Assessment of the Arthritic Knee: Patient Selection for Oxford Unicompartmental Knee Arthroplasty

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Abstract

Assessment of the Arthritic Knee:
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The aim of this thesis was to establish the long-term outcomes of the Oxford medial Unicompartmental Knee Arthroplasty (OUKA), define patient selection criteria and to develop and externally validate an evidence based method of patient selection for this procedure.

In the hands of the developer surgeons, outcomes following medial OUKA were found to be good with an implant survival of 94% (95%CI 92 to 96) at ten-years and 91% (95%CI 83 to 98) at fifteen-years. Across the published literature, however, variation in outcomes was observed with a meta-analysis of published series of OUKA finding estimates of ten-year survival ranging from 57% to 100%, mean 88% (95%CI 85 to 90).

It was identified that both increased surgical caseload (volume) and increased surgical usage (proportion of primary knee arthroplasty that are OUKA), a surrogate marker of indications, were associated with improved outcomes. Surgical usage, however, was more important, with good results following OUKA seen with high surgical usage, representing broad indications, independent of the surgical volume. This finding, coupled with differences in patient demographics and failure mechanisms between usage groups, highlighted that differences in indications for OUKA may explain the variability in outcomes observed.

One reason surgeons may have a low usage is if they apply previously recommended patient factor contraindications based on age (<60 years), weight (≥82kg) and activity level (high activity). When disease factors are standardised, however, it was found that patients with these previously reported contraindications often actually did better than those without, and outcomes of knees implanted where all these factors were present were as good as where none were present. Therefore, the decision to proceed with OUKA should be based on the pathoanatomy of disease.

Optimal candidates for OUKA should have full-thickness cartilage loss, with bone on bone arthritis, in the medial compartment, as knees with partial thickness cartilage loss were found to have worse functional outcomes and almost three-times the reoperation rate, predominantly for unexplained pain. Provided there was full-thickness preserved cartilage laterally and functionally normal ligaments, the presence of lateral osteophytes and the macroscopic status of the anterior cruciate ligament was not found to influence outcomes, nor did the presence of patellofemoral joint disease (with the exception of lateral facet disease with bone loss and grooving) or anterior knee pain.

The pathoanatomy of disease can be identified radiologically, however, standing knee radiograph were found to perform poorly. To identify medial compartment full-thickness cartilage loss either a varus stress radiograph or fixed flexion radiograph, both at 20° flexion and aligned to the joint surface, were identified as the optimum views. To confirm preserved lateral compartment full-thickness cartilage a valgus stress radiograph at 20° flexion, aligned to the joint surface, was identified as the most appropriate technique. As stress radiographs are time and resource consuming, a novel stress device was developed in line with the IDEAL-D framework and validated against the gold standard of manual, clinician performed stress radiographs, as well as independently tested in clinical practice.

Finally, to simplify patient selection, an atlas based Decision Aid, combined with a structured radiographic assessment, was developed and externally validated with an accuracy of over 90% at identifying suitability for OUKA. The routine use of this approach would be expected to standardise patient selection and ultimately translate into improved long-term outcomes.

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Abbreviations

ACL Anterior Cruciate Ligament

AKSS American Knee Society Score

AKSS-F American Knee Society Score - Functional

AKSS-O American Knee Society Score - Objective

AMOA Anteromedial Osteoarthritis

AP Anteroposterior

ASA American Society of Anesthesiologists (grading system)

BMI Body Mass Index

CI Confidence Interval

FFV20 Fixed-Flexion View 20°

FFV45 Fixed-Flexion View 45°

FTCL Full-thickness Cartilage Loss

IDEAL Idea, Development, Exploration, Assessment, Long-term study

JSW Joint Space Width

LEAS Lower Extremity Activity Scale

MCID Minimal Clinically Important Difference

MCL Medial Collateral Ligament

MINORS Methodological Index for non-randomised studies

MRI Magnetic Resonance Imaging

N Newton

NICE National Institute for Clinical Excellence

NPV Negative Predictive Value

NJR National Joint Registry for England, Wales and Northern Ireland

OA Osteoarthritis

OARSI Osteoarthritis Research Society International

OKS Oxford Knee Score

OUKA Oxford Unicompartmental Knee Arthroplasty

%pa Percentage Revision rate per Year (Revisions per 100 Observed Component Years)

PA Posteroanterior

PCL Posterior Cruciate Ligament

PFJ Patellofemoral Joint

PROMS Patient Reported Outcome Measures

PPV Positive Predictive Value

PTCL Partial-thickness Cartilage Loss

PTIR Patient-Time Incidence Rate

QALY Quality Adjusted Life Year

RA Rheumatoid Arthritis

RCT Randomised Controlled Trial

SD Standard Deviation

SEV Standing Extension View

SONK Spontaneous Osteonecrosis of the Knee

TAS Tegner Activity Scale

TKA Total Knee Arthroplasty

TOPKAT Total Or Partial Knee Arthroplasty Trial

UCLA University of California, Los Angeles Activity Score

UKA Unicompartmental Knee Arthroplasty

VAS Visual Analogue Scale

X-KIDS X-ray Knee Instability and Degenerative Score

Chapter 1 Introduction and literature review

1.1 Background and aims

Knee arthritis is common with around one in every two people developing symptomatic disease by the age of eighty-five-years[1]. Where non-operative treatment fails, knee arthroplasty is often performed with the number of knee arthroplasties increasing globally over recent years due to changing population demographics amongst other factors[2]. Knee arthroplasty can either be total knee arthroplasty (TKA) where all of the articulating joint surfaces are replaced or unicompartmental knee arthroplasty (UKA) where only the diseased portion of the knee, typically the medial compartment, is replaced.

In appropriate patients UKA has been reported to have significant benefits to the patient, healthcare provider and healthcare payer, over TKA. For patients, compared to TKA, UKA is associated with a lower morbidity and mortality[3]. For healthcare providers UKA is associated with higher levels of satisfaction with lower resource utilisation, and for healthcare payers UKA is associated with higher quality of life and lower lifetime costs[4,5].

Whilst excellent results following UKA are seen in appropriate patients, there is significant variability in outcomes and globally higher revision rates of UKA are observed when compared to TKA. The reasons for this higher revision rate are multi-factorial and include variation in patient selection, surgical technique as well as differing thresholds for revision of UKA, as compared to TKA[6].

At present guidelines for patient selection for UKA are, at best, based on medium-term data with no externally validated method of patient selection for this procedure in existence. This is reflected by the variability in current UKA utilisation which ranges between 0% and 60% of all primary knee

arthroplasties at different centres across the UK with a current mean utilisation in the UK at around 10%[7].

The purpose of this thesis is to develop an evidence-based method of patient selection for Oxford Unicompartmental Knee Arthroplasty (OUKA). As such, this thesis has three broad aims:

- To establish the local and global long-term outcomes of OUKA
- To define patient selection criteria for OUKA
- To develop and externally validate a method of patient selection for OUKA

The hypothesis for this thesis is that outcomes of OUKA are not influenced by patient characteristics, such as age weight and activity level, but rather by the pattern and severity of disease. Therefore, patient suitability for OUKA can be determined by structured radiological assessment of the knee in combination with an atlas based decision aid.

