (i.e. weight-bearing), antero-posterior (AP) long-leg radiograph as a standardised method of measuring mechanical lower limb alignment. Plain radiographs of this nature are clinically convenient in routine practice and incur less exposure to ionizing radiation than CT. In a sample of 40 patients, with 3 observers, Babazadeh et al found high intra-observer repeatability and inter-observer correlation for pre-op and post-op standing long-leg radiographs. There was also high correlation with alignment measured on CT [Babazadeh et al, 2013]. In another study, of 56 patients awaiting navigated TKA, the authors found high intra-observer and inter-observer ICC (0.984-0.997) in measurements of MFTA on long-leg radiographs [Rauh et al, 2007]. Thus there is evidence that the standing, long-leg plain radiograph can give a reliable measurement of MFTA. There is also evidence that this is a more reliable method of assessing mechanical alignment than radiographs which do not include the entire lower limb anatomy. In a sample of 68 patients, van Raaij et al compared mechanical alignment measured on standing long leg radiographs versus alignment measured on a cropped image of the knee joint (representing a typical AP knee film). Using mid-diaphyseal lines as a measure of measuring alignment on the cropped image was found to have unsatisfactory inter-observer agreement. Using lines transecting the knee joint centre on the cropped image was also found to have poor correlation with long-leg films [van Raaij et al, 2009].

Interestingly, there is evidence that measurement of mechanical alignment may be affected by a supine position versus a weight-bearing stance. This is particularly relevant if we consider a patient supine and anaesthetised on the operating table then walking post-operatively.Brouwer et al measured alignment on long-leg radiographs in a sample of 20 patients, both supine and standing, finding a mean discrepancy of 2° varus with the patient weight-bearing [Brouwer et al, 2003]. In measuring mechanical alignment on long-leg radiographs with patients supine, standing with two-legged stance then one-legged stance, Specogna et al found a mean difference of ±2° in alignment between different patient positionings [Specogna et al, 2007]. The complexity of lower limb mechanical alignment, and that it may be a dynamic parameter, leads to questions - as yet not fully answered - of the alignment which should be aimed for in a patient undergoing knee joint reconstruction in the form of arthroplasty.

1.3 Osteoarthritis and knee arthroplasty in context

Osteoarthritis remains the major indication for knee replacement. A recent report published by the

UK National Joint Registry records that a total of 85,920 primary total knee arthroplasties were performed in the UK in 2013, of which 97% were performed as procedures for osteoarthritis [Powers-Freeling et al, 2013]. Osteoarthritis is a highly prevalent disease, with approximately 13% of patients over the age of 55 years experiencing symptomatic knee osteoarthritis [Felson, 2004]. The knee is the most commonly affected large joint in the body [Felson, 2004].

A number of patient factors have been associated with increased risk of knee osteoarthritis, including increasing age, female sex, obesity and history of knee injury (a previous diagnosis of meniscal or cruciate injury) [Emery et al, 2012]. Osteoarthritis in patients with a history of knee injury, septic arthritis or inflammatory arthritides (for example rheumatoid arthritis or gout) has been described as 'secondary' osteoarthritis. Evidence for genetic risk factors has been reported in twin and other family history studies, and may account for 50% of risk of incidence of osteoarthritis; the evidence, however, is particularly strong for polyarticular osteoarthritis with hand and hip involvement [Cimmino and Paradi, 2005].

Macroscopically, the pathology of osteoarthritis is well described, as a chronic, progressive disease process of articular cartilage destruction and disorganised regeneration. The hyaline cartilage covering the joint surfaces becomes dehydrated, thinned and develops fissuring; the subchondral bone substance becomes hardened, or *sclerotic*. Remodelling manifests as osteophytes, which are spur-like bony outgrowths. The process may lead to inflammation of the joint synovium (synovitis), one source of the associated pain. At a cellular level, the pathogenesis and pathophysiology of osteoarthritis is more obscure. Various forms of calcium phosphate crystals are found in the synovial fluid in knee osteoarthritis, but it is not clear whether these are simply a product of the disease process, or the promoting factor of the pathology [Nalbant et al, 2003]. Consequently, pharmacotherapy can alleviate symptoms but has yet to be targeted at a level which halts disease progression.

While UK National Institute of Clinical Excellence (NICE) guidelines recommend that a diagnosis of osteoarthritis can be made clinically in a patient over the age of 40 with chronic, use-related knee pain without the need for imaging, the first-line investigation in osteoarthritis is a plain knee radiograph. Severity of osteoarthritis is based on the presence, and extent of, a number of classical findings. The Kellgren and Lawrence Score, graded from 0-4, was first described in 1963 and remains in common use, being adopted as a WHO standard. With 0 defined as the absence of radiographic evidence of osteoarthritis, the findings range from doubtful narrowing of joint space with possible marginal osteophytes (Grade 1), to large osteophytes, significant joint space narrowing, significant subchondral sclerosis and bony deformity [Kellgren et al, 1963].

It is worth discussing at this stage that there is some evidence that coronal alignment is of significance in the pathological knee - that is, in the development and progression of osteoarthritis. Altered alignment of the lower limb is a common clinical feature of knee osteoarthritis. This is caused by the fact that the medial and lateral compartments can be affected to differing degrees by the disease process. In osteoarthritis that is predominantly medial, loss of joint space in this compartment leads to the lower limb mechanical axis shifting medially - giving a varus deformity. In valgus deformity, which is less common, increased loss of the lateral compartment with respect to the medial shifts the axis laterally.

Cerejo et al followed-up a cohort of 377 knees in 230 patients with established, symptomatic osteoarthritis. MFTA was measured on long-leg radiographs at baseline, with severity of osteoarthritis graded using the Kellgren and Lawrence score. At 18 months, in knees with initial moderate osteoarthritis (Grade 3) the authors found a statistically significant increase in the risk of increased severity of osteoarthritis with either varus or valgus alignment [Cerejo et al, 2002]. In a previous study, also of 230 osteoarthritic patients, Sharma et al found a four-fold increased risk of increased severity of medial compartment osteoarthritis severity score with baseline varus malalignment; valgus malalignment at baseline was associated with a five-fold increased risk of progression of lateral compartment osteoarthritis at follow-up. The authors also concluded that varus or valgus malalignment of more than 5° at baseline significantly increased the risk of disease progression compared with knees within these limits [Sharma et al, 2001].

Studies such as these suggest that the malaligned osteoarthritic knee is prone to more rapid disease progression. However, the cause and effect are unclear - are those who have an alignment outwith neutral in their 'normal', asymptomatic knee susceptible to osteoarthritis, or is malalignment simply a manifestation of osteoarthritis? In a study of 2958 knees, in 1752 participants with no evidence of osteoarthritis, varus alignment (defined as >2° deviation from neutral MFTA) on baseline long-leg radiograph was associated with an odds ratio of 1.49 for development of evidence of osteoarthritis at 30 month follow-up radiograph [Sharma et al, 2010]. However, in a study published in 2007 of 356 knees in 178 patients, with a mean follow-up of 8.75 years, mechanical alignment (as measured on AP leg radiographs at baseline with anatomic axis and tibial plateau angle) was not found to be a statistically significant risk factor for developing osteoarthritis [Hunter et al, 2007]. Conflicting studies of this nature make it difficult to draw conclusions on the exact significance of pre-existing lower limb alignment in an individual in the risk of developing osteoarthritis.

The extent to which any deformity in the coronal plane is correctable may influence the surgical technique used in total knee arthroplasty. ‘Correctability’ is assessed clinically by applying a varus or valgus force when examining the knee. There is currently no accepted means of quantifying this objectively. A reliable, non-invasive method of doing so with navigation technology could therefore be a valuable tool in operative planning.

The management of osteoarthritis is typically described as either conservative (non-operative) or surgical. Current evidence-based guidelines published by NICE recommend that a number of ‘core treatments’ should be offered initially to patients with diagnosed osteoarthritis. A topical NSAID, such as diclofenac gel applied to the skin surrounding the knee, and/or oral paracetamol are first-line pharmacotherapies. Oral NSAIDs and opioids such as codeine, dihydrocodeine or tramadol preparations are offered as second-line analgesics. Intra-articular injections are a further pharmacotherapy option for the knee. A systematic review published in 2006 of 28 clinical trials found evidence of short-term (2-3 week) syptomatic benefit in using intra-articular steroid in the knee (triamcinolone acetonide/hexacetonide are routinely-used preparations) [Bellamy et al, 2006]. Evidence is supportive, however, only for patients with surgical risk factors which would preclude eventual arthroplasty and those with mild osteoarthritic changes for whom conservative management has failed [Cheng et al, 2012]. There is currently insufficient evidence to support the use of intra-articular injection with hyaluronic acid (a component of synovial fluid), also termed viscosupplementation, with a meta-analysis of 89 trials published in 2012 finding no clinically significant benefit, with increase risk of adverse side-effects including increased symptoms and infection [Rutjes et al, 2012]. There has also been controversy over whether intra-articular injections increase the risk of complications, such as infection, in knees subsequently undergoing arthroplasty [Papavasilou et al, 2006].

1.4 Surgical management of knee pathology

The current recommendation from NICE is that patients with symptomatic osteoarthritis which has a “substantial impact on quality of life and is refractory to non-surgical treatment” may be considered for surgical management.

There are a number of options for the knee joint, aside from arthroplasty. Arthroscopic lavage and debridement were previously offered to patients; however aspersions were cast on efficacy in key randomised control trials which found no improvement in pain or function versus conservative management or placebo surgery [Moseley et al, 2002][Kirkley et al, 2008]. In realignment surgery, the rationale is to reduce the load on the osteoarthritic compartment. A number of realignment osteotomy techniques have been described; most commonly, a wedge of bone is removed from the tibia (opening or closing-wedge high tibial osteotomy, or HTO). In common practice, patient selection is limited to younger patients with higher functional demands, who have unicompartmental osteoarthritis and a less limited range of movement. A Cochrane review from 2007 of 11 studies of HTO for medial compartment OA found evidence that the technique could be of clinical benefit, but its efficacy versus non-operative management was unclear, as there were no RCTs of HTO versus conservative management [Brouwer et al, 2005].

With the belief that replacing the pathological joint surfaces in osteoarthritis with prothestic implants would alleviate pain and improve function, the first knee arthroplasties were performed in the 1950s. Initial implants were hinged in design and failed early due to their constrained nature, which placed undue force through the prosthesis. They were also poorly fixed to the underlying bone as cement was not available. Hinged prostheses and arthrodesis (fusion of the knee joint) are now used as salvage procedures, for example in cases of extensive bone loss following revision, or chronic intractable infection.

An alternative to total knee arthroplasty (TKA) is the unicondylar knee arthroplasty (UKA). With somewhat similar indications to HTO, UKA is offered to younger patients with OA confined to a single compartment, with correctability of any malalignment to neutral on examination. Studies show clinical benefit in the form of improved post-op functional scores [Berger et al, 2005], and a survivorship of 91% at 16 years [Price and Svard, 2011].

Current TKA implants are condylar by design; the femoral condyles and proximal tibial surface are resected, with components replacing the resected area, a design which more closely resembles the native anatomy. The anterior cruciate ligament and menisci are removed in resecting the tibia, and the posterior cruciate ligament can be retained (CR) or sacrificed in a posterior-stabilised (PS) implant. Theoretical advantages of the former have been described as increased patient proprioception and decreased AP laxity, which may be of benefit in some functional activites such as climbing stairs. The latter is considered by some to be a more forgiving procedure technically and can give greater range of flexion post-op [Luo et al, 2012]. Recent meta-analyses have found evidence of increased range of flexion with posterior-stabilised implants; however, there are no statistically significant differences found in clinical outcome scores or implant survivorship [Verra et al, 2013][Li et al, 2014].

This thesis explores an application of computer-assisted orthopaedic surgery (also known as knee navigation). In contrast, conventional (non-navigated) TKA instrumentation uses alignment rods and jigs to position the prosthesis. With an extramedullary tibial jig, a cutting block (saw guide) is positioned on the proximal tibia to allow bone to be resected at right angles to the anatomical axis. Using an intramedullary femoral guide, access is gained to the femoral canal distally using a drill hole. The intramedullary guide is inserted into the canal and used to position the cutting block for an appropriate distal femoral cut, as described in Chapter 1.2.

1.5 Navigated knee arthroplasty

The origins of computer-assisted orthopaedic surgery (CAOS) are found in neurosurgical use, beginning in the 1980s, of CT images of the head to guide stereotactic brain surgery. This concept evolved into computer-assisted technology for spinal surgery, with pre-operative imaging guiding instrumentation and the positioning of pedical screws in vertebrae [Langlotz and Nolte, 1999], [Lavalle et al, 1995].

Essentially, the goal of using computer technology in knee arthroplasty was to increase the reliability of implant positioning - to place components more frequently within the biomechanical parameters thought to be associated with optimum patient function post-operatively and with greatest longevity of the arthroplasty.

Computer assisted knee arthroplasty, also known as *navigation*, has been classified as either *image-based* or *image-free*. As with the computer-assisted systems introduced in spinal surgery, image-based knee navigation uses plain radiography/fluoroscopy, CT or MRI imaging to outline anatomical landmarks and guide bone cuts and implant placement [Cheng et al, 2011]. Our research uses a non-invasive application of an image-free navigation system. Image-free systems do not require pre or intra-operative radiological imaging, relying instead on localisation of anatomical landmarks with electromagnetic or infra-red emission. With electromagnetic tracking largely falling out of favour, most current knee navigation systems are optical, image-free systems where localisation of anatomical positions with fixed trackers gives kinematic data intra-operatively.

The essential components of an image-free navigation system are *trackers* and an infra-red detector/localiser. *Active* trackers emit infra-red radiation and thus require a cable or battery power source. *Passive* infra-red trackers use spheres with reflective coating, with infra-red radiation emitted by a separate source, usually incorporated into the localiser unit. In current image-free navigation systems, trackers are fixed to bony anatomical landmarks by attaching to drilled cortical bone screws. The localisation of bony landmarks facilitates the measurement of knee alignment and kinematics (i.e. movement in the sagittal, coronal and axial planes) intra-operatively.

A number of studies have attempted to quantify error in the registration process of knee navigation systems through their development. Review of these studies is relevant to the research presented here as it can help to contextualise the error of our non-invasive navigation system.

Image-free Orthopilot navigation software [B. Braun Aesculap, Tuttlingen, Germany] was found to have high reliability in research published by Jenny et al in 2004. The software used was a predecessor of the currently available Orthopilot system, differing in that it required an infra-red tracker to be drilled into the anterior iliac crest, and a tracker secured to the dorsum of the foot with a base plate and strapping in order to register the hip and ankle centres [Jenny et al, 2004]. Using a series of 20 consecutive TKAs with 2 operating surgeons, MFTA as measured by the Orthopilot package was recorded at knee extension and 90° of flexion. Mean intra-observer variations in MFTA were ±0.1° and ±0.2° at maximum extension and 90° flexion, respectively, while inter-observer variations were found to be ±0.1° and 0°.

Yau et al conducted a study in 2005 to quantify the errors in registering anatomical landmarks with Vector Vision CT Free Knee [BrainLAB AG, Heinstetten, Germany], an image-free navigation system. This system used 2 clusters of passive infra-red trackers, one secured to the femur and one to the tibia [Yau et al, 2007]. A single surgeon performed 100 registrations on a cadaveric knee specimen. Mean errors in registration, in anterior/posterior and medial/lateral directions, were greatest for the medial epicondyle of the femur and the lateral malleolus of the fibula [2.8mm and 1.9mm respectively, with ranges 0.2-6.4mm and 0.2-6.2mm]. A maximum potential error in registration of the MFTA was calculated as ±1.32°. A limitation of this study was that it lacked a ground truth definition of anatomical landmarks, with the target coordinates calculated from the 100 points taken for each landmark.

Hauschild et al tested the Orthopilot navigation system on 4 cadaveric knee specimens with 5 different operators in a study published in 2009. A contemporary version of the software package was used which required infra-red trackers to be fixed to the distal femur and tibia only [Hauschild et al, 2009]. MFTA of each specimen was initially measured manually with a goniometer and rigid cable aligned from femoral head, to intercondylar eminence, to centre of the ankle joint. When the Orthopilot system was used to measure MFTA, intra-observer and inter-observer agreements were satisfactory with the knee in extension. However, agreement was poorer with the knee at 90°of flexion. There was also a tendency for improved agreement in senior operators with more clinical experience. The mean difference in MFTA between navigated measurements and initial manual method was ±1.55°, which was not statistically significant.

Davis et al conducted a study of anatomical landmark registration in cadaveric lower limb specimens using the image-free Stryker Knee Navigation System [Stryker Corporation, Kalamazoo, MI]. Five surgeons performed a standard medial parapatellar surgical approach on a specimen as for TKA, each performing the registration 5 times. The target landmarks were then defined by a single operator after stripping all tissues from the specimens [Davis et al, 2013]. Mean anterior/posterior errors and medial/lateral errors were calculated for each landmark defined by the navigation system. These equated to a mean error in MFTA of ±0.09°.

One of the key limitations of the evidence base evaluating knee navigation systems is the difficulty in defining the ‘ground truth’ - in other words, accurate values for anatomical landmarks, alignment and kinematics. Many studies therefore assess precision (repeatability). International standards for navigation systems have been agreed and published by the American Society for Testing and Materials in *ASTM F2554-10: Standard Practice for Measurement of Positional Accuracy of Computer Assisted Surgical Systems*. Standards set by this publication include that landmarks should be able to be localised to an error of 1mm, and alignment should be accurate to 1° [ASTM, 2010]. These values have been based on manufacturer and surgeon consensus, and there is a need to burgeon the evidence base of both cadaveric and in-vivo/clinical studies to establish the gold standards of error and accuracy required for safe and effective TKA navigation systems.

1.6 Measuring the outcome of TKA

It is worth mentioning at this stage that there are a number of methods of quantifying clinical benefit to patients in knee arthroplasty. Assessing the domains of pain, function and activity, and biomechanical parameters, has led to an array of scoring systems being described in the literature. Commonly used scores which are not specific to knee arthroplasty include the Short Form Health Survey (SF-12 and SF-36) [Ware and Sherbourne, 1992] and Western Ontario and McMasters University Arthritis Index (WOMAC) [Bellamy et al, 1997].

The Oxford Knee Score (OKS), in common use in the UK, is a 12 point questionnaire of patient reported outcome measures of pain and function. Each question is rated 1-5, giving a range of 12-60. The Oxford Knee Score has been shown to have good internal consistency with repeated scoring, and lack of bias [Conaghan et al, 2007], [Xie et al, 2011]. Another widely used system is the American Knee Society Score. This combines a patient-reported ‘Function Score’ of mobility with an objective ‘Knee Score’ which tallies biomechanical findings on post-operative examination including range of flexion, varus/valgus alignment and balancing, AP laxity and pain score. In a sample of 190 patients, Medalla et al found that OKS correlated well with AKSS over a 10 year period, supporting the use of the OKS alone as a measure of patient reported outcomes [Medalla et al, 2009]. In a recent study, Maempel et al found good correlation between AKSS and OKS at 5 years follow-up, and used a regression model to predict OKS from AKSS, finding good correlation between predicted and actual OKS [Maempel et al, 2015]. One of the limitations of the OKS lies in assessing clinical outcome in cases of bilateral TKA. The questionnaire includes specifically functional questions which may reflect symptoms in both knees, such as relating to stair-climbing and kneeling, although the OKS was designed to be limb-specific [Murray et al, 2007]. It may thus be difficult to compare clinical benefits in patients who have undergone (simultaneous or staged) bilateral TKA.

Currently, there is no universal, gold-standard measure of clinical outcome following arthroplasty, which leads to difficulties in comparing the results of studies. It is recommended that all published studies specify the patient scoring system used in quantifying clinical outcome [Maempel et al, 2015].

1.7 Biomechanical outcomes of arthroplasty: coronal alignment

The literature of orthopaedics and biomedical engineering has explored a number of biomechanical outcomes of knee arthroplasty, including coronal alignment, rotational alignment and soft tissue balancing. Debate remains over which, if any, correlates most significantly with clinical outcomes - patient satisfaction, relief of symptoms, and implant longevity.

In primary knee arthroplasty, it is clearly advantageous to have implants in situ for as long as possible to avoid the need for further surgery (revision). Unfortunately, arthroplasty has a finite longevity. Survivorship analysis of modern TKA designs is an ongoing process in the field of orthopaedics. The UK National Joint Registry, presenting data from 2003-2013, found an overall risk of revision at 10 years of 4.47% of a primary TKA [Powers-Freeling et al, 2013]. Indications for revision include isolated polyethylene wear, aseptic loosening (of femoral and/or tibial components), infection, malalignment and periprosthetic fracture [Sharkey et al, 2002].

Retrieval studies suggest that mechanical alignment - specifically MFTA, as defined above - correlates with implant survivorship. One such study, dating from 1994, examined 55 tibial inserts retrieved at time of revision arthroplasty; inserts had been in situ for a mean of 34.2 months (range 2.5-80 months). Significantly increased polyethylene wear was found on the medial side in pre-operative varus knees, and increased lateral wear was found in pre-operative valgus knees, even if mechanical axis had been restored to a satisfactory alignment following arthroplasty. In this study, however, only 20 of the retrieved inserts were made from ultra-high molecular weight polyethylene - the vast majority of contemporary TKA designs use tibial inserts made from this material [Wasielewski et al, 1994]. A more recent paper from 2007 assessed 81 unicondylar arthroplasties and 89 TKAs inserted between 1984 and 1998 which were retrieved at time of implant revision or patient death. The authors found that loss of polyethylene thickness in the medial compartment of the knee was associated with post-operative varus MFTA alignment on linear regression analysis [Collier et al, 2007]. In a study published in 2005, Werner et al placed cruciate-retaining knee arthroplasty components in cadaveric lower limb specimens at 0°, 3° and 5° varus and valgus mechanical alignments and loaded the joint with a simulator of physiological weight-bearing, finding significant changes in loading of the medial or lateral compartments with a change of 3° or more [Werner et al, 2005].

A well-described aim of TKA is to place implants such that the MFTA post-operatively is within a margin of 0±3°. These parameters were advocated by a number of authors; oft-quoted papers include a study by Jeffrey et al published in 1991of 115 TKAs, and an analysis of 351 TKAs conducted by Ritter et al, published in 1994. TKAs with alignment outlying ±3° of a neutral (0°) MFTA were associated with decreased survivorship - a need for earlier revision [Jeffrey et al, 1991][Ritter et al, 1994]. Evidence for the significance of MFTA was indeed one of the rationales for the development of knee navigation. However, a review of up-to-date literature suggests that coronal alignment and the recommendation of a 0±3° MFTA may not be as clinically significant as once thought.

A recent paper to have explored this issue was a retrospective analysis at 15 years post-op of 398 primary TKAs performed on 280 patients between 1985 and 1990 by a single surgeon [Parratte et al, 2010]. MFTA alignment was measured 2 to 3 months post-operatively using long-leg radiographs. Patients were split into 2 groups, a well-aligned cohort of MFTA 0±3º, and a cohort of outlierswith MFTA measured as more than 3º from neutral. The authors found no statistically significant improvement in implant survivorship in the well-aligned group at 15 years. The findings of the Parratte paper were somewhat corroborated by a 2011 study of 501 TKAs in a cohort of 396 patients. The patient sample was split into an aligned group within 0±3° and a malaligned group. With 15 year follow-up there was tendency for decreased rate of revision for aseptic loosening but this was not statistically significant [Bonner et al, 2011].

Berend et al analysed 3152 primary TKAs in 2125 patients implanted between 1983 and 2000 with a mean follow-up of 5 years (range 2-14.2 years). Post-op radiographs, which did not include long-leg views (currently an accepted standard for mechanical lower limb alignment, as discussed in Chapter 1.2), were taken for all patients and assessed for radiolucent lines, implant alignment and limb alignment. Medial bone collapse requiring revision was found to have a statistically significant correlation with varus tibial component alignment >3°, and any degree of overall varus limb alignment post-op [Berend et al, 2004].

An MFTA of 0±3° representing a ‘well-aligned’ TKA prosthesis has thus been challenged; from another point of view on the issue of coronal alignment, some authors have questioned whether ‘neutral’ alignment is a valid aim for TKA in the first place. In a 2012 study, Bellemans et al analysed standing long-leg radiographs in a cohort of 250 healthy subjects aged 20-27 years, finding 32% of males and 17% of females had a ‘constitutional varus’ MFTA of >3° [Bellemans et al, 2012]. The authors proposed that aiming for varus TKA alignment may be more appropriate, yet recognised the difficulty of trying to reconcile this concept with previous studies. In the study by Deep et al published in 2015, 264 healthy knees in 132 subjects were assessed using the Orthopilot navigation system non-invasively. Mean supine MFTA was 1.2° varus in full extension but 2.0° and 3.4° with standing bipedal and monopedal stance, respectively. The authors concluded that ‘neutral’ MFTA was not seen natively in the majority of subjects, and emphasised that MFTA can be observed to change with posture [Deep et al, Apr 2015]. These studies, however have stopped short of explicitly recommending aiming for restoration of a ‘constitutional varus’ in TKA.

1.8 Biomechanical outcomes of arthroplasty: soft tissue balancing

As with the concept of mechanical alignment, the theory of achieving a *balanced* knee joint in the arthroplasty process has been described in the literature through the evolution of the procedure [Insall, 1985]. As described in Chapter 1.1, the stability of the knee joint about its axes of movement is dependent on supporting soft tissues, including, in the coronal plane, the medial and lateral collateral ligaments. A ‘balanced’ TKA is one which exhibits consistent stability throughout its range of movement. This is described in turn as the rectangular ‘gap’ between the resected femoral and tibial surfaces being equal in flexion and extension intra-operatively [Mihalko et al, 2008]. As the process of TKA balancing lacks robust objective measures, a goal of knee navigation is to standardise the measurement of varus and valgus correctability. There is currently no agreed standard in the literature, particularly for knees with a valgus deformity.

A number of authors have described techniques for releasing medial soft tissue structures in knees with varus deformity. Varus deformity is more common in osteoarthritis, and is felt to be less technically challenging to correct than significant valgus deformity. Whiteside et al published a study in 2000 in which 76% of TKA procedures in a sample of 80 varus knees were felt to require soft tissue release; the technique is described sequentially as incision of the posterior or anterior portions of the medial collateral ligament, or complete ligament release [Whiteside et al, 2000]. In a more recent study, Koh et al described release initially of the posterior MCL in all patients, followed by incision of the semimembranosus tendon as the next step in varus knees which continued to have ‘tightness’ medially on stress testing [Koh and In, 2013]. There is a general lack of evidence of correlation of knee ‘balancing’ with clinical outcomes. In one study with a sample of 410 TKAs, Unitt et al used a gap balancing device similar to a laminar spreader which gave a reading of the degree of varus/valgus correctability with flexion and extension gaps. Medial and lateral soft tissue releases in varus and valgus knees were described as minimal, moderate or extensive with a balanced knee described as within ±3° deviation of neutral mechanical axis. All knees achieved satisfactory balance, but at 12 month follow-up there were no statistically significant differences in AKS and OKS clinical scores between patients requiring differing levels of soft tissue release [Unitt et al, 2008].