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1.2 Oxford Unicompartmental Knee Arthroplasty

The principal indication for OUKA is anteromedial osteoarthritis (AMOA) which represents the primary diagnosis in around 98% of cases and will be the focus of this thesis[8]. Spontaneous osteonecrosis of the knee (SONK) represents another important indication although it is less common and patient selection for this particular indication will not be discussed here.

Osteoarthritis (OA) is a clinical syndrome consisting of activity-related joint pain associated with functional limitation and reduced quality of life[9]. The diagnosis of arthritis can be made based on clinical symptoms alone and, in the absence of clinical signs and symptoms indicating an alternative

diagnosis such as gout, other inflammatory arthritis, septic arthritis or malignancy, the National Institute for Clinical Excellence (NICE) considers a patient to have knee osteoarthritis if they are aged over 45 years and present with activity related joint pain, provided any morning joint stiffness lasts no longer than thirty minutes[9].

Osteoarthritis develops when there is failure of cartilage homeostasis. On a microscopic level the cartilage within the joint is continually subject to biomechanical and biochemical insults and, when damage occurs, in the majority of cases cartilage repair, mediated by chondrocytes, is initiated and regeneration occurs[10]. In some cases, however, due to failure of the repair mechanism the cartilage is unable to adequately compensate resulting in structural evidence of disease which presents macroscopically as localised cartilage loss with associated inflammation and remodelling of adjacent bone[10].

Whilst osteoarthritis can be considered a systemic disease, with elevated inflammatory markers recorded in peripheral blood, the macroscopic presentation of the disease is typically more discrete[11]. In the majority of cases, where the cruciate and collateral ligaments are intact, the cartilage lesion typically presents anteriorly on the tibia in the medial compartment, progressing posteriorly as the disease progresses[11,12]. Provided the anterior cruciate ligament (ACL) is intact, posterior cartilage within the medial compartment on the tibia is preserved. This in turn prevents shortening of the medial collateral ligament (MCL) as its length is maintained, as is intraarticular alignment, in full flexion[13]. Upon rupture of the ACL, due to trauma, biomechanical or biochemical insult, the wear pattern on the medial tibia has been observed to progress to involve the posterior aspect of the joint with subsequent development of lateral compartment disease[13,14].

Knee osteoarthritis can be managed symptomatically through pharmacological and non-pharmacological interventions, however, if these approaches fail, knee arthroplasty becomes a treatment option. In the UK around 100,000 primary knee arthroplasty procedures are performed per year[15]. Given projected population changes in age and body mass index (BMI) it is estimated

that the number of knee arthroplasties carried out per year will increase significantly over the next few decades[16]. At present TKA constitutes around 90% of primary knee arthroplasty procedures with UKA making up the remaining 10%. The majority of UKAs, 9%, are unicondylar prostheses with OUKA being the most commonly used implant[15]. Patellofemoral arthroplasty remains relatively rare representing around 1% of UKA[15].

Whilst the utilisation of UKA has remained relatively constant over the last decade there is significant variation in practice across the UK with some surgeons not implanting any UKA and others using UKA in high proportions of their practice. Whilst referral pathways, and specialisation of some centres, will contribute to some of the variability observed, differences in indications for UKA is likely to be a major factor.

1.2.1 Development of the Oxford Unicompartmental Knee Arthroplasty

The OUKA was first marketed in 1976 and today represents the most commonly implanted UKA[15]. The Phase 1 OUKA, was initially developed as a bi-unicompartmental implant however, following the observation that in the majority of cases the disease was isolated to the medial compartment, anteromedial osteoarthritis, since 1982 it has predominantly been implanted as a medial unicompartmental prosthesis[17].

The OUKA is unique in being a fully unconstrained implant with a congruent mobile-bearing with there being several theoretical advantages to this design which have been borne out with the passage of time. Firstly, the fully congruent design over the entire range of movement means there is a large contact area, and consequentially small contact stresses, resulting in low levels of polyethylene wear. In clinical studies of retrieved components the wear of the OUKA has been reported as 0.02mm/year, which is significantly less than similar studies involving non-conforming UKA[18-20]. Additionally, reduced stresses across the knee may also translate into reduced component micro-motion with revisions of OUKA for wear and aseptic loosening being extremely rare[21].

Secondly, as the prosthesis is ligament preserving, the unconstrained bearing is free to move under their control resulting in preserved knee kinematics which may contribute to OUKA having an increased range of movement and better PROMS compared to TKA[22-24]. Thirdly, the design of the implant, with its spherical femoromeniscal articulation and the ability to adjust ligamentous tension through different bearing thicknesses once the femoral and tibial components have been implanted mean that the prosthesis is relatively tolerant to positioning with implant orientation not found to be related to clinical outcomes across several studies[25,26]. Finally, minimal bone resection is required, preserving bone stock and facilitating revision if required.

The original OUKA has gone through two re-designs, however, throughout these the core design features of the implant have remained the same. The first re-design was in 1987, when the Phase 2 OUKA, specifically designed for unicompartmental implantation, was introduced. In contrast to the Phase 1, in which femoral preparation was by way of chamfer cuts using a saw and a cutting-block, the Phase 2 introduced a femoral mill to provide a spherical femoral cut for which the non-articulating femoral component surface was re-designed to accommodate[17].

The second, and most recent, re-design was in 1998 when the Phase 3 OUKA was introduced. The Phase 3 was specifically designed for minimally invasive implantation, and in contrast to the Phase 2 which was implanted using a medial parapatellar approach, the Phase 3 is implanted through a shortened medial parapatellar arthrotomy without eversion or dislocation of the extensor mechanism[17]. More recently modifications of the Phase 3 implant have been made including: anatomical bearings to reduce the rate of bearing dislocation, two-peg femoral component to improve fixation in deep flexion, as well as cementless versions of the design to eliminate the risk of errors associated with cementing[17].

1.2.2 Early clinical results of the Oxford Unicompartmental Knee Arthroplasty

The first clinical results for the OUKA, implanted as a bi-unicompartmental prosthesis, were published in 1986[27]. Goodfellow *et al.* reported the results of OUKA in 125 knees (107 patients) with the indication for surgery being osteoarthritis in 59% (74 knees) and rheumatoid arthritis (RA) in 41% (51 knees). Patients were considered suitable for surgery if they could achieve at least 75° of flexion, had a flexion deformity of no greater than 40°, and varus or valgus deformity no greater than 30°. Posterior cruciate ligament (PCL) deficiency was considered a contraindication but ACL deficiency was not. The average age of the patients at surgery was 65 years (range 45 to 83) and the average weight 72kg (range 47 to 115).

At a mean follow-up of 49 months (range 24 to 72) 89% of the knees were reported to be pain-free or, at most, had mild pain with activity with similar results reported in the knees at rest. Of the 125 knees, where failure was considered removal of OUKA with replacement by another design of prosthesis or arthrodesis, the five-year implant survival was 89% with four knees failing due to tibial component loosening, one due to recurrent bearing dislocation and one due to infection. No difference in outcomes was noted in knees operated on for osteoarthritis or rheumatoid arthritis, however in knees where the ACL was functionally intact (63 knees) at the time of surgery the failure rate was zero, with all revisions occurring in knees where the ACL was damaged or absent.

In a follow-up paper in 1992, assessing 301 OUKA (205 bicompartmental, 65 medial, 31 lateral) this finding was confirmed with the six-year survival found to be 95% where the ACL was functionally intact compared to 81% where the ACL was damaged or absent[28]. As a consequence since this time a functionally intact ACL has been considered a prerequisite for OUKA.

In 1993, the first results of OUKA implanted for AMOA in the presence of a functionally intact ACL, fully correctable deformity, and full-thickness preserved articular cartilage in the lateral compartment were published[29]. Between November 1982 and April 1989, 121 consecutive knees (96 patients) underwent OUKA for the above indications. At a mean follow-up of 44 months 75% of

knees had no pain on activity, 22% mild pain, and 3% moderate pain with only one revision case to TKA which was performed for loosening of the tibial component and subsequent bearing dislocation. The cumulative survival of the prosthesis at nine-years was 99%. The full ten-year results of this cohort were published in 1998 where a survival of 98% (95%CI 93 to 100) was found with five cases of revision, all to TKA, at a mean of 6.6 years (range 2.2 to 12.5), two for lateral compartment disease progression, one for infection, one for component loosening and one for unexplained pain with no cause found at operation[30].

Despite good results with the Phase 1 and 2 implants (**Table 1.1**), it was not until the release of the Phase 3 OUKA, implanted via a minimally invasive approach, that there was a resurgence in interest in OUKA. With the Phase 3 OUKA, whilst studies by the developer surgeons demonstrated similar excellent results to those seen with the Phase 2 design with a 96% (95%CI 93 to 100) ten-year survival with 94% of patients being very or fairly pleased with their outcome at last review, it was reported that these results were not representative of the global experience in which revision rates on average 2.7 times higher than those seen by the developer surgeons were reported[8,31]. More recently, National Joint Registries, have also reported higher revision rates for OUKA than TKA (**Table 1.2**). Should we therefore conclude that, as revision rates following OUKA appear higher than TKA, we should abandon the prosthesis? Or perhaps that OUKA should only be used in the hands of specialist surgeons?

Before drawing conclusions from this data it is important to ensure that when comparing the performance of OUKA against other implants that these comparisons are appropriate. One of the issues with analysing case series and joint registry data is that raw data analysis does not take into account differences in baseline characteristics between groups undergoing these procedures which may lead to inappropriate comparisons being made. An example of this confounding by indication is age at surgery with data from the National Joint Registries indicating that, compared to patients receiving a TKA, patients who receive an OUKA are typically younger, have higher activity levels and

in the long-run have increased failure rates[32,33]. As such, by analysing raw data, as a consequence of these baseline imbalances, it is not possible to differentiate whether these differences in activity levels and failure are driven by population differences or by differences in performance of prostheses.

Age is not the only potential confounding factor with Liddle *et al.* identifying several other differences in patient (gender, ethnicity, medical comorbidity, socioeconomic status) as well as operative characteristics (seniority of operating surgeon, surgical caseload) between patient undergoing OUKA and undergoing TKA, all of which may influence implant survival[34].

One way of accounting for these differences in baseline characteristics is to perform a propensity score matched comparison, a statistical technique to account for covariates that predict treatment allocation, and when this is done to the National Joint Registry for England, Wales and Northern Ireland (NJR) patients who receive a UKA are found to have lower morbidity and mortality, better functional outcomes and be 30% more likely to be highly satisfied with the outcome compared to TKA[34,35]. Whilst after propensity score matching revision rates for UKA remain higher than TKA, it is worth considering what other differences may exist between groups that have not been accounted for and what effect these would have on revision rates, as well as considering what outcomes matter to patients before a valid decision as the superiority of one treatment over another can be made.

Ultimately the best way to directly compare treatments is by way of a well conducted randomised controlled trial (RCT), however due to the feasibility and expense of running such trials only a limited number have been conducted. At the time of writing, five RCTs comparing UKA against TKA have been published (**Table 1.3**). With the exception of the Total Or Partial Knee Arthroplasty Trial (TOPKAT; preliminary results only), which found a 1.9 point (95%CI 0.2 to 3.6; p=0.03) difference in post-operative Oxford Knee Score (OKS) in favour of UKA, no significant differences in functional outcomes or implant survival between UKA or TKA have been seen.

Table 1.1: Survival of the Phase 1 and 2 OUKA: Results from case series.

Study	Implant	Number of knees	Survival (%)	95%CI
Ten-Year Survival				
Murray 1998[30]	Phase 1 & 2	143	98	93 to 100
Kumar 1999[36]	Phase 1 & 2	100	85	78 to 92
Koskinen 2007[37]	Phase 1 & 2	1145	80	72 to 89
Price 2011[8]	Phase 1, 2 & 3	682	94	55 to 100
Rajasekhar 2004[38]	Phase 2	135	94	84 to 98
Vorlat 2006[39]	Phase 2	149	84	Not reported
Twenty-Year Survival				
Barrington 2010[40]	Phase 2	54	84	Not reported
Price 2011[41]	Phase 1, 2 & 3	682	91	55 to 100

Table 1.2: Ten-year survival of the Phase 3 OUKA: Results from registries.

Registry	TKA Survival (%)	95%CI	Ten-year OUKA Survival (%)	95%CI
England, Wales, Northern Ireland and Isle of Man (2016)[7]	96.6	96.5 to 96.6	88.0	87.5 to 88.5
New Zealand (2016)[33]	95.1	94.9 to 95.3	86.0 Cemented 93.0 Uncemented	84.6 to 87.3 91.1 to 94.7
Australia (2016)[42]	94.7*	94.6 to 94.8	85.1	4.2 to 15.7
Danish (2016)[43]	92.5	92.3 to 92.7	84.3	80.8 to 87.9
Emilia-Romagna (2016)[44]	95.1	94.8 to 95.2	86.0	83.2 to 88.4

*for a primary diagnosis of OA

A final consideration as to our treatment decision in this patient group is health economics of each procedure. In a recent systematic review of twelve studies we have reported that in the short-term, UKA is associated with better health outcomes and lower costs than TKA with the initial cost savings associated with UKA being maintained over patients' lifetimes, even after accounting for increase revision rates with UKA[5]. This has been supported by a large Health Economic propensity score matched analysis of 3,519 UKA and 10,557 TKA which, using routinely collected data from the UK, found that for all age and gender subgroups UKA lead to greater gains in Quality Adjusted Life Years (QALYs), a measure of disease burden assessing both the quality and the quantity of life lived, compared to TKA as well as reduction in costs over a patient's lifetime[5].

Whilst the long-term results from TOPKAT are awaited the current data from all published RCTs suggests that, when UKA is performed in the same population as TKA there is no difference in implant survival, and functional outcomes following UKA may be superior. Whilst at a national level outcomes following UKA are inferior to TKA many surgeons do achieve excellent results. Data from joint registries has highlighted that population differences exist between those achieving good and poor results with UKA suggesting that on a national level this variability in outcome following UKA may, in part, be explained by patient selection.