Navigation systems in TKA can provide real-time, on-screen quantification of knee kinematics. Attempts have been made to use CAOS to standardise the approach to knee balancing. Picard et al developed an algorithm for soft tissue release in varus osteoarthritic knees using image-free navigation, published in 2007. Intra-operatively, before the insertion of implants, MFTA was measured in extension with a manually applied valgus force [Picard et al, 2007]. The degree of correctability of varus MFTA displayed on-screen was used to determine the degree of medial soft tissue release, described as none, moderate or extensive. The algorithm was validated in a sample of 42 patients, where all knees were released to give a limit of 3° of valgus stress angle in extension. Hakki et al performed 93 (66 varus and 27 valgus knees) navigated TKAs using the image-free Orthopilot system, aiming to have the TKA ‘balanced’ in extension with ±2° of coronal laxity from neutral MFTA with manually applied varus or valgus force [Hakki et al, 2009]. The authors aimed to predict if 2 measures, using the navigation system, could be used to guide the need for soft tissue release. Firstly, if deformity could be manually corrected to on-screen neutral MFTA in extension with applied force, and secondly if there was greater than 5mm difference in medial and lateral ‘gap’ in flexion and extension when bony cuts were made. 10% of patients required medial or lateral collateral ligament release with this algorithm. With regards to patient outcomes in TKA balancing, there is scanty evidence that the ‘well-balanced’ TKA leads to clinical improvements. In balancing a series of 135 TKA patients, Gustke et al used a tibial insert system intraoperatively fitted with load sensors corresponding to the medial and lateral compartments [Verasense Knee System; OrthoSensor Inc, Dania Beach, FLA]; satisfactory balancing was based on the difference in medial and lateral load distribution with stress testing. In a series of 135 patients, there was a statistically significant increase in the proportion of patients who reported as being “satisfied” or “very satisfied” on questionnaire at 12 months post-op in knees which were deemed to be ‘well-balanced’ (n=113) versus unbalanced TKAs [Gustke et al, 2014].

1.9 Biomechanical outcomes of arthroplasty: rotational alignment

Rotational alignment of femoral TKA components (i.e. in the axial plane) is commonly described as being centred on the transepicondylar axis (TEA), a straight-line visualised passing between the medial sulcus of the medial epicondyle and the prominence of the lateral femoral epicondyle [Berger et al, 1998]. However, there is no globally accepted method of obtaining optimal implant rotational alignment; femoral component rotation has also been described in relation to the axis of the posterior aspect of the femoral condyles, or perpendicular to the axis of the femoral trochlea. Rotation of tibial TKA components is classically described as centred on the medial aspect of the tibial tubercle [Lutzner et al, 2010].

While rotational alignment and range of movement in the axial plane is not a specific biomechanical measure in our work, it is worthwhile recognising that malrotation of femoral and tibial components is a recognised cause of poor clinical outcome and requirement for early revision in TKA. Quantification of rotation is therefore of interest. In particular, rotational malalignment of femoral components has been associated with anterior knee pain after TKA with patellofemoral dysfunction; Berger et al found that increasing internal rotation of femoral components with respect to the TEA was associated with increased risk of abnormal patellar tracking and subluxation [Berger et al, 1998].

A number of studies have evaluated the precision of rotational alignment with navigation technology. Stockl et al analysed the rotational alignment of components using an image-free Stryker Knee Navigation System. 32 patients were randomized to conventional TKA and 32 to navigated arthroplasty. Both the conventional TKA instrumentation and navigation software aimed for a rotational alignment of within 3° of external rotation with respect to the posterior condylar axis [Stockl et al, 2004]. Rotation was measured post-operatively with CT imaging. The authors found a statistically significant difference in deviation from the neutral rotational alignment (0°) for component placement in conventional TKA versus the navigated group, suggesting more reliable rotational alignment in navigation.

Other studies, however, suggest higher levels of error in registration of rotational alignment. In a cadaveric study by Stockl et al, 4 surgeons repeatedly marked positions on the lateral and medial femoral epicondyles of 6 knee specimens with active infra-red navigation trackers to identify the transepicondylar axis. The authors found that the level of intra-observer variance equated to a possible error in femoral component rotational positioning of ±8° [Stockl et al, 2004]. Jenny et al evaluated the reproducibility of the transepicondylar axis in a clinical setting in a study published in 2004 [Jenny and Boeri, 2004]. 2 surgeons performed repeated registrations of the transepicondylar axis in theatre using the Orthopilot navigation system; the angle between this registration and a constant reference plane was recorded. Intra-observer variations between the reference and transepicondylar axes were 5° and 6 °, with a mean inter-observer variation of 9°.

1.10 Non-invasive navigation

Using image-free knee navigation markers and software in a non-invasiveway - that is, attached to the skin surface rather than secured to bone - is a relatively novel concept.

A key study which sought to develop and validate non-invasive navigation has been published as *Non-invasive Computer-assisted Measurement of Knee Alignment* [Clarke et al, 2012]. The system used in this study consisted of an infra-red localiser with an Orthopilot navigation software package originally developed for high tibial osteotomies. Active infra-red trackers were attached to metal base-plates and positioned at the dorsum of the foot, proximal tibia and distal femur. Base plates were secured to the skin as tightly as tolerated using custom-made adjustable elastic webbing.

The anatomical registration process followed the software workflow as for a navigated HTO. This began with registration of the hip joint centre in space with circumduction, followed by ankle centre registration (dorsiflexion and plantarflexion) and knee joint centre registration (flexion and extension through the range 0-90° and rotation of tibia at 90° of knee flexion). The software gave an on-screen measurement of the baseline extension MFTA as calculated from these points.

The non-invasive system was first assessed for tracker stability by comparing measurements of MFTA from a single knee of a single volunteer with a mechanical simulation of the knee made from metal models of the femur and tibia. Securing the trackers rigidly to the metal model aimed to give a comparison of conventional invasive navigation with trackers secured non-invasively to the skin surface which may have been susceptible to artefact from movement of underlying soft tissues. In this testing the authors found, between multiple registrations, a standard deviation in measurement of MFTA of <1° for both metal model and volunteer. Analysis of the non-invasive system for repeatability was then conducted using 30 volunteers with no history of knee pathology. 2 full registrations were performed on one knee per test subject, with MFTA recorded in full extension while supine, and with bipedal stance. There was satisfactory intra-observer repeatability with CR and LOA <2 (see Chapter 2.3).

This formative research used pre-existing software designed for theatre use in a novel, non-invasive method. More recently, software has been developed specifically for non-invasive navigation, as used in this study (Physiopilot v1.0; B. Braun Aesculap, Tuttlingen, Germany). Initial research of this software was published as *Non-invasive quantification of lower limb mechanical alignment in flexion* [Russell et al, 2014]. In this study, a single researcher tested 6 cadaveric knee specimens. Navigation trackers were attached to the specimens using metal baseplates and fabric strapping, rubber strapping (previously unused) and metal baseplates, and cortical bone screws (as used in the operating theatre in navigated TKA). MFTA was measured using the non-invasive software at full knee extension, and then at 30°, 40°, 50° and 60° of flexion. Varus and valgus force was then applied to the specimens at extension and through the same increments of flexion. A force of 12Nm was applied in a standardised fashion using a handheld electronic force application device. The registration process was performed on each knee specimen 4 times.

The authors found an acceptable [≤2] repeatability coefficient for MFTA through the range of 0-60° range of flexion when using fabric strapping and bone screws to secure navigation trackers. When trackers were secured with rubber strapping, the repeatability was 2.3° when the specimen was flexed beyond 50°. With applied varus or valgus force, the repeatability of the on-screen MFTA became unacceptable once the knee was flexed beyond 30°. This study of the Physiopilot system used cadaveric specimens; these had a mean starting fixed flexion of 12.8° and 1 specimen was only able to flex to 58°. A need was identified for in-vivo testing of the system on a sample of volunteers. This forms the rationale of the experiment methodology presented in this thesis.

1.11 Navigated knee arthroplasty: current evaluation

While there is a body of evidence to suggest that navigation improves the alignment of arthroplasty components, it remains controversial whether this equates to a benefit in terms of clinical outcomes; patient function, satisfaction and implant longevity.

In a meta-analysis published in 2007, the results from 33 studies of computer-assisted knee arthroplasty were examined [Bauwens et al, 2007]. Versus conventional arthroplasty, the paper found that the risk ratio of components being placed with a MFTA outlying the margin of 0±3° was 0.79. There were no statistically significant differences between navigation and conventional TKA for incidence of joint infection, thromboembolism or functional outcomes. The mean operative time for navigation was greater by 17 minutes. Another meta-analysis published in December 2007 [Mason et al, 2007] reached a similar conclusion; the risk of implant placement outlying±3° of a neutral mechanical axis was significantly greater for conventional TKA versus navigation. The analysis, however, did not address patient functional outcomes. Cheng et al published a meta-analysis specifically of image-based navigation systems only which included 5 randomised controlled trials of CT-based systems, finding a higher proportion of arthroplasties aligned within 3° but no statistically significant differences between CAOS and conventional TKA with regards to post-operative complications and patient functional scores [Cheng et al, 2011]. A meta-analysis by Hetaimish et al published in 2012 also found a significantly lower risk of component malalignment for navigation versus conventional TKA on post-op standing long-leg radiographs, but did not analyse functional outcomes [Hetaimish et al, 2012].

Recent trials of navigation systems find similar results. A trial published in 2011 randomized 107 TKA patients to 3 operative groups: navigated, conventional with intramedullary tibial alignment, and conventional with extramedullary tibial alignment [Blakeney et al, 2011]. All were performed by the same surgeon with the same implant and approach. Patients with tibial or valgus deformity pre-op were excluded. On 6 week post-op long leg radiograph and using the ±3° margin, it was found that the navigated group had significantly less malalignment. This was also found on CT at 3 months post-op. There were no significant differences between the groups on CT femoral rotation or tibial posterior slope. A retrospective analysis of 27 navigated and 27 conventional TKAs at a follow-up of 5 years found that MFTA alignment was significantly improved in navigated patients, with a statistically significant improvement also found in patient functional score [Ishida et al, 2011]. In another recent randomized trial of navigated TKA versus conventional in 111 patients, it was found that navigation was more likely to align components within 3° of neutral MFTA, and that this gave improved patient functional scores at 6 weeks, 3 months, 6 months and 12 months [Choong et al, 2009]. With the same patient sample followed-up at 5 years, functional scores continued to be better in the navigated group versus conventional [Huang et al, 2012].

More recently, Rebal et al published a meta-analysis of Level 1 evidence of navigation systems. 21 randomised control trials of image-free navigation systems alone, which analysed functional outcomes, were included. As well as reduced risk of alignment outlying ±3°, image-free navigation patients were found to have statistically significantly higher functional scores at 3 month and 12-32 month follow-up [Rebal et al, 2014]. Most recently, an analysis of data from the Australian National Joint Replacement Registry published in the Journal of Bone and Joint Surgeryin April 2015 found decreased rates of TKA revision with use of computer navigation [de Steiger et al, 2015]. 10 different knee navigation systems were used in the patient cohort (which included 44,573 navigated TKAs and 270,545 conventional TKAs) with 14 years follow-up from 1999-2013. Revision rates at 9 years were 5.2% for conventional TKA versus 4.6% for navigated TKA. A lower revision rate, of statistical significance, was found for patients under 65 for navigated TKA; the difference was not significant for over 65s. This is the first study to suggest that navigation can lead to improved TKA survivorship, and it benefits from a large patient cohort.

Review of the literature however reveals studies which suggest that the clinical benefit of navigation in knee arthroplasty remains uncertain. As discussed above, early meta-analyses did not conclude that functional outcomes were superior in navigated TKA.

A study published in 2009 analysed the outcomes of 637 TKAs performed by a single surgeon over a 5 year period. These were divided into a navigated cohort and conventional cohort and followed-up at 1-5 years post-operatively. The authors did not find any statistically significant differences in Oxford Knee Score between the 2 groups, however it was found that knees (navigated or conventional) which were malaligned with a MFTA outlying the 0±3° margin had significantly poorer Oxford Knee Scores [Kamat et al, 2009]. On linear regression analysis, Widmer et al found low correlation between biomechanical parameters measured intra-operatively with a Stryker Knee Navigation System (on-screen coronal alignment and varus/valgus range at full extension, maximum flexion and extension, external tibio-femoral rotation) and patient satisfaction scores 1 year post-TKA [Widmer et al, 2013].

In a 2011 study, the post-operative morbidity of 146 patients undergoing navigated TKA was compared with a conventional group of 181 TKAs; groups were matched for age, BMI and ASA grade. The authors found that tourniquet and operative times were significantly increased for the navigated group. There were no statistically significant differences between the groups in VTE rates, time to reach 70° of flexion, drop in haemoglobin post-operatively, or total length of stay [Graham et al, 2011]. Another study from 2011 randomized 141 knees in 120 patients to either navigated or conventional TKA. Using long-leg radiographs for MFTA and CT for axial rotation, no statistically significant differences in alignment were found between the 2 groups. There were also no significant differences in early post-op functional outcomes [Hiscox et al, 2011]. A study published in March 2013 analysed a group of 54 patients who had undergone sequential bilateral total knee arthroplasty with one side performed using navigation and the contralateral TKA performed conventionally. The patients were followed up at a mean of 2.5 years. There was a statistically significant decrease in outlying TKAs in the navigated knees although this did not correspond to a significant difference in functional outcomes [Johnson et al, 2013].