At present there is no long-term evidence as to what constitutes the appropriate patient for OUKA and how they should be identified. As a consequence there is huge variability in UKA utilisation, ranging from between 0% and 60% of all primary knee arthroplasties at different centres across the UK[7]. If results from OUKA are to improve then defining patient selection criteria and developing an evidence based method to achieve this are of paramount importance as only once this has been done can a truly fair comparison of OUKA with different treatment options be performed.

Table 1.3: Randomised controlled trials comparing Unicompartmental against Total Knee Arthroplasty.

Study	Number of knees	Number of UKA	Number of TKA	UKA	TKA	Mean follow-up (years)	Follow-up range (years)
Beard 2017[45]	528	Not stated	Not stated	Various designs	Various designs	1	Not stated
Costa 2011[46]	68	34	34	Stryker	Stryker	5	2 to 7.4
Newman 2009[47]	102	52	50	St George Sled	Kinematic	15	Not stated
Murray 2014[48]	34	18	16	Various designs	Various designs	10	Not stated
Sun 2012[49]	56	28	28	OUKA	AGC	4.3	3 to 6.7

1.2.3 Patient selection for Oxford Unicompartmental Knee Arthroplasty

The indications for UKA remain controversial. Based on their experience with fixed-bearing designs, to optimise outcomes Kozinn and Scott and others advised strict patient and disease criteria for this procedure[50]. In their seminal paper they stated that UKA should not ideally be used in patients aged under 60 years, who weighed more than 82kg (180lb), who undertook heavy labour or who had exposed bone in the patellofemoral joint. In particular they stated that UKA should not ideally be performed in patients who meet all of these criteria, and are male, as their experience was that these patients had particularly poor outcomes[50,51].

Conversely, Goodfellow's experience with the mobile-bearing OUKA was that the decision to proceed with OUKA should be based on the pathoanatomy of disease and that, with the exception of patients with inflammatory arthritis, provided the knee ligaments remained intact, it is appropriate to implant OUKA and as such patients with AMOA represent ideal candidates for this procedure[52].

Whilst indications may vary between implant designs much of the evidence to support the indications for OUKA has been derived from short to medium-term observational data. The questions that this thesis sets out to answer are whether the decision to proceed with OUKA should be based on the indications and contraindications proposed by Kozinn and Scott, or whether it should they be based on the pathoanatomy of disease, and if it should be based on the pathoanatomy of disease how should these features be identified?

1.2.3.1 Age

One of the factors reported to affect outcomes of UKA is age at operation with the NJR reporting young age to be associated with an increased probability of revision, with the ten-year revision rate of UKA (all designs) being 20.0% (95%CI 17.4 to 22.8) in men aged under 55, compared to 6.4%

(95%CI 4.9 to 8.3) in men aged over 75, with a similar relationship seen in women, as well as reported in other National Joint Registries[7,33,42].

Whilst this data would appear to support Kozinn and Scott's argument that UKA should not be used in patients aged under 60 years, for OUKA this relationship has not typically been observed outside of joint registries with only one study, Kuipers *et al*. 2010, of the seven published series that have assessed the influence of age on outcome of OUKA finding survival to be worse in younger compared to older patients (**Table 1.4**). Furthermore, when patient reported outcome measures (PROMS) are assessed these are found to be better in younger patients which would suggest that, at least for OUKA, age should not be a contraindication for this procedure (**Table 1.4**).

Why such stark differences exist between the findings based on NJR data and case series is unclear. One suggestion by Labek, who is an advocate of registries, is that it is bias in clinical studies that limits the interpretation of their results[31]. Whilst the effect of bias on the results cannot be excluded, the fact that these published series represent consecutive knees in populations where surgeons were performing a high-proportion, typically >20%, of their knee arthroplasty as OUKA, with low loss to follow-up reduces the risk of selection and attrition bias. Additionally, whilst reporting and publication bias may exist the absence of any relationship between age and outcome is notable.

Another possible explanation, as discussed previously, is that age may be a confounding variable for another factor that influences outcome. In these published series of OUKA the indications for OUKA were standardised based on the pathoanatomy of disease, as stated by Goodfellow *et al.*, whereas the indications for OUKA in the NJR are unclear[52]. Whilst many surgeons submitting data to the NJR will use the indications of Goodfellow *et al.* some may not, and as such age may be a confounder for other variables, such as disease factors like partial-thickness cartilage loss, that have been reported to influence outcomes[53].

Table 1.4: Outcomes of published series of OUKA by age.

Study	Mean Follow-up (years)	Age Groups	Knees	Survival (%)	95%CI	PROMS
Pandit 2011[54]	5.6	 <60 ≥60	 245 755	*10-year survival* 97 95 *p*=0.60	 91 to 100 91 to 99	AKSS-F and TAS better in those <60
Price 2005[55]	Not stated	 <60 ≥60	 52 512	*10-year survival* 91 96 *p*=0.60	 Not stated Not stated	HSS knee score better in those <60
Kristensen 2013[56]	4.6	 <60 ≥60	 248 447	*10.7-year survival* 87 82 *p*=0.98	 79 to 92 69 to 91	Not reported
Kuipers 2010[57]	2.6	 <60 ≥60	 437 total	5-*year survival* 77 89 *p*=0.03	 68 to 87 85 to 94	Not reported
Ingale 2013[58]	3.9	 <60 60-69 70-79 >79	 110 164 145 51	*6-year survival* 84 91 94 95 *p*=0.08	 Not stated Not stated Not stated Not stated	No difference AKSS-F or O improvement
Matharu 2012[59]	4.4	Regression analysis	459 total	No difference *p*=0.11	Not stated	Not reported
Berend 2007[60]	Not stated	 <60 ≥60	318 total	No difference	Not stated	Not reported

Whilst the published series of OUKA suggest that age may not be a factor that influences implant survival or functional outcomes in the largest study, Pandit *et al.*, the number of knees at risk at ten-years was small (121 knees) and as such further, long-term evidence is needed[8]. To develop this evidence, in **Chapter 3,** the effects of patient factors on outcomes of OUKA will be explored including whether, when disease factors are standardised, age influences the long-term functional outcomes and implant survival of OUKA.

1.2.3.2 Weight

Another factor reported to be associated with an increased failure rate following UKA is increased weight or BMI. Kandil *et al*., utilising health insurance databases from the United States, reported a seven-year revision rate of 2.7% in individuals with a BMI of under 30 (non-obese) increasing to 4.5% in those with a BMI of between 30 and 40 (obese) and 5.7% in individuals with a BMI of 40 and over (morbidly obese)[61,62].

Again whilst this data would appear to support Kozinn and Scott's statement that UKA should not be used in patients who weigh more than 82kg (180lb) this relationship has not been observed in case series where indications for OUKA have been standardised based on the pathoanatomy of disease (**Table 1.5**). Furthermore, in the largest study of 2438 OUKA increasing BMI was associated with greater improvement from baseline in OKS suggesting that obese patients may have more to gain from this procedure than non-obese patients.