Studies have been conducted to evaluate the cost-effectiveness of navigation as an operative method for TKA. A 2008 analysis used a theoretical population of 65 year old patients with osteoarthritis in the USA as a model with the conclusion that cost-effectiveness would decrease with a decreased volume of navigated arthroplasties per year - a centre with 250 navigated cases would require a 2% reduction in annual revision rate for navigation to be cost-effective [Slover et al, 2008]. Another study of cost-effectiveness concluded that navigation could reduce revision rates at 15 years such that savings would be made if navigation incurred an additional cost of $629 or less per operation [Novak et al, 2007].

1.12 Conclusion

This review of the literature aims to provide an introduction to the context and current evidence-base of navigated total knee arthroplasty. While controversy remains over the role of coronal alignment in the aetiology and natural history of knee osteoarthritis, we find a body of evidence to suggest that the alignment of the knee in the coronal plane following arthroplasty is of clinical significance, both in terms of patient satisfaction and the more objective measure of implant longevity before the need for revision. Indeed, this was the rationale behind the development of knee navigation; that implants would be placed more reliably in a satisfactory coronal alignment. Image-free navigation systems, which use infra-red trackers, have been shown to be a repeatable and accurate method of knee arthroplasty. Non-invasive navigation has been developed and used in a number of studies; infra-red trackers are secured to the skin surface allowing assessment of knee kinematics outwith the operating theatre. Early studies suggest that non-invasive navigation can give a reliable measure of mechanical alignment with the knee in extension or early flexion.

CHAPTER 2: TRIAL OF NON-INVASIVE NAVIGATION SYSTEM

2.1 Research aims and objectives

The aim of the research presented in this thesis was to evaluate a non-invasive knee navigation system (Physiopilot) in the measurement of lower limb mechanical femoro-tibial angle (MFTA), with manually applied varus and valgus force, in knee extension and through the range of knee flexion.

As discussed in Chapter 1, there is evidence to suggest that mechanical alignment of the lower limb is relevant to navigated TKA on a number of levels; osteoarthritis is associated with coronal malalignment, which may even form part of its aetiology. The degree of correctibility of deformity is significant for operative planning, as is the concept of soft tissue balancing to give the post-operative knee an appropriate coronal laxity through its range of motion. Post-operative mechanical alignment is also thought to be of significance for implant survivorship. A non-invasive navigation system providing a reliable measure of MFTA could therefore be of clinical value in assessing deformity and laxity pre-operatively, and alignment and balancing post-operatively.

While the use of the Physiopilot system in flexion has been studied in cadavers, as yet there has been no in-vivo evaluation of this nature. We therefore aimed to recruit a number of volunteers, with testing of each knee in each volunteer, to give a sample size of healthy knees which would be of adequate statistical power. In the interests of practicality, we aimed for a sample size of at least 30. The Central Limit Theorem proposes that a sufficient number of iterates of a random variable - in this case, differences between user measurements of MFTA - will have a randomly distributed mean, and many researchers consider 30 as an adequate sample size in trials [Corder and Foreman, 2009]. We aimed to perform varus and valgus stress testing through the range of 0°-90° with 15° increments, to give an experiment protocol which would be practical yet also reflect the intra-operative process of soft-tissue balancing (as described in Chapter 1.8 [Insall, 1985]) and allow identification of trends in coronal laxity with increasing flexion.

With the absence of a comparative ‘gold-standard’ measurement of MFTA, the experiment protocol was developed to allow for the calculation of appropriate intra-observer and inter-observer statistics - repeatability for a single user and inter-observer correlation. There were two system operators, one being the author and the other a post-graduate student in Biomedical Engineering. Both operators were medical graduates, with formal training in clinical examination of the knee and lower limb with 3 years of post-graduate clinical experience.

2.2 Development of non-invasive system

The system used was a non-invasive, image-free knee navigation system similar to that originally developed by Clarke et al in the published study *Non-invasive Computer-assisted Measurement of Knee Alignment* [Clarke et al, 2012]. The system aims to provide reliable kinematic data for the tested knee, including real-time mechanical alignment, similar to the measurements which would be obtained by using a conventional 'invasive' image-free navigation package in the operating theatre.

This consisted of an infra-red Polaris camera [B. Braun Aesculap, Tuttlingen, Germany], navigation base plates [B. Braun Aesculap, Tuttlingen, Germany], fabric strapping, passive infra-red trackers [B. Braun Aesculap, Tuttlingen, Germany], navigation pointer [B. Braun Aesculap, Tuttlingen, Germany], and the Physiopilot® v.1.0 software package [B. Braun Aesculap, Tuttlingen, Germany]. An overview of the system setup is illustrated in Figure 2.1.

Trackers used in computer-assisted orthopaedic surgery are devices which are fixed to a patient in order to mark an anatomical reference point. As discussed previously, the majority of current navigation systems use the emission and detection of infra-red light to determine kinematics. An activetracker emits infra-red light at its point of attachment, which is then detected by the navigation sensor (camera). This necessitates a battery or cable power source for the tracker itself. Passive trackers, as used in this system, use a cluster of reflective points; the navigation camera is thus the source of infra-red emission and detection.

The passive trackers were mounted to metal base-plates, as illustrated in Figure 2.2. These were originally designed for use in theatre in earlier image-free knee navigation systems, to attach navigation trackers to the dorsum of the foot in the registration of the kinematic centre of the ankle. Base-plates were secured to the skin surface using fabric strapping. This consisted of 45mm width elastic webbing with a series of eyelets for attachment of the base-plate; this was identical to that used in the non-invasive navigation system developed by Clarke et al. Various lengths of strapping were available, allowing the base-plate to be secured firmly to differing thigh and calf diameters.

Figure 2.1: Overview of Physiopilot system set-up. The Polaris camera, positioned on the tripod, acts as the source of infra-red emission and detection. Trial participants are positioned, initially supine, on the examination trolley and stand in front of the trolley for bipedal and monopedal stance. To the right of the picture the Physiopilot workflow is shown on-screen.

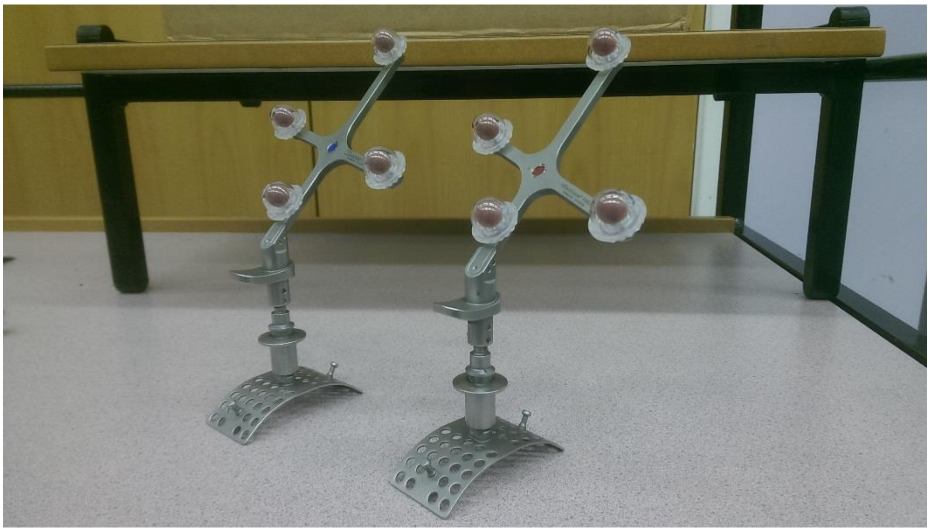

Figure 2.2: Passive navigation trackers - clusters of reflective spheres - attached to base-plates.

2.3 Trial methodology

A submission was made to the University of Strathclyde Department of Biomedical Engineering Departmental Ethics Committee, with ethical approval granted for testing the Physiopilot system on volunteers. The approved submission is found in Appendix 2. Exclusion criteria were previous knee surgery, known knee pathology, and skin lesions, oedema or poor skin quality which would have risked cutaneous damage when attaching the infra-red trackers. All volunteers signed a written informed consent proforma.

The experiment protocol proceeded as follows for each volunteer:

The participant was asked to lie supine on an examination trolley, wearing shorts so that the thigh and leg were exposed, as illustrated in Figure 2.3.

Figure 2.3: Passive navigation tracker clusters are secured to the thigh and leg with fabric strapping. The examination trolley is positioned so that the tested limb is approximately 2m from the camera, as per manufacturer's recommendations.

Base-plates with trackers were attached to the lower limb, with positioning as described in the clinical studies conducted previously by Clarke [Clarke et al, 2012] and Russell [Russell et al, 2014], which are based on manufacturer's recommendations for tracker placement in use of the conventional, invasive Orthopilot® navigation system [B. Braun Aesculap, Tuttlingen, Germany]:

- The thigh tracker, corresponding to the recommended position of a distal femoral navigation tracker, was secured to the skin overlying the vastus medialis anteriorly, just proximal to the superior pole of the patella.
- The leg tracker, corresponding to the recommended position of a tibial navigation tracker,

was secured to the skin overlying the tibial crest, anteriorly, at the level of mid-leg.

The Polaris IR camera and Physiopilot workflow do not include any calibration procedure prior to the registration of landmarks in the tested knee. There are thus no additional registration steps required in use of the system prior to the registration of anatomical landmarks.

The protocol followed the standardised workflow for registration as per the Physiopilot software package:

- Palpable bony landmarks were registered with the navigation pointer, in turn; medial epicondyle, lateral epicondyle, centre of the knee joint (see Figure 2.4), medial malleolus, lateral malleolus, centre of the ankle joint (see Figure 2.5).
- With the limb relaxed and the knee extended, and avoiding movement of the pelvis, the centre of the hip joint was registered by the operator holding the heel and passively circumducting the lower limb.
- The Physiopilot registration process was then completed by passively flexing the knee from the limit of extension to 90° of flexion, and internally and externally rotating the tibia to end points at 90° of flexion.

With the registration process complete, the mechanical femoro-tibial angle (with participant supine with knee extended) calculated by the software was displayed on the screen and recorded.

- With the knee extended, but in an ‘unlocked’ position, a varus force was applied manually by the operator until an end-point in the knee joint was reached. A valgus force was then applied manually by the operator until end-point was reached. The variation/range of MFTA with applied force was displayed on-screen and recorded.
- Force was applied with one hand on either the medial or lateral side of the distal femur to stabilise the thigh, and the other hand gripping the participant’s ankle, to stress the tibia (and hence the knee joint itself) in a varus or valgus direction in the coronal plane.
- The knee was then tested through the range of flexion to 90° in 15° increments; with the on-screen flexion angle at 15°, 30°, 45°, 60°, 75°, 90°, a varus and then valgus force was applied manually by the operator until an end-point was reached. The range/variation of MFTA with applied force was recorded
- The maximum extension/hyperextension and maximum tolerated flexion were recorded
- The Physiopilot workflow was completed by recording the bipedal and monopedal MFTA; the participant was asked first to stand, fully weight-bearing, facing the navigation camera. The MFTA in the tested limb was recorded. The patient was then asked to balance on the

tested foot, and the MFTA in the tested limb was recorded with monopedal stance.

Figure 2.4: Registration of knee centre. The pointer is placed anteriorly, in the pre-patellar area, aiming towards the tibial spines. This corresponded to the midway point on screen between the registered medial and lateral epicondyles.

Figure 2.5: Registration of ankle centre. The pointer was aimed at the lateral border of the palpable tibialis anterior tendon, which has been shown to be a reproducible landmark clinically in registration of the kinematic centre of the ankle joint [Rajadhyakasha et al, 2009]. On screen, we aimed for this to correspond to midway between the registered medial and lateral malleoli.

The trackers, strapping and baseplates were then removed, and the protocol was repeated on the same knee, this time by the second operator. Each operator performed 2 registrations on each knee. Each participant therefore underwent 8 registrations with the Physiopilot software, 4 on each knee.

In order to avoid the operator obscuring the field of the IR camera, and to avoid the operator having to lean over the contralateral limb to conduct stress testing (which may have led to alteration in technique), the patient was asked to turn on the examination trolley when switching between testing of the right and left knees. As can be seen in Figure 2.3, the lower limb contralateral to the tested knee is closer to the IR camera, and we found this patient positioning facilitated easier, and subjectively more reproducible, stress testing of the knee.

2.4 Data Analysis

A group of 23 participants was recruited, all with asymptomatic, ‘healthy’ knees; 13 male and 10 female, with mean age 32.6 years (range 23-59 years) and mean BMI 24.1 (range 18.8-43.1). This gave a sample of 46 knees.

The complete data set for all participants is found in Appendix 2. The efficacy of the Physiopilot system as a measurement tool for mechanical alignment was evaluated by calculating intra-observer CR and inter-observer ICC.

Intra-observer repeatabilities are described using the Coefficient of Repeatability (CR). Using a 95% confidence interval, the Coefficient of Repeatability gives a value below which the absolute difference between consecutive measurements would occur with a probability of 0.95 [Vaz et al, 2013]. The lower the CR, the less likely there is to be a large discrepancy between repeated measurements taken by a user and thus the more reliable or ‘repeatable’ the tool. CR, as advocated by Bland and Altman initially in 1986, is an established means of assessing measurement tools where repeated measurements of a variable are taken by a user. CR for each operator was determined using the standard deviation of the absolute difference between the first and second readings taking for each knee. The value is calculated using the formula:

$$\mathbf{CR = 1.96 \times \sqrt{\Sigma(d2 - d1)^2/(n - 1)}}$$

where d2-d1 is the difference between the repeated readings of MFTA. This statistic accounts for both random and systematic errors in measurement[Vaz et al, 2013]. While conventional, clinically approved knee navigation systems aim for a maximum error of 1°, for the non-invasive system a maximum CR of 2 was considered as acceptable due to the likelihood of additional errors incurred by soft tissue artefacts (see Chapter 3.2).

Inter-observer correlation was assessed with calculation of the Intraclass Correlation Coefficient

(ICC). ICC is an accepted method in clinical trials of measuring correlation between 2 methods of measurement when taking repeated measurements [Bland and Altman, 1986]. Each operator (A and B) performed 2 registrations of the Physiopilot system on each knee, with each user's registration taken as a representation of an individual 'method' of examining the knee for the purposes of this model. Using the 2 readings taken by each operator, a mean was found and used to find ICC [McGraw and Wong, 1994]. Calculated as a value between 0 and 1.00, a higher value of ICC indicates a greater degree of correlation between 2 users measurements of the same variable. Correlation is considered 'poor' when ICC<0.40, fair with ICC 0.40-0.70, and good when ICC>0.70 [Fleiss, 1986]. ICC was calculated using SPSS statistics software [SPSS v.20.0; IBM Corp, Armonk, NY, USA].

Data is represented graphically in this section in the form of Bland-Altman plots for intra-observer agreement. The mean of each user's 2 readings (X axis: Mean) is plotted against the difference between the first and second readings (Y axis: Difference). Points which are duplicate appear as bold. Using a 95% confidence interval, Limits of Agreement (LOA), indicated by the blue lines, give the values with which the difference between the first and second reading would lie with a probability of 0.95. These are calculated using the mean difference between the first and second readings and the standard deviation of the difference between first and second readings [Bland and Altman, 1986]:

$$\mathbf{LOA = mean\ difference \pm 1.96 \times \sqrt{\Sigma(d2 - d1)^2/(n - 1)}}$$

Figures 2.6 and 2.7 show that, with data from all volunteers included, the intra-observer Limits of Agreement for both users fall outwith acceptable values. In addition, when agreement between User A and User B is illustrated in the Bland-Altman plot in Figure 2.8, there is decreased agreement when compared with intra-observer repeatability.

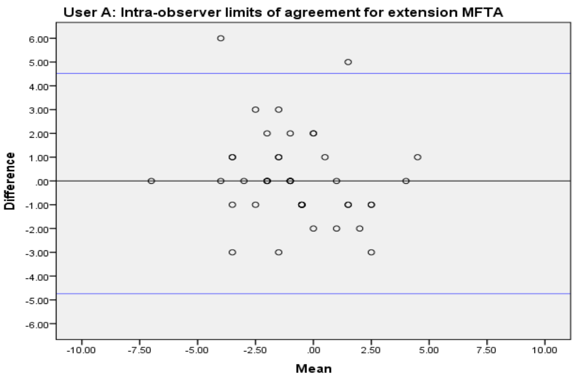

Figure 2.6: Bland-Altman plot with the mean of User A's 1st and 2nd readings plotted against reading 2 subtracted from reading 1. Limits of Agreement with a 95% confidence interval are found to fall outwith acceptable values.

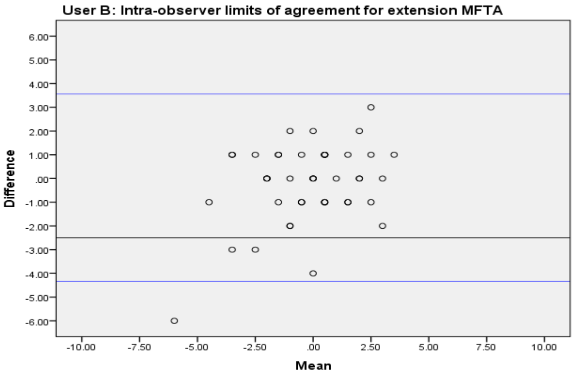

Figure 2.7: Bland-Altman plot of mean of 1st and 2nd readings of User B plotted against reading subtracted from reading 1. Limits of Agreement with a 95% confidence interval are again seen to fall outwith acceptable limits.

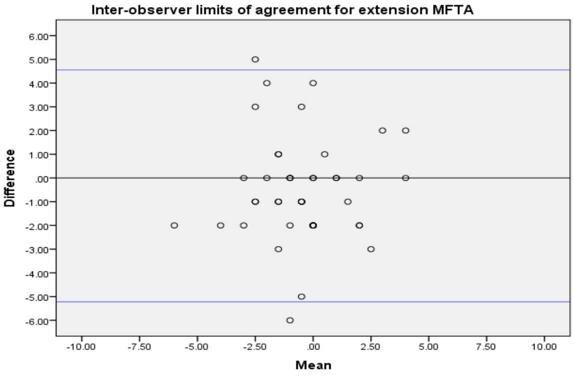

Figure 2.8: Using the mean of 1st readings for MFTA taken by User's A and B, the differences are plotted in this Bland Altman chart, which illustrates a poorer value for agreement between users.

Exclusion of results with inadequate initial agreement:

Analysis of data from registrations for our first 8 volunteers (equating to 16 knees) found that there was inadequate initial agreement for supine MFTA in extension. As with the trial conducted by Clarke in *Non-invasive Computer-assisted Measurement of Knee Alignment* in *Computer Aided Surgery* [Clarke et al, 2012], repetitions of the registration process which did not give an initial measurement of MFTA in extension within ±2° of the first registration were discounted, and the registration workflow was restarted. Indeed, in the use of invasive navigation systems in the context of the operating theatre, it is common practice for initial registrations of MFTA in extension which are thought to be erroneous by the surgeon to be discounted and the registration process repeated [Jenny et al, 2008]. The limit of 2° proposed by Clarke was based on the accepted standard for commercial navigation systems of 1° (see Chapter 1.5) with an additional 1° in anticipation of soft tissue artefacts. A difference in agreement of greater than 2° in extension MFTA was likely to lead to unsatisfactory agreement for MFTA in flexion.

The decision was made therefore to retrospectively discard data (supine, flexion and stance MFTA values) from the first 8 consecutive participants due to unsatisfactory agreement between repeated registrations - that is, a difference of >2° between each operator's 1st and 2nd registrations. Further values were then calculated for intra-observer agreement with this data excluded. No other measurements from the initial sample of 46 knees were excluded except those from the 1st consecutive 16. This gave a final sample of 15 volunteers, equating to 30 knees. The excluded raw data is highlighted in yellow in Appendix 2. Results are illustrated in Figures 2.9 and 2.10 below, which show satisfactory agreement of supine MFTA in extension.

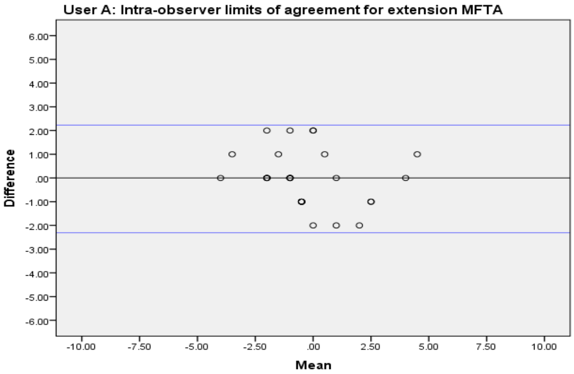

Figure 2.9: Repeatability for the sample of 30 knees show satisfactory improvement for User A in measurement of supine MFTA with the knee extended, with no differences outlying the Limits of Agreement

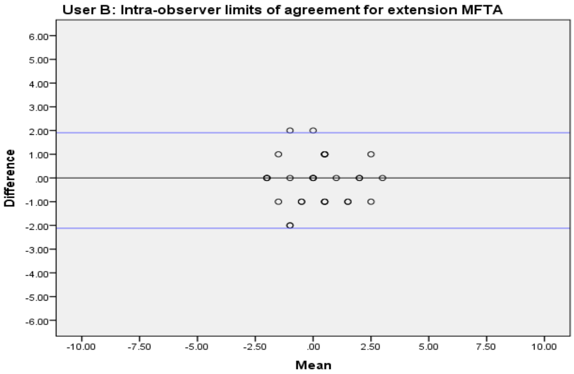

Figure 2.10: There is satisfactory agreement for User B in supine MFTA in extension with the sample of 30 knees

Agreement with applied coronal force:

A varus and valgus force was applied manually to the knee to the palpable limit of coronal laxity. These manoeuvres were initially performed in extension with the knee in an 'unlocked' position. Figures 2.11-2.14 show that, for both users, intra-observer repeatability falls outwith acceptable limits for measurement of MFTA when force is applied. Values for CR for each user at each 15°

increment of flexion are given in Chapter 2.3; Figures 2.11-2.14 illustrate agreement in extension with applied force, with Figures 2.15-2.18 illustrating agreement at the limit of flexion.

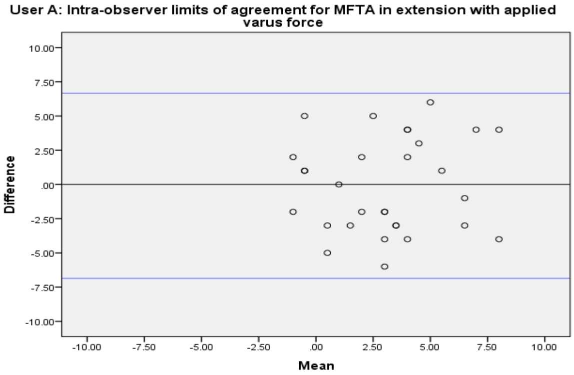

Figure 2.11: Limits of Agreement are greater than the accepted values when a varus force is applied

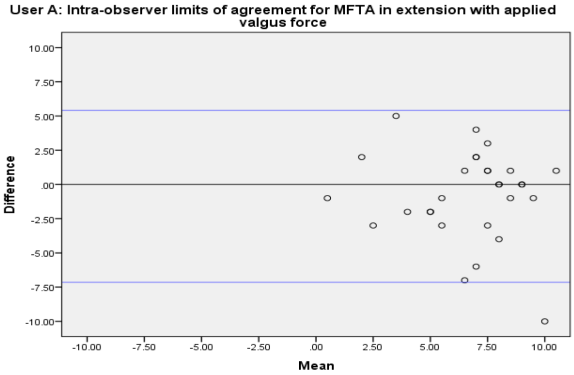

Figure 2.12: Bland-Altman plot illustrating intra-observer agreement for MFTA in extension with valgus force for User A

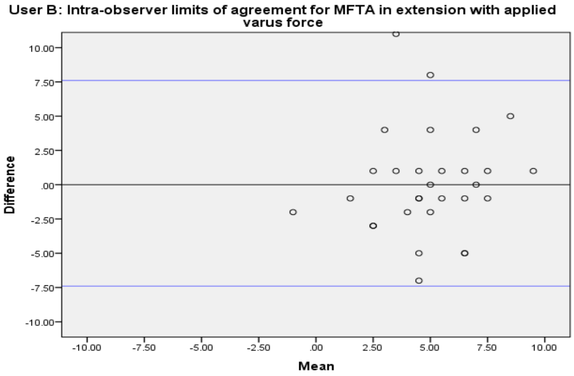

Figure 2.13: Bland-Altman plot illustrating intra-observer agreement for MFTA in extension with varus force for User B

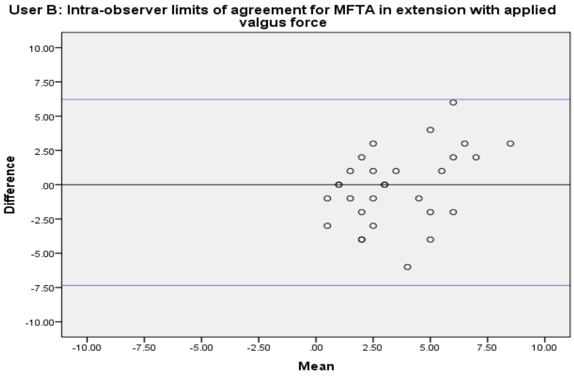

Figure 2.14: Bland-Altman plot illustrating intra-observer agreement for MFTA in extension with valgus force for User B

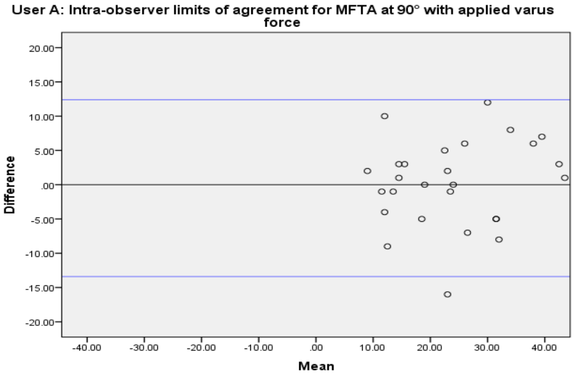

Figure 2.15: There is a significant increase in the Limits of Agreement for measured MFTA at 90° flexion with applied force

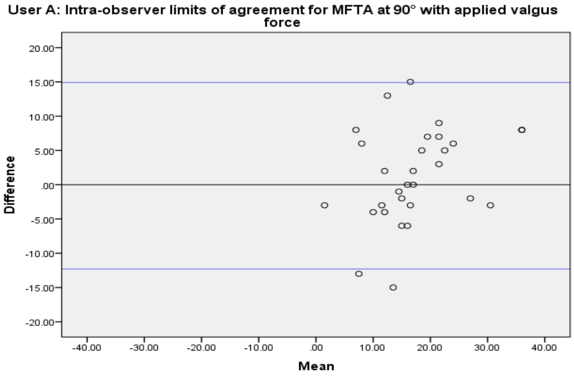

Figure 2.16: Bland-Altman plot illustrating agreement for User A at 90° flexion with valgus force

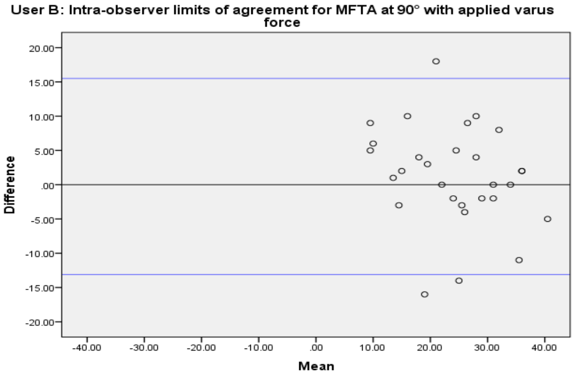

Figure 2.17: Bland-Altman plot illustrating agreement for User B at 90° flexion with varus force

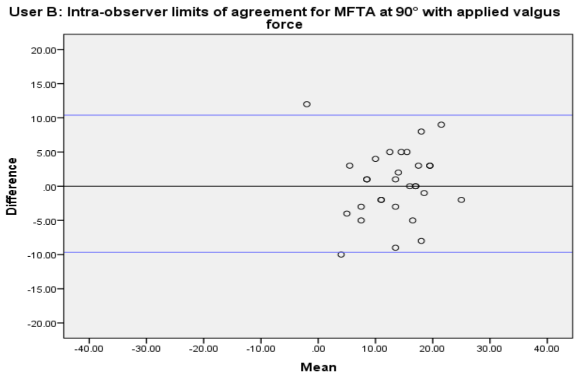

Figure 2.18: Bland-Altman plot illustrating agreement for User B at 90° flexion with valgus force

Table 2.1, below, shows the mean MFTA in extension and stance found for each user, and Figures 2.19 and 2.20, illustrate the mean varus and valgus knee angulations found for each user as an illustration of the trend found in coronal range of movement. As described above, results for the first 8 participants have been excluded due to unsatisfactory agreement in initial supine MFTA. The given angles are the on-screen MFTAs displayed with the knee taken to its palpable limits of coronal laxity at the measured increments of flexion.