As with age, it is unclear whether increased weight or BMI represent confounders or directly result in an increased failure rate. To guide patient selection and to investigate whether, when disease factors are standardised, increased weight is associated with an increased fifteen-year failure rate and worse functional outcomes at ten-years the influence of increased weight on the first 1000 consecutive OUKA performed by the developer surgeons will be investigated (**Chapter 3**).

Table 1.5: Outcomes of published series of OUKA by weight.

Study	Mean Follow-up (years)	Weight Groups	Knees	Survival (%)	95%CI	PROMS
Pandit 2011[54]	5.6			*10-year survival*		
		<82kg	551	96	91 to 100	TAS better in those ≥82kg
		≥82kg	449	96	91 to 100	
				p=0.49		
Murray 2013[63]	5.0	BMI		*10-year survival*		
		<25	378	95	91 to 99	Increasing BMI associated with greater improvement in OKS
		25 to <30	856	93	89 to 97	
		30 to <35	712	95	93 to 98	
		35 to <40	286	94	89 to 99	
		40 to <45	126	95 (5-year)*	91 to 100	
		≥45	80	100 (5-year)*		
				p=0.57		
Berend 2007 [60]	Not stated					
		<82kg	318 total	No difference	Not stated	Not reported
		≥82kg				
Kuipers 2010 [57]	2.6	BMI				
		≤30	437 total	No difference	Not stated	Not reported
		>30				
				p=0.08		

*Too few at risk at ten-years to calculate survival

1.2.3.3 Activity level

As has been highlighted patients undergoing OUKA are typically younger with higher activity levels than those undergoing TKA and it has been reported that up to two thirds of patient undergoing OUKA participate in regular sporting activity before they became symptomatic with between 80 and 90% of those who participated in sports successfully returning to their regular sporting and physical activities following surgery[64,65]. Whilst high activity is believed to increase wear and risk of revision data regarding the impact of activity level on outcomes following OUKA is limited[50,51].

Assessing outcomes from the first consecutive 1000 cemented Phase 3 OUKA performed by the developer surgeons at a mean 5.6 year follow-up Pandit *et al*. found that activity level did not influence survival with no difference in ten-year implant survival seen between high and low activity groups. However, with increasing patient demands, and joint arthroplasty being performed in younger patients compared to a decade ago, further long-term data is required to inform patients and surgeons about the impact of high activity on outcomes. In **Chapter 3** the relationship between activity levels and outcomes will be explored and the mean ten-year follow-up of this cohort will be reported.

1.2.3.4 Partial-thickness cartilage loss

In addition to patient factors, various disease factors have been reported as influencing outcomes. One such disease factor is partial-thickness cartilage loss (PTCL) in the medial compartment with Goodfellow *et al.* stating that to achieve optimum outcomes with OUKA knees should have exposed bone on the tibia with a reciprocal lesion on the femur, representing full-thickness cartilage loss (FTCL) bone on bone arthritis[52].

This factor is particularly relevant as PTCL is reported to be seen in over a quarter of secondary care consultations for osteoarthritis which have failed non-operative treatment[66,67]. In most cases the pain and functional scores of these patients are the same as, if not worse than, patients with more advanced structural changes and as such it is unclear whether OUKA represents an appropriate treatment option in this population[66,67].

Whilst, in the setting of PTCL outcomes following OUKA are believed to be poor there is limited evidence to support this statement. Of the two published studies that report the outcomes of OUKA in knees with PTCL, one study (29 knees with PTCL, mean follow-up 2 years) found functional outcomes to be significantly worse in those knees with PTCL, whereas the other study (32 knees with PTCL, mean follow-up 4 years) found no difference. Only one of these studies assessed implant survival and the 5-year survival-rate in knees with PTCL was 84% (95%CI 72 to 92; 4 knees at risk) compared to 97% (95%CI 91 to 100; 5 knees at risk) for knees with FTCL however this difference did not reach statistical significance (p=0.10)[53,68].

Based on these studies it remains unclear whether PTCL represents a contraindication to OUKA and as such in **Chapter 4** a propensity score matched analysis is performed to assess whether PTCL influences functional outcomes or implant survival following OUKA.

1.2.3.5 Anterior cruciate ligament

Another disease factor reported to impact on the outcomes of OUKA is the status of the ACL. Based on the original studies of OUKA by Goodfellow *et al.*, where a high failure rate, due predominantly to tibial loosening, was observed in ACL deficient knees, ACL deficiency has been considered a contraindication to OUKA[52]. Whilst recent experience suggests that there may be groups of patients in which ACL deficiency does not present a contraindication, it is known when OUKA is implanted

in ACL deficient knees this is associated with abnormal knee kinematics and bearing movement, and as such knees with ACL deficiency cannot be considered optimal for OUKA[69,70].

Whilst the ACL has been reported to be intact in up to two-thirds of patients undergoing joint arthroplasty (range 25% to 68%), not all of these cases have a macroscopically normal ACL[71,72]. As the grade of macroscopic disease increases it is known that the wear pattern on the tibia moves more posteriorly due to altered biomechanics of the joint, however, the outcome of OUKA in these patients who have macroscopic abnormalities, yet intact, ACL is unknown[13]. As a significant number of patients presenting with AMOA will have macroscopically abnormal, yet intact, ACL it is important to establish whether it is safe to perform OUKA in these cases[71,73]. **Chapter 4** will explore whether the macroscopic status of the ACL influences the long-term functional outcomes and implant survival of OUKA.

1.2.3.6 Full-thickness lateral cartilage

Lateral progression has been reported as a common cause of failure for OUKA with the thickness of the cartilage in the lateral compartment at operation being identified as a significant predictor of this failure mechanism[74,75]. Female gender, pelvic geometry including reduced femoral offset and more valgus neck-shaft angle as well as lateral osteophytes have been associated with an increased incidence of lateral compartment OA[76-81].

In patients with osteoarthritis osteophytes are commonly seen in the lateral compartment, and it has been reported that the incidence of full-thickness cartilage defects in the lateral compartment increases as the grade of lateral osteophyte increases from under 2% in knees without lateral osteophytes to 10% in knees with large (Grade 3) osteophytes[82]. In many cases however, even in the presence of osteophytes the lateral compartment will be intact and it is unclear whether, in this

scenario, they represent a failing lateral compartment and as such a contraindication to medial OUKA or are a general manifestation of intraarticular disease[50,82-84].

As a significant number of patients presenting with AMOA have lateral osteophytes, and progression of arthritis in the retained lateral compartment is a common failure mechanism following OUKA, it is important to establish whether it is safe to perform a OUKA in these cases [85]. In **Chapter 4** whether the presence and size of lateral osteophytes influences the long-term functional outcomes and implant survival of OUKA will be explored.

1.2.3.7 Acceptable patellofemoral joint

The final disease factor which will be investigated is the status of the patellofemoral joint (PFJ) and its relationship to outcomes following OUKA. PFJ disease and anterior knee pain are common in the population of patients undergoing joint arthroplasty and there is uncertainty as to whether these factors represent a contraindication to OUKA.