	User A	**User B**
Supine MFTA at extension	0.33° varus	0.13° valgus
Bipedal MFTA	0.43° varus	0.33° varus
Monopedal MFTA	0° (neutral)	0.5° varus

Table 2.1: Mean MFTA values calculated for each user

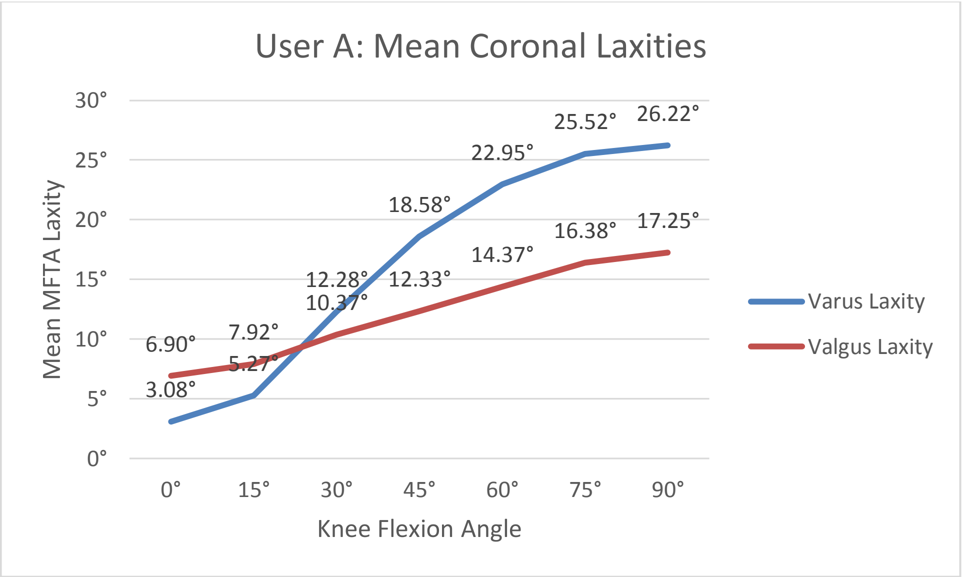

Figure 2.19: Mean angulation in the coronal plane with applied force observed for User A. Readings for 15 volunteers

are used (excluding 1st 8), giving 30 knees, using both registrations performed by User A in each case

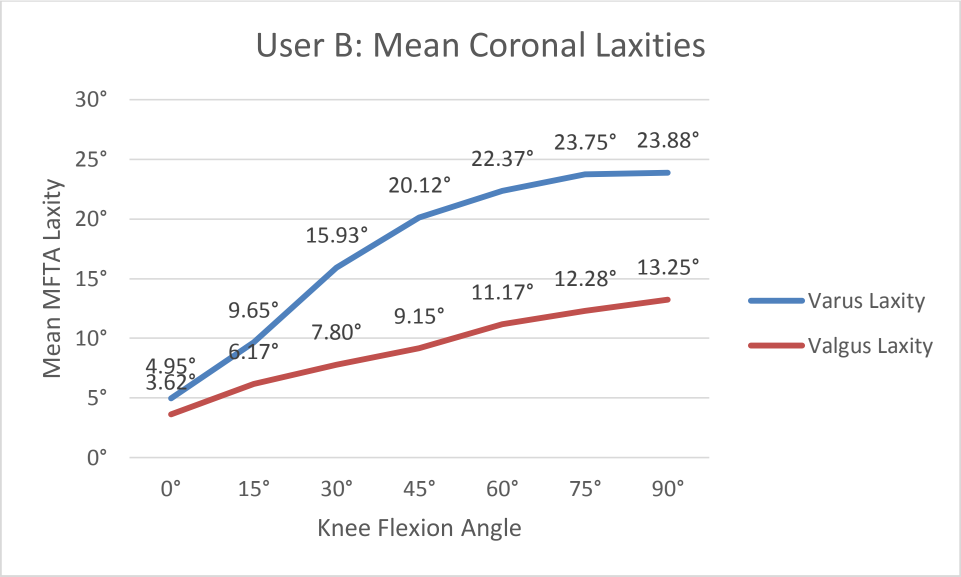

Figure 2.20: Mean angulation in the coronal plane with applied varus or valgus force observed for User B. Both registrations performed by User B are used in each case

The overall trends for Figures 2.19 and 2.20 are similar, with an increase in coronal laxity as flexion increases - that is, with increasing increments of flexion, both users found that a greater increase in MFTA in a varus or valgus angulation was measured by the non-invasive system. In addition, the general trend in laxity illustrated is for greater varus angulation than valgus when force is applied. By comparison, these results are in keeping with 2 recent studies of coronal laxity. In a sample of 50 normal knees, Okazaki et al found a mean limit in extension of 4.9° varus and 2.4° valgus with stress testing [Okazaki et al, 2006]. With a standardised force of 15Nm, Heesterbeek et al found 2.3° varus laxity and 2.8° in extension, with increased coronal laxity when flexion was introduced [Heesterbeek et al, 2008].

Additional data analysis:

Further statistical testing was carried out on the final sample of 30 knees to determine if the participant independent variables of sex, BMI and age had any statistically significant effect on the outcomes of MFTA in extension and coronal laxity in extension and flexion with applied force. In this analysis non-parametric tests were selected so that there was no assumption that the measured outcomes followed a normal distribution. The SPSS statistics software package was also used for these calculations [SPSS v.20.0; IBM Corp, Armonk, NY, USA]. The level of significance was taken as 0.05. For the ordinal variable of sex, a Mann-Whitney U-test was conducted to determine if there were any significant differences in MFTA and laxity for either user at the increments of flexion. BMI and age were taken as continous variables and therefore a Spearman's rank correlation coefficient was calculated. As a correlation coefficient, this gives a value between -1.00 and 1.00, with values closer to 1.00 indicating a greater degree of correlation, and values closer to -1.00 indicating a greater degree of inverse correlation (i.e. the dependent variable decreases as the independent variable increases) [Corder and Foreman, 2009]. Results are given in Chapter 2.5 and further discussion is found in Chapter 3.5.

2.5 Results summary

Supine MFTA in extension/monopedal stance/bipedal stance:

Using data from all 23 volunteers, equating to 46 knees, the agreements for measurement of MFTA are found in Table 2.2, with inter-observer correlation given in Table 2.3. Table 2.3 illustrates a ‘good’ level of inter-observer correlation for supine MFTA measured in extension.

	User A	**User B**
Supine MFTA at extension	3.61	3.01
Bipedal MFTA	4.48	6.94
Monopedal MFTA	5.11	6.76

Table 2.2: Intra-observer CR calculated for supine MFTA at extension (initial registration MFTA), bipedal MFTA in extension and monopedal MFTA in extension

	Intraclass Correlation Coefficient
Supine MFTA at Extension	0.72
Bipedal MFTA	0.57
Monopedal MFTA	0.57

Table 2.3: Inter-observer ICC (correct to 2 decimal places) calculated for supine MFTA at extension (initial registration MFTA), bipedal MFTA in extension and monopedal MFTA in extension

Supine MFTA with applied force:

Due to a software problem at the time of testing, the results of MFTA with applied force from 15-90° could not be recorded for one participant. The initial sample size for the analysis of these results was thus 22 volunteers, equating to 44 tested knees. Intra-observer agreements for Users A and B are given in Tables 2.4 and 2.5, respectively, with inter-observer correlation given in Table 2.6. The general trend is for increased loss of intra-observer agreement with increasing flexion, particularly with applied varus force. Inter-observer correlation remains ‘fair’ throughout flexion.

Flexion Angle	Applied Varus Force	Applied Valgus Force
0°	3.97	5.25
15°	6.12	5.64
30°	8.64	7.72
45°	11.99	8.48
60°	11.53	7.63
75°	10.17	6.73
90°	8.54	12.62

Table 2.4: Intra-observer CR calculated for User A with applied varus and valgus force through the range of flexion

Flexion Angle	Applied Varus Force	Applied Valgus Force
0°	5.01	5.50
15°	7.54	7.96
30°	6.75	7.55
45°	10.29	10.77
60°	12.86	8.15
75°	14.48	7.80
90°	14.65	7.69

Table 2.5: Intra-observer CR calculated for User B with applied varus and valgus force through the range of flexion

Flexion Angle	Applied Varus Force	Applied Valgus Force
0°	0.70	0.58
15°	0.49	0.44
30°	0.68	0.72
45°	0.65	0.62
60°	0.69	0.65
75°	0.60	0.53
90°	0.69	0.64

Table 2.6: Inter-observer ICC for applied varus and valgus force through the range of flexion

Exclusion of results with unsatisfactory initial agreement:

As discussed above, data from the first 8 participants was excluded due to unsatisfactory agreement of initial supine MFTA with repeated readings.Tables 2.7-2.11 below summarise the intra-observer CRs and inter-observer ICCs for the sample of 30 knees. There is satisfactory intra-observer agreement in extension, however this remains unacceptable with applied force through the range of flexion. The general trend is again towards increasing loss of agreement with increasing flexion, especially with varus force. Inter-observer correlation again remains fair throughout:

	User A	**User B**
Supine MFTA at Extension	1.55	1.33
Bipedal MFTA	4.02	6.43
Monopedal MFTA	5.17	6.52

Table 2.7: Intra-observer CR calculated for supine MFTA at extension (initial registration MFTA with no force applied), bipedal MFTA in extension and monopedal MFTA in extension for 30 knees

	Intraclass Correlation Coefficient
Supine MFTA at Extension	0.67
Bipedal MFTA	0.32
Monopedal MFTA	0.54

Table 2.8: Intra-observer CR calculated for supine MFTA at extension (initial registration MFTA), bipedal MFTA in extension and monopedal MFTA in extension

Flexion Angle	**Applied Varus Force**	**Applied Valgus Force**
0°	3.02	4.42
15°	4.51	5.69
30°	5.84	8.13
45°	11.36	7.92
60°	11.90	7.39
75°	9.60	5.95
90°	8.00	8.10

Table 2.9: Intra-observer CR calculated for User A with applied varus and valgus force through the range of flexion for

30 knees

Flexion Angle	Applied Varus Force	Applied Valgus Force
0°	5.08	4.74
15°	5.70	7.07
30°	6.79	6.97
45°	11.45	9.41
60°	14.19	5.80
75°	15.00	5.74
90°	15.78	6.23

Table 2.10: Intra-observer CR calculated for User B with applied varus and valgus force through the range of flexion for 30 knees

Flexion Angle	Applied Varus Force	Applied Valgus Force
0°	0.57	0.54
15°	0.45	0.50
30°	0.61	0.72
45°	0.57	0.61
60°	0.64	0.61
75°	0.51	0.38
90°	0.65	0.61

Table 2.11: Inter-observer ICC for applied varus and valgus force through the range of flexion

Significance of sex:

A Mann-Whitney U-test was used to determine if there were any significant differences in MFTA or laxity between males and females. P-values correct to 3dp at extension and each increment of flexion are given in Table 2.12, with values indicating statistical significance highlighted in blue. This illustrates a tendency for a difference with sex observed with increasing flexion, however the results are not equivocal for both users. Further discussion is found in Chapter 3.5.

	User A	User B
Supine MFTA at Extension	0.126	0.1

Bipedal MFTA	0.203	0.495
Monopedal MFTA	0.161	0.815
0° varus	0.441	0.03
0° valgus	0.184	0.066
15° varus	0.418	0.187
15° valgus	0.383	0.12
30° varus	0.039	0.148
30° valgus	0.383	0.034
45° varus	0.022	0.085
45° valgus	0.09	0.046
60° varus	0.018	0.059
60° valgus	0.017	0.071
75° varus	0.012	0.034
75° valgus	0.008	0.097
90° varus	0.028	0.003
90° valgus	0.003	0.094

Table 2.12: Mann-Whitney U-test p-values for effect of sex on trial outcomes

Significance of BMI:

Spearman’s rank correlation coefficients were calculated to determine the degree of correlation of participant BMI with MFTA in extension and coronal laxity. Values correct to 3dp at extension and each increment of flexion are given in Table 2.13, with those corresponding to a statistically significant p-value highlighted in blue. The largely negative values suggest a tendency for coronal laxity in flexion to decrease if BMI is increased, although this is not entirely uniform and is rarely at a level of statistical significance. Further discussion is found in Chapter 3.5.

	User A	**User B**
Supine MFTA at Extension	0.241	0.292
Bipedal MFTA	0.022	0.181
Monopedal MFTA	-0.008	0.098
0° varus	0.23	0.403 (p=0.027)
0° valgus	-0.329	-0.372 (p=0.043)
15° varus	-0.073	-0.001

15° valgus	-0.371 (p=0.043)	-0.283
30° varus	-0.232	-0.123
30° valgus	0.01	-0.321
45° varus	-0.226	-0.146
45° valgus	-0.16	-0.214
60° varus	-0.105	-0.087
60° valgus	-0.135	-0.034
75° varus	-0.252	-0.071
75° valgus	-0.243	-0.068
90° varus	-0.158	-0.101
90° valgus	-0.18	-0.105

Table 2.13: Spearman rank correlation coefficients for effect of BMI on measured outcomes

Significance of age:

Spearman’s rank correlation coefficients were calculated to determine the degree of correlation of participant age (in years) with MFTA in extension and coronal laxity. Values correct to 3dp at extension and each increment of flexion are given in Table 2.13, with those corresponding to a statistically significant p-value highlighted in blue. Again, largely negative values in flexion suggest a tendency for coronal laxity to decrease with increasing age, although this is not uniform. Further discussion is found in Chapter 3.5.

	User A	**User B**
Supine MFTA at Extension	0.254	0.088
Bipedal MFTA	0.119	-0.075
Monopedal MFTA	0.118	-0.083
0° varus	0.235	0.312
0° valgus	-0.408 (p=0.025)	-0.2
15° varus	-0.068	-0.157
15° valgus	-0.33	-0.169
30° varus	-0.045	-0.105
30° valgus	-0.028	-0.218
45° varus	-0.379 (p=0.039)	-0.15
45° valgus	-0.177	-0.201

60° varus	-0.202	-0.123
60° valgus	-0.091	0.001
75° varus	-0.299	-0.102
75° valgus	-0.095	0.023
90° varus	-0.149	-0.116
90° valgus	-0.015	0.01

Table 2.14: Spearman rank correlation coefficients for effect of age on measured outcomes

CHAPTER 3: DISCUSSION OF FINDINGS

3.1 Reliability in extension versus knee in flexion

As discussed in detail in Chapters 1.7 and 1.11, the literature suggests that MFTA following TKA (with or without use of a navigation system) can have a significant effect on patient functional outcome and implant survivorship [Jeffrey et al, 1991], [Ritter et al, 1994], [Berend et al, 2004], [Kamat et al, 2009], although this is not agreed unequivocally [Paratte et al, 2010]. We felt that there was sufficient evidence to give a justifiable rationale for a study of coronal alignment in the use of a navigation system. Repeat calculations of CR were made with our first 8 volunteers excluded due to unsatisfactory initial agreement. This gave a sample of 30 normal knees. With values of 1.55 and 1.33 calculated for intra-observer Coefficients of Repeatability, and 0.72 calculated for interobserver Intraclass Correlation Coefficient, our study found that after each user trialling 8 participants, an acceptable level of repeatability for the measurement of supine mechanical alignment in extension was achieved. These results are in keeping with the findings previously demonstrated by Russell et al in *Non-invasive quantification of lower limb mechanical alignment in flexion*. As discussed in Chapter 1.10, in this trial the non-invasive Physiopilot system was tested on a sample of 12 cadaveric limbs, and compared with a conventional, invasive navigation system using Orthopilot software. The authors found an adequate limit of agreement for MFTA for the range of flexion 0-30° using Physiopilot with applied varus or valgus stress. With flexion above these limits, the repeatability was unacceptable [Russell et al, 2014].

Our view is that the improvement in agreement observed after testing the first 16 consecutive knees may represent a ‘learning-curve’ of registrations required before satisfactory, repeatable use of the system is achieved. There is evidence in the literature that more precise results are obtained with navigation systems after an initial ‘training’ period of usage - as yet not clearly quantified. Learning-curve in CAOS is discussed more fully in Chapter 3.3.

As discussed in Chapter 1.5 and Chapter 1.7, engineering standards for invasive CAOS systems state that navigation should aim for an error of 1° or less in measurement of alignment, while a margin of error of ±3° from neutral is frequently accepted in the literature as an aim for post-operative lower limb alignment. While our calculations show 'fair' inter-observer ICC values for applied force through the range of flexion, CR values show inadequate intra-observer agreement when varus or valgus force is applied, both in extension and through the range of flexion from 0-90°. In addition, CR and ICC fall outwith acceptable limits for extension MFTA with bipedal and monopedal stance. The general trend for inter-observer correlation is for ‘fair’ ICC in flexion, which does suggest a degree of similarity between the MFTAs measured by each user at each increment of flexion. However, when agreement between users is also plotted, even in extension (see Figure 2.8), this is unsatisfactory.

Our study of the Physiopilot system at this point in time did not involve clinical and ethical approval for radiographic assessment of volunteers (for example, standing long-leg radiographs, an accepted method of measuring mechanical alignment, as discussed in Chapter 1.2). Volunteers did not undergo TKA subsequently, and thus did not have alignment measured by a conventional, invasive knee navigation system. Our research therefore does not assess agreement of the Physiopilot system measurements with a 'ground-truth' or 'gold-standard' measurement, but rather evaluates the system solely in terms of intra-observer and inter-observer agreement. Despite this, in keeping with previous research, our work can support the use of the Physiopilot system in the measurement of lower limb MFTA in extension. However there is insufficient evidence from our trial to support its use in measuring MFTA with manually applied force in standard clinical examination.

This invokes a discussion of possible sources of error which could account for unsatisfactory reliability of the non-invasive system with applied force in flexion.

3.2 Soft tissue artefacts

As discussed in Chapter 1.5, in the context of the operating theatre, conventional, invasive image-free knee navigation systems use passive or active infra-red trackers which are attached to bony anatomy with drilled cortical bone screws. They are assumed to be fixed and immune - as possible - to any artefactual movement which would result in loss of registered position. It is therefore intuitive to assume that attaching trackers non-invasively to the skin surface could result in a significant level of error.

In performing varus and valgus stress testing in the context of the non-invasive system, force is applied directly to the skin, subcutaneous tissue and muscle in close proximity to the attached markers. It is therefore assumed that error in marker position would be incurred due to deformation and movement of these structures. As illustrated in Figure 2.2, the reflective infra-red markers used in the Physiopilot system are attached to metal base plates which project the markers upwards. Movement of underlying muscle and tissue may lead to a higher relative movement in positioning of markers due to a pendulous movement of the cluster set moving to either side on its mounting.

Additionally, conventional invasive navigation systems are used in anaesthetised patients with muscle relaxation. Variation in limb muscle activation and tone is negligible; this is evidently not the case for our sample of volunteers. While patients in the operating theatre are supine, our volunteers were additionally assessed with bipedal and monopedal stance. Stress testing of the knee joint may be associated with discomfort, which may lead to variations in muscle tone and activation. It is possible that these factors may all lead to error in registered position of markers attached to the skin.

Attempts were made to minimise these sources of error by careful prior definition in the experiment methodology of the surface anatomical landmarks we wished to register in each trial participant. In addition, in performing the examination on each patient we aimed to direct varus or valgus force only through the medial or lateral malleolus while steadying the proximal thigh; if soft tissue movement was seen in the calf or thigh then the manoeuvre was repeated.

In the initial studies by Clarke, attempts were made to quantify the errors incurred by using a navigation system non-invasively. In preliminary in-vivo testing of non-invasive trackers, varus and valgus stress testing of the knee was found to increase the limits of agreement by ±0.5 when supine MFTA in extension was subsequently registered again. Standing (bipedal stance) was associated with an ±0.2 increase in limits of agreement. These calculations do give an estimate of the error which may be incurred by muscle activation and weight-bearing in stance, and with muscle activation due to stress testing. However, it is important to note that these quantifications relate specifically to the repeat measurement of supine extension MFTA *after* stress testing or weight-bearing, which cannot be easily extrapolated to the stress testing in flexion performed in our trial. In addition, the studies by Clarke found a CR of 3 for measurement of MFTA with bipedal stance, which indicates a loss of repeatability for weight-bearing versus measurements when supine [Clarke, 2012]. Our own values for this were higher; 4.02 and 6.43 for Users A and B, respectively. It is entirely possible that increased muscle activation while standing leads to a soft tissue artefact and change in positioning of skin surface markers which incurs significant error.

A (limited) number of other studies of relevance found in the literature have investigated the errors associated with soft tissue movement in using optical trackers. Using fluoroscopy, Sati et al found that skin overlying the medial and lateral condyles could move in position by up to 17mm [Sati et al, 1996]. On 2 patients following TKA, Stagni et al used X-ray fluoroscopy to define bony anatomy and stereophotogrammetry with skin surface optical markers simultaneously with the subjects performing sitting, standing and stair-climbing. The standard deviation of movement of trackers on the skin surface from original position after movement was 31mm for the thigh and 21mm for the calf [Stagni et al, 2005]. Other authors have directly compared skin-mounted trackers with trackers fixed to bony landmarks in gait analysis trials. In a study of this nature from 2002, Manal et al used bone trackers fixed to the medial and lateral malleoli, and skin trackers attached to the calf skin surface simultaneously on a group of 3 subjects. Results were given as moments (i.e. torque) of the lower limb measured using invasive versus skin-mounted trackers; an error of 1 Nm was found in moment about a longitudinal axis [Manal et al, 2002].

It is somewhat difficult to compare the results of these studies with the methods in our own trial as they involved gait analysis rather than supine or stance alignment, and do not specifically address errors in angular coronal alignment. Nevertheless, they suggest that significant errors due to soft tissue artefacts can occur which could equate to difficulties in reliably measuring coronal mechanical alignment with non-invasive infra-red trackers.

One of the limitations of our methodology in applying coronal force with the introduction of flexion is that this manoeuvre invariably results in a rotational movement of the femur and hip joint. In our study the examination technique attempted to minimise lower limb rotation in assessing extension MFTA and coronal laxity with one hand firmly holding the thigh/femur while the other hand applied force from the ankle. However it was impossible to eliminate rotation of the tested limb, particularly when flexion was introduced. Studies in the biomechanical literature have referred to ‘crosstalk’ - a (motion-capture) system designed to measure kinematics can interpret movement about one axis (e.g. flexion in the sagittal axis), as movement in another. Internal and external rotation of the femur with flexion and extension have been well described in knee biomechanics [Johal et al, 2005], although the potential effect of this on the measurement of coronal alignment by a navigation system has not.

Baker et al analysed a gait analysis system with different limb marker positions in children with cerebral palsy and found significant error in measured coronal alignment with maximum knee flexion in swing and stance phase [Baker et al, 1999]. Kannan et al measured mechanical alignment in a prosthetic model of the lower limb using long-leg radiographs with 5° increments of knee flexion and lower limb internal and external rotation up to 20°. A combination of knee flexion and lower limb external rotation was found to progressively alter measured MFTA up to an error of 5° [Kannan et al, 2012]. Prior, similar studies of prosthetic limb models of lower limb internal and external rotation with knee flexion [Lonner et al, 1996] or without knee flexion [Radtke et al, 2010] also show statistically significant effects in radiographically-measured coronal alignment. Studies of this nature suggest that if rotation, with knee flexion, is introduced to the lower limb when assessing subjects with our non-invasive navigation system, a significant error can occur in MFTA which may considerably contribute to the unacceptable repeatability found. A recent study used MRI to assess rotation of the tibia with knee flexion. 30 patients were asked to lie supine with the foot fixed in position; when flexion was introduced to the knee joint up to 40°, the tibia was observed to internally rotate to a mean of 11.55° [Chen et al, 2014]. An IR tracker was fixed to the tibia in our study; while there is no clear quantification of the subsequent error in coronal alignment due to tibial movement, it is possible that this is an additional source of artefact. It is clear that complex interactions of movements about the sagittal, axial and coronal axes lead to difficulties in accurately measuring the kinematics of the knee joint. Unfortunately, there is no clearly defined method of eliminating lower limb rotation in routine clinical examination. A variety of operating table and patient positioning paraphernalia are used in orthopaedic surgery, such as the 'Durham' thigh side support which prevents lower limb adduction, to more advanced technology such as automated limb traction and positioning devices. There is no evidence for use of these in knee examination and measurement of mechanical alignment, however.

It is also worth commenting on the fact that our study assesses the knees of healthy participants only, with those with any history of knee pathology or previous knee surgery excluded. Table 2.1 shows that the mean alignment in extension (supine and with bipedal/monopedal stance) for our healthy participants was close to 'neutral'. However, knee osteoarthritis is associated with coronal deformity [Brouwer GM et al, 2007], pain and loss of range of movement in the sagittal axis. The ultimate purpose of the non-invasive system would be in the clinical assessment of knees with OA and post-TKA, and it is possible that these conditions may impose further error. Unfortunately there is a general paucity of evidence to quantify the potential additional error of the kinematics, symptoms and deformity of the osteoarthritic knee versus a healthy sample.