Short and medium-term data has demonstrated that whilst the presence of medial facet PFJ disease and location of pre-operative knee pain do not influence functional outcomes following OUKA, in knees with lateral facet PFJ disease, lower improvements from baseline function and absolute functional outcome at two-years postoperatively have been reported[27,54,86-88]. The influence of PFJ disease and anterior knee pain on long-term functional outcomes and implant survival following OUKA has not been evaluated and it is important to establish whether it is safe to perform OUKA in these cases.

Data from six studies has investigated the impact of exposed bone at the patellofemoral joint on outcomes. Four studies[60,86,89,90] found no association between the presence or location of exposed

bone at the PFJ whereas two studies[91,92] have reported severe arthritis of the lateral facet of the patella to be associated with worse outcomes than knees without this finding.

To investigate the long-term outcomes of OUKA in the setting of PFJ disease the influence of clinical, radiographic and intra-operative PFJ disease on fifteen-year implant survival and ten-year functional outcomes will be reported in **Chapter 4**.

1.2.4 Imaging in unicompartmental knee arthroplasty

As discussed the pattern and severity of arthritis within the knee is believed to significantly influence outcomes following OUKA and it has been suggested that if disease factors are standardised then patient factors such as age, weight and activity level should not be seen as contraindications to this procedure. If the long-term data presented in **Chapters 3** and **Chapter 4** confirms these findings then it is important to consider how the pattern and severity of disease should be identified pre-operatively.

Currently there is a lack of consensus amongst orthopaedic surgeons as to the best way to image the knee joint to establish the degree and pattern of arthritis[93,94]. At present plain radiographs represent the most frequently used imaging of the arthritic knee with the standing anteroposterior (AP) and lateral radiograph representing standard care and requested in all cases of knee arthritis[94]. Posteroanterior (PA) fixed-flexion radiographs, mostly at 30°, are requested by 22% of surgeons, and skyline radiographs to assess the patellofemoral joint by 41% of surgeons, except where anterior knee pain is reported where 87% request this view[94]. Varus and valgus stress radiographs are used in 17% to assess the medial and lateral compartments respectively as well as assess the integrity of the collateral ligaments[95]. Utilisation of magnetic resonance imaging (MRI) is highly variable between centres but it is estimated that around a fifth of patients aged over 40 referred to secondary care with knee pain have undergone MRI[96].

When deciding between UKA and TKA the detection of the degree and pattern of arthritis is of critical importance[52]. Whilst radiographs are the most frequently used imaging test as they are accessible, non-invasive, safe and cost-effective, it has been argued that MRI is a more powerful diagnostic tool[52,53,97]. Ultimately, however, the optimum imaging protocol is one that is acceptable to patients, involves the fewest procedures to obtain the most clinically relevant information and one that utilises the least resources in terms of staff and equipment. To assess the performance of different imaging techniques to identify key pathoanatomical features that have been reported to influence the outcome of OUKA a review of the literature has been performed.

1.2.4.1 Assessment of the medial compartment

For a long time it has been known that weight-bearing views are a better method of establishing the true joint space width compared to non-weight bearing views due to the increased forces across the joint[98-100]. Data from the rheumatology literature has demonstrated that fixed-flexion radiographs are superior to full-extension views to identify joint space narrowing[101,102]. In cross sectional studies it has been reported that one in three knees considered to have joint space narrowing, PTCL, on weight-bearing full-extension radiographs demonstrating joint space obliteration with FTCL, bone on bone arthritis, on fixed-flexion imaging[101,102]. Whilst the performance of fixed-flexion radiographs in early arthritis has been extensively evaluated there is little data on these views and their role in patient selection for OUKA. Furthermore, there remains uncertainty over the optimum flexion angle of the knee for these[103].

An alternative radiographic technique to assess for FTCL in the medial compartment is stress radiography. Varus stress radiographs are performed with the patient supine, knee flexed, with a varus force applied to the leg whilst the knee is fixed. In this position the X-ray beam is aligned to the tibial plateau and a radiograph is taken with the medial compartment under compression.

Whilst Gibson and Goodfellow reported stress radiography to be a reliable assessment of the pattern and severity of the disease within the arthritic knee there have been few studies evaluating its performance in clinical practice since[104].

Finally, an alternative to plain radiography is MRI. Whilst predominantly used to assess for soft tissue injuries within the knee, as well as to assess for early arthritic change, there is some data as to the performance of MRI in more advanced disease. Smith *et al.* in their systematic review found the sensitivity and specificity of MRI at detecting a cartilage defect with exposed subchondral bone within the tibiofemoral joint to be 81% (95%CI 76 to 84) and 99% (95%CI 98 to 100) respectively[105]. Overall, however, the diagnostic accuracy of MRI at detecting chondral lesions (all grades) of the tibiofemoral joints is lower on account of the diagnostic specificity decreasing as grade of lesion decreases (overall sensitivity 88% (95%CI 86 to 89) and specificity 82% (95%CI 81 to 83). As such Smith *et al*. concluded that, due to the risk of obtaining a false positive results to incorrectly inform clinical decision making, arthroscopic assessment should remain as the gold-standard to assess adults with possible chondral lesions of the tibiofemoral or patellofemoral joints.

In the workup for medial OUKA the observation that the diagnostic accuracy of MRI decreases as the grade of lesion decreases is of particular relevance. Due to the additional cost and time associated with obtaining an MRI, its role in assessing the medial compartment is typically reserved for patients in which bone on bone arthritis is not demonstrated on standing AP or fixed-flexion radiographs. As such the group of knees undergoing MRI will likely be heterogeneous and skewed towards lower disease grades where the performance of MRI is known not to be optimum.

There have been two studies assessing outcomes of OUKA based on MRI findings of the medial compartment with both studies investigating whether bone marrow oedema, which has been reported to be associated with FTCL, seen on pre-operative MRI influenced outcomes following surgery.

The first study by Jacobs *et al.* assessed the outcomes of 28 OUKA who had had pre-operative MRI, in which 11 (39%) had medial tibial bone marrow oedema, and found those knees with this finding had higher levels of pre-operative pain as assessed by the Knee Society Pain Score, but similar improvements from baseline pain score at a mean of two-years.

Conversely, a second study, again by Jacobs *et al*. in a separate population of 153 knees at a mean of 3.4 years, found no pre-operative differences in Knee Society Objective, Functional or Pain Score between knee with medial sided tibial, femoral or patellofemoral bone marrow oedema but that knees with anteromedial tibial, but not femoral or patellofemoral, bone marrow oedema reported greater gains in Knee Society Functional Score compared to knees without this finding. In a follow-up study by Berend *et al.* where this data was stratified by disease severity, FTCL vs. PTCL, the association of anteromedial tibia bone marrow and superior outcomes was lost highlighting, that due to the relationship between bone marrow oedema and FTCL, disease severity was likely a confounding factor in the first analysis.

As the current evidence suggests that bone marrow oedema does not influence outcomes following OUKA once disease severity has been accounted for, if plain radiographs can quantify disease severity by identifying FTCL then the role of MRI may be limited. In **Chapter 5** the performance of standing full-extension AP radiographs, fixed-flexion radiographs as well as varus stress radiographs at assessing the severity of arthritis by identifying FTCL within the medial compartment of the arthritic knee will be investigated.