3.3 Learning-curve in CAOS

The two operators in our study were junior trainees with training and experience in clinical examination of the knee, but no prior experience with the use of the non-invasive navigation system. While the operators conducted multiple registrations (>20) on each other as test subjects before commencing the trial, it was felt that the relative inexperience with knee navigation systems was a significant source of error and may have contributed to the unsatisfactory values for repeatability with flexion. Indeed, there is some evidence in the literature to suggest that there is a significant learning curve in the use of navigation systems before reliable, repeatable results are produced. In a paper from 2004 [Donnelly et al, 2004], a single surgeon performed 32 TKAs using a Stryker Knee Navigation System, as their first experience with CAOS technology. An unsatisfactory complication rate was found, with complications in 4 cases, including errors in pin placement and outlying initial MFTA registration. In a further 3 cases the navigation system was abandoned in favour of conventional instrumentation.

A study published by Maniar et al found that lack of experience with navigation systems had an effect on operative outcome. A single surgeon switched from conventional TKA to an image-free navigation system; 3 patient groups were identified - 100 consecutive conventional TKAs before switching, 100 consecutive TKAs in the second month of navigation use, and 100 consecutive TKAs after the operator had performed over 500 navigated procedures [Maniar et al, 2011]. With mechanical axis measured on long-leg radiographs post-operatively, it was found that 66% of the conventional group, 94% of the early navigation group and 100% of the final navigation group had an axis within the margin of 0±3°.

In a study from 2008, however, Jenny et al concluded that the effect of inexperience could become negligible after a small number of registrations. A sample of 368 TKAs using the Orthopilot system was assessed; 150 were performed at 5 centres with previous experience of the system, and 218 were performed at 8 centres using Orthopilot for the first time for the purposes of the study. There were no significant differences between the experienced and beginner groups in the outcome measures of alignment (MFTA measured on post-op long-leg films, with 0±3° taken as satisfactory), clinical outcome (Knee Society Score), and intra-operative and post-operative complications. Operating time was initially 10-20 minutes in the beginner group but this difference decreased to an insignificant level after the operator had performed 20 procedures. 2 cases were abandoned due to difficult registration of hip centre, 2 due to persistently questionable initial MFTA registration, and 2 due to software problems [Jenny et al, 2008].

We feel that the CAOS learning curve is itself evident in our work, in that repeated registrations in our initial 8 volunteers found unsatisfactory agreement in extension. There was, however, satisfactory initial agreement thereafter - that is, after each operator had performed 32 registrations in the trial. With initial registration in supine extension inadequate, results for these knees for MFTA with applied force in flexion were subsequently excluded and intra-observer agreements recalculated, which showed improved agreement.

It was thought in particular that difficulties with adapting clinical examination technique with use of the non-invasive system hardware may have led to error when flexion was introduced. This may be particularly related to user inexperience with navigation systems. In stress testing participants, care was taken by each user to perform stress manoeuvres which were as reproducible as possible, with one hand placed on the medial/lateral malleolus and medial/lateral knee joint margin to apply a coronal force. However, it was essential not to accidentally move the marker sets attached to the skin surface in doing so, or to obscure the markers from the view of the infra-red camera. This inherently made clinical examination a more difficult process. In introducing flexion to the knee, the users will additionally have introduced flexion to the hip joint. Quantification of the way in which these movements may affect measured MFTA with a non-invasive navigation system is unclear. In one relevant cadaveric study, Mayr et al found that flexion of the hip joint to 90° could result in an error of up to 2.5° in the mechanical alignment measured using a corresponding distal femoral navigation tracker [Mayr et al, 2006].

3.4 Force standardisation

As would be performed in a routine clinical examination of the knee, the joint was stressed with varus and valgus force to what was felt to be an 'end-point' - as deemed subjectively by the operator. There was therefore no quantification of the force (torque) applied to the joint from volunteer to volunteer. Measurement of applied torque is not viewed as a standard aspect of clinical examination of the knee, and there is no consensus found in the orthopaedic literature as to a preferred method of doing so.

There are a number of studies of relevance to this area. To attempt to reliably quantify the moment applied to the knee joint in the coronal plane, Clarke developed a force application device which consisted of a right-angled padded aluminium bracket fitted with torque sensors linked to a data acquisition software package. The bracket was positioned over the medial or lateral malleolus and moment determined by force acting on a horizontally aligned transducer [Clarke et al, 2012]. The mean coronal force applied was measured as 19Nm, range 13-33Nm. Unfortunately, it was not technically feasible at the time of our study to incorporate this force application device into the Physiopilot workflow. In Russell's cadaveric study of the Physiopilot system, torque in the coronal plane was standardised at 15Nm using a manual hand held force transducer; however, this equipment was attached to the distal tibia using cortical bone screws, which was not suitable for our in-vivo trial [Russell et al, 2014]

Other methods of applying a standardised force to the knee can be found in the literature. A description of applying force in the process of intra-operative soft tissue balancing using laminar spreaders has been mentioned previously, in Chapter 1.8 [Unitt et al, 2008]. In a recent study, Panzica et al attempted to simulate lower-limb weight-bearing conditions intra-operatively by applying a standardised load in the axial plane to the extended knee. A force equivalent to half the patient's body weight was applied to foot using a foot-plate. MFTAs were recorded using the image-free navigation system, with and without applied force. With a sample of 30 patients, and 2 operators, high intra-observer and inter-observer ICCs of 0.997 and 0.998 were reported in achieving the target force. This study, however, did not standardise force application to the complexities of varus and valgus angulation, or to forces on a knee through the range of flexion [Panzica et al, 2014]. Crottet et al had previously described a similar approach, using the distance of medial or lateral knee joint compartment opening with a standardised applied axial force to determine soft tissue balancing technique [Crottet et al, 2007]. It is difficult to see, however, a way in which these invasive, intra-operative techniques from single studies could be adapted to the setting of non-invasive navigation.

Rather than quantification of force itself, other studies have used a measurement of 'joint opening' in relation to varus and valgus applied force, that is the distance gap which appears in the medial or lateral compartment of the knee with manual stressing of the joint. This has been particularly described in relation to assessment of medial collateral ligament injuries, the primary constraint to valgus force in the knee. An example is found in the American Medical Association Standard Nomenclature of Athletic Injuries, which grades (specifically) medial joint opening, as assessed in subjective clinical examination, as 3-5mm, 6-10mm or >10mm when compared with the contralateral side [Wijdicks et al, 2010]. This, however, relates to the injured knee, and quantifying or standardising assessment of the normal knee in this manner in our own study would be inappropriate.

The significance of coronal alignment in osteoarthritis and knee arthroplasty has already been discussed in detail in Chapters 1.2 and 1.7, and a non-invasive, image-free/IR navigation system could be a valuable tool in assessing coronal alignment. With regards to coronal stress testing in pre-operative clinical assessment, the importance of ‘correctibility’ on examination of any valgus or varus deformity due to OA has been emphasised by a number of studies. For example, for valgus deformity found pre-operatively, Ranawat et al grouped knees according to the extent of malalignment, with a ‘Grade 3’ non-correctable deformity of >20° valgus MFTA recommended as a relative indication for use of a constrained TKA implant [Ranawat et al, 2005]. An accurate and repeatable tool for measuring coronal alignment with stress testing could thus guide surgical technique. Coronal laxity in the intra-operative process of soft tissue balancing and its relevance to navigation systems has been discussed in Chapter 1.8, with note made of the lack of robust evidence quantifying a target laxity. In the post-operative period, and moving to longer-term follow-up, some authors have recommended a varus/valgus laxity of ±2° as satisfactory [Deep et al, Nov 2015], although again this lacks a clear evidence base. Interestingly, using a standardised force in a sample of 71 TKAs, Sekiya et al found that medial collateral (valgus) laxity remained largely constant immediately post-arthroplasty until 12 months follow-up, however lateral collateral (varus) laxity was found to be increased from 0-3 months post-op, then decreased - any significance of this with regards to clinical outcome was not addressed [Sekiya et al, 2009]. We can therefore envisage that an accurate non-invasive measure of coronal laxity may be useful in assessing TKAs post-operatively for studies addressing these unresolved issues.

3.5 Effects of sex, BMI and age

As illustrated in Figures 2.19 and 2.20, in both users' measurements, varus and valgus coronal laxity was seen to increase with increasing flexion. However, the repeatability of the non-invasive system was also seen to decrease with increasing flexion; one may therefore envisage that if a participant factor (for example age) were to affect coronal laxity, this may in turn affect the precision of the system.

There was a tendency observed for a statistically significant difference between males and females in coronal laxity with increased knee flexion, particularly at 60° and greater. However, this was not equivocal between the 2 users. Increased generalised ligamentous laxity in female knees has been described in a number of studies, particularly in relation to AP laxity with the ACL and PCL [Rozzi et al, 1999]. This has also been observed in the MCL and LCL [Shultz et al, 2011]. In a study of osteoarthritic patients, van der Esch et al found a mean of 7.7° varus/valgus laxity in females in extension versus 4.6° in males [van der Esch et al, 2007]. It would therefore not be unexpected to encounter an effect with sex in our results, however given the poor precision of the Physiopilot system with increasing flexion it would be difficult to consider the results as convincing evidence of sex as a significant factor in coronal laxity.

There has been some criticism of the general clinical use of Body Mass Index (BMI) as an accurate reflection of body fat composition [Rothman KJ, 2008], however BMI (body weight in kg divided by the squared value of height in m) is commonly measured in patients undergoing knee arthroplasty as its significance with regards to clinical outcome is well documented. Obesity, taken as a BMI of greater than 30, is a risk factor for the development of knee osteoarthritis, and meta-analysis has shown higher infection and revision rates following TKA in obese patients [Kerkhoffs et al, 2012]. There is also evidence that obese patients have lower post-TKA functional scores [Issa et al, 2013]. Watts et al found that, in a sample of morbidly obese patients undergoing TKA, increased anterior knee subcutaneous fat thickness was associated with an increased risk of post-op wound infections [Watts CD et al, 2016]. As seen in Table 2.13, Spearman rank correlation coefficients for BMI have largely (although not universally) negative values for both users at increments > 0°, suggesting a tendency for increased BMI to decrease laxity as flexion is introduced to the tested knee. However, only 2 of these values correspond to a statisically significant effect at the 0.05 level, and indeed user B found a significant *positive* correlation for BMI with varus force in extension. It is again therefore difficult to reach any definitive conclusion on the effect of BMI on our use of the non-invasive system.

As illustrated in Table 2.14, the largely negative values for Spearman correlation coefficients for increasing age with coronal laxity in flexion suggests that laxity would tend to decrease with age, however this again is not uniform for both users and only 2 values are at a level of statistical significance. There is limited evidence of a relationship between age and coronal knee alignment and laxity. One small study indeed found that an older age group (20-40 years versus 54-85 years) had a slightly higher mean varus/valgus laxity in extension, which was not statistically significant, however this was study of osteoarthritic patients [Sharma et al, 1999].

3.6 Future work

The clear issue with the Physiopilot non-invasive system which arises from our study are the findings of unsatisfactory reliability for coronal alignment in flexion, and unsatisfactory reliability when a non-standardised varus or valgus force is manually applied, both in extension and through the range of flexion 0-90°. Our results do not indicate value in conducting further in-vivo trials of the system in its current form with non-standardised force. Progressing to clinical testing, including pre-operative assessment in OA and laxity assessment, would not be appropriate based on our results. With the potential sources of inaccuracy and imprecision outlined above, including soft tissue and skin deformation, muscle activation and femoral rotation, it is this author’s opinion that further non-clinical studies (cadaveric or in-vivo) are required to address these errors before progress can be made. An initial step for testing on the part of the manufacturers may be to attempt to quantify the error incurred in MFTA measurement when flexion is introduced to the knee, as it may be that this precludes any further use of the system in the measurement of coronal alignment in flexion. A further key issue is that the fact that repeated registrations in our initial 16 tested knees showed an unacceptable intra-observer repeatability, which we have attributed to inexperience with CAOS systems. With a current lack of convincing evidence in the literature to define the length of training time - i.e. the number of registrations required by a user before satisfactory precision is achieved - it may be useful for the manufacturers to conduct further trials to this effect.

Nevertheless, the Physiopilot system was able to give an acceptably repeatable measure of static MFTA in extension when supine, and a non-invasive image-free/IR system has the distinct advantage of avoiding the ionizing radiation incurred by long-leg radiographs or CT scanning. The potential to conduct future studies of coronal alignment in larger samples of both healthy and osteoarthitic patients may develop a better understanding of ‘normal’ MFTA versus alignment in OA, and guide a standardised/algorithmic approach to surgical technique to establish the most appropriate target alignment in TKA. Indeed, Deep et al (see Chapter 1.7) used an Orthopilot non-invasive navigation system in their recent study of MFTA in healthy knees [Deep et al, Apr 2015]. Monitoring of coronal alignment in long-term follow-up post-arthroplasty may develop evidence of its role in functional outcome and survivorship. If the Physiopilot system were developed to be able to reliably measure MFTA with applied coronal force (which, in this author’s opinion, is likely to require equipment to standardise force application), future studies could include assessing laxity in ‘normal’ and pathological knees, and long-term assessment post-arthroplasty, with the ultimate goal of a continuous, standardised process of measuring coronal alignment and laxity through the pre-operative and post-operative periods to evaluate the impact of these parameters on clinical outcome.

CONCLUSION

Given the clinical significance of coronal alignment described in the literature, it certainly seems intuitive that a reliable, yet non-invasive navigation system could be a powerful tool in patient management. In keeping with previous studies, our research suggests that the Physiopilot system, under clinical examination conditions in vivo, can give a reliable measurement of MFTA in extension. As such it may have potential as a tool in the clinical assessment of deformity in osteoarthritis, and the correctability of deformity. However, we found that the system gave unacceptable agreement with manually applied varus and valgus force when flexion was introduced. This may have been due to errors incurred by soft tissue artefact, lack of operator experience with navigation systems, and lack of force standardisation. There are a number of opportunities for further work with the non-invasive system, particularly, in this author's opinion, with attempts to integrate a validated force standardisation tool with the Physiopilot software.

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