1.2.4.2 Assessment of the anterior cruciate ligament

The clinical evaluation of the ACL in the setting of osteoarthritis can be misleading due to the presence of osteophytes and joint contracture and as such the functional status may be best determined using imaging[106,107]. Radiographically the status of the ACL can be determined from a

true lateral radiograph taken with the knee slightly flexed and the femoral condyles overlapping. On the true lateral radiograph where the ACL is functionally abnormal or absent, the tibial erosion extends to the back of the tibial plateau and may be accompanied by posterior femoral subluxation. If the tibial erosion cannot be seen or does not extend to the back of the tibia there is a 95% chance that the ACL is functionally normal[13,108].

Alternatively, MRI can be used to assess the status of the ACL. The sensitivity and specificity of MRI at detecting ACL tears has been reported as 87% (95%CI 77 to 94) and 93% (95%CI 91 to 96) respectively although its performance is known to be lower in older patients, possibly due to the higher number of chronic, as opposed to acute, ruptures in this group[109].

Waldstein *et al*. assessed the performance of radiographs against MRI in 93 knees with medial compartment arthritis and found good correlation between the MRI findings and the evaluation of the wear pattern on lateral radiographs. One of the key findings from their study however was that ACL degeneration was observed in 58% of ACL with the clinical significance of these findings with respect to patient selection for, and outcomes of, OUKA being unclear[110]. This finding has also been reported by Sharpe *et al.* who found evidence of ACL degeneration on MRI in 33% of patients with AMOA, compared to only 13% on surgical inspection[111].

Based on the early studies by Goodfellow *et al*. it is known that an intact ACL is a requirement to optimise outcomes following OUKA[28,70]. Currently however, the impact of the macroscopic status of the intact ACL on outcomes is unclear but will be reported in **Chapter 4**. If macroscopic appearance of the ACL is associated with clinical outcome then there may be a role for MRI in delineating which patients are optimum for OUKA. If however the macroscopic status of the intact ACL is not related to outcomes then it is likely that MRI findings of ACL degeneration are also not related to patient outcome and as such given that good correlation between the MRI findings and

the wear pattern on lateral radiographs exists the latter is likely to be the more cost-effective choice.

1.2.4.3 Assessment of the lateral compartment

The lateral compartment can be evaluated by plain radiographs or by MRI. When determining the optimum radiographic view of the knee is important to appreciate that when evaluating radiographs we interpret joint space width to be equal to cartilage thickness and that whilst this may be true when the compartment is under compression, this is not true if the compartment is unloaded.

Ahlbäck *et al.* noted that upon weight-bearing the joint space of the more affected compartment, typically the medial compartment, narrowed whereas in the less affected compartment it often widened[100]. This finding was confirmed by Thomas *et al.* and is why standing AP radiographs in full-extension are believed to perform poorly when assessing the pattern and severity of arthritis within the knee[98].

To improve the performance of plain radiographs in evaluating the lateral compartment it has been proposed that fixed-flexion views at 45° should be performed. There are several theoretical reasons why the fixed-flexion 45° radiograph may be best at evaluating the lateral compartment as it is known that as the knee goes into flexion the forces move laterally across the tibial plateau, that defects in the lateral compartment typically starts at this degree of flexion and that at 45° flexion maximum compressive force are being exerted by the quadriceps across the knee which may further assist in demonstrating lateral compartment disease[12,112]. Whilst there is some evidence for the use of the 45° fixed-flexion view to assess the lateral compartment in early lateral compartment disease, its utility at assessing the lateral compartment in the presence of medial compartment

AMOA is unknown, furthermore, there remains uncertainty over the optimum flexion angle of the knee for these views[103].

An alternative method of radiographically assessing the lateral compartment is by using stress radiographs. Valgus stress radiographs are performed with the patient supine, knee flexed to relax the posterior capsule, with a valgus force applied to the leg whilst the knee is fixed. In this position the X-ray beam is aligned to the tibial plateau and a radiograph is taken with the lateral compartment under compression. Whilst Gibson and Goodfellow reported stress radiography to be a reliable assessment of the pattern and severity of the disease within the arthritic knee there have been few studies evaluating its performance in clinical practice[104].

Waldstein *et al*. assessing 100 consecutive knees undergoing TKA found that the joint space width on valgus stress radiographs correlated well with the combined cartilage thickness in the lateral compartment of the knee[113]. Whilst, in a sub study they found cartilage thickness to be a poor predictor of cartilage degeneration, both macro- and microscopically, the ability of this cartilage to repair once limb biomechanics are restored is unknown[114]. As the long-term results from Goodfellow's series, where all patients had a joint space width of more than 5 mm in the lateral compartment on valgus stress, were good this would suggest that that knees with preserved full-thickness cartilage loss, independent of the presence of surface degeneration, are appropriate for OUKA[104,115].

MRI may also be used to assess the lateral compartment however, as discussed previously, due to its low specificity in low grade cartilage lesions there is a risk of false positives where MRI suggests a cartilaginous lesion exists where one does not which may lead to patients being considered contraindicated for OUKA. Hurst *et al*. assessed the outcomes of 33 OUKA with MRI evidence of lateral compartment, patellofemoral compartment, and/or deficiency of the ACL at a mean follow-up of 43 months and found no difference in Knee Society Objective, Functional or Pain Scores or

implant survival compared to the remainder of a consecutive 1000 knee cohort (967 knees; 11 with normal MRI findings outside of the medial compartment, 956 with no MRI) who underwent OUKA for AMOA[116]. Based on this finding the authors concluded that abnormal pre-operative MRI findings do not have an influence on the outcome of OUKA when radiographic and clinical criteria are met.

1.2.4.4 Assessment of the medial collateral ligament

In addition to identifying preserved posterior tibial cartilage in the medial compartment on the true lateral radiograph, indicating an intact ACL, and implying that the MCL length is maintained in full flexion, shortening of the MCL can be assessed by valgus stress radiographs. Using the same technique as reported to assess for lateral compartment disease, in the presence of a functionally normal MCL on valgus stress the medial compartment opens fully demonstrating that the MCL is not shortened[13].

Restoring MCL length through the range of movement is a key principle of OUKA and outside of the scope of this thesis and as such will not be discussed further.

1.2.4.5 Assessment of the patellofemoral joint

To evaluate the PFJ radiographically sagittal or transverse plane imaging is required. A study by McDonnell *et al*. assessed 100 consecutive knees with lateral and skyline radiographs and compared these findings to those identified intra-operatively. The authors found skyline views to be highly sensitive (sensitivity 90%; specificity 73%) at identifying lateral patella facet bone loss with grooving and as such reliable at identifying knees that may represent a contraindication to OUKA[117]. Conversely, lateral views had a sensitivity of 23% and specificity of 94% leading to these views not being recommended to assess for lateral patella facet bone loss with grooving [117].

An alternative method of assessing the PFJ is by MRI. Through meta-analysis Smith *et al.* found the sensitivity and specificity of MRI at identifying subchondral bone loss to be 68% (95%CI 56 to 79) and 99% (95%CI 98 to 100) respectively[105]. Whilst the specificity of MRI at assessing for bone loss with grooving of the lateral facet is higher than seen with skyline radiographs due to the lower sensitivity of MRI, if it was used to assess knee pre-operatively, due to the higher number of false negatives, more patients would be excluded from undergoing OUKA than if skyline radiographs were used. Conversely, if skyline radiographs were used, compared to MRI more patients with lateral patella facet bone loss with grooving would be listed for OUKA.

This observation was confirmed in a study of 100 consecutive knees in which MRI, skyline and intra-operative assessment of the lateral patella facet was performed at operation[118]. Of the 100 knees where one knee was found to have lateral facet bone loss at operation, lateral facet bone loss was identified on skyline radiographs in four knees and on MRI in fifteen knees. As the number of knees with lateral patella facet bone loss with grooving is low, 1% in this series, and the lateral facet of the patella is readily assessable at operation, it would seem prudent to use skyline radiographs as a screening tool to assess for lateral patella facet bone loss with grooving as the use of MRI would result in a high proportion of knees being considered contraindicated for OUKA[118].

The literature suggests that radiographs may be able to accurately identify disease factors reported to influence outcomes following OUKA. Whilst radiographic analysis is a slightly blunt tool to assess knee pathology, radiographs are readily available, cost-effective and easily interpretable. Whilst MRI may provide more information about the pathological processes going on within the knee the clinical relevance of these MRI findings on outcomes of OUKA is unknown and in practice, in the absence of long-term evidence that MRI signs of disease in the unaffected compartments and structures do not compromise clinical outcomes, they may be viewed as contraindications to OUKA.

Whilst MRI in general has a very high specificity, its sensitivity at identifying those disease factors reported to influence outcomes following OUKA is often lower leading to a higher number of false negatives. As such, as a screening tool to identify appropriate patients for OUKA its widespread use would be expected to exclude appropriate patients from undergoing this procedure and decrease the caseload, as well as usage, of OUKA, both of which have been associated with worse outcomes.

Conversely, radiographic assessment, with its lower specificity compared to MRI may result in patients, who are inappropriate for OUKA, being identified as suitable for this procedure. As, ultimately the decision to proceed with OUKA is made at the time of operation following direct assessment of the joint, radiographic assessment would seem the most appropriate method of assessment as, provided the number of false positive for OUKA remains at an acceptable level, the number of cases converted from OUKA to TKA at operation would be expected to be low.

The performance of the various radiographic techniques to assess the medial and lateral compartments of the knee will be assessed in **Chapter 5** and a full assessment of their combined performance will be assessed in **Chapter 7**.

1.3 Scope and structure of thesis

As stated in **Section 1.1** (**1.1 Background and aims**), the aim of this thesis is to develop an evidence based method of patient selection for OUKA and will be structured as follows:

In the first experimental chapter, **Chapter 2**, local and global long-term outcomes of OUKA will be established. The first part of the chapter will report the local outcomes of the cemented Phase 3 OUKA by assessing the ten-year functional outcomes and fifteen-year implant survival of the first 1000 consecutive procedures by the developer surgeons. In the second part of the chapter the

global outcomes of OUKA will be reported by systematic review with meta-analysis of all published case series with subgroup analysis based on surgical caseload and usage of OUKA.

The next two chapters, **Chapter 3** and **Chapter 4**, will focus on indications and define patient selection criteria for OUKA. In **Chapter 3** the influence of patient factors, including age, weight and activity level, which have previously been proposed to be contraindications to UKA are explored using the 1000 consecutive patient cohort presented in **Chapter 2**. In **Chapter 4** the influence of disease factors, including the presence of PTCL in the medial compartment, the macroscopic status of the ACL, the presence of lateral osteophytes and the status of the PFJ, on long-term functional outcomes and implant survival is investigated using local data.

The final part of the thesis reports on the development and validation of a method of patient selection for OUKA. In **Chapter 5**, assessment of the medial and lateral compartments is considered and the performance of standing full-extension AP radiographs against fixed-flexion PA radiographs and stress radiographs in a controlled setting as well as in clinical practice is assessed. **Chapter 6** looks at the development and validation of a novel device for performing stress radiographs of the knee and the final experimental chapter, **Chapter 7**, builds on the first five experimental chapters and outlines the development and external validation of a radiographic decision aid for OUKA. **Chapter 8** summarises the important findings and conclusions from this thesis with recommendations subsequently made for relevant future work. **Table 1.6** outlines each of the cohorts used for each of the experimental chapters.

Table 1.6: OUKA performed by Professor DW Murray and Mr CAF Dodd June 1998 to March 2009

	Knees	**Chapter**
Met inclusion criteria: ▪ medial bone on bone arthritis ▪ functionally intact ACL ▪ full thickness lateral cartilage ▪ functionally normal MCL ▪ acceptable PFJ	1000	Chapter 2.1 Oxford Experience: Results of a consecutive series of 1000 knees Chapter 3: Patient Factors affecting outcome of Oxford Unicompartmental Knee Arthroplasty
Intraoperative data on ACL available	820	Chapter 4.2.2 Macroscopic status of the anterior cruciate ligament
Radiographs available	458	Chapter 4.2.3 Lateral Osteophytes
Intraoperative data on PFJ available	805	Chapter 4.2.4 Patellofemoral joint disease
Did not meet inclusion criteria:	97	
Reasons:		
▪ without functionally intact ACL	37	
▪ combined ACL / OUKA	22	
▪ medial PTCL	20	Chapter 4.2.1 Partial thickness cartilage loss in the medial compartment ▪ These 20 plus 74 with PTCL performed outside initial study period
▪ medical OCD	7	
▪ prior HTO	5	
▪ PCL laxity	3	
▪ von Willebrand's Disease	2	
▪ previous MCL repair	1	

OUKA – Oxford Unicompartmental Knee Arthroplasty; ACL – anterior cruciate ligament; MCL – medial collateral ligament; PFJ – patellofemoral joint; OCD- osteochondritis dissecans; HTO – high tibial osteotomy; PCL – posterior cruciate ligament

Chapter 2 Outcomes of Oxford Unicompartmental Knee Arthroplasty

2.1 Oxford Experience: Results of a consecutive series of 1000 knees

2.1.1 Introduction

To improve patient selection, and ultimately outcomes, it is first important to establish the current experience with the Oxford Unicompartmental Knee Arthroplasty (OUKA). This chapter reports our local experience by assessing the results of the first consecutive 1000 cases implanted by the developer surgeons, as well as assessing the global experience by performing a meta-analysis of published case series.

The first consecutive 1000 cemented Phase 3 medial OUKA implanted through a minimally invasive approach represent the experience of the developer surgeons and in this series patient selection was standardised, and was based on the pathoanatomy of the disease as outlined by Goodfellow *et al.*[52]. Patient factors including: age, weight and level of activity; radiographic factors including chondrocalcinosis and lateral osteophytes; and operative factors including the presence of a chondral ulcer on the medial side of the lateral femoral condyle were not considered contraindications. All patients had anteromedial osteoarthritis (AMOA) or medial spontaneous osteonecrosis of the knee (SONK) with suitability for OUKA confirmed at the time of operation. In cases of AMOA the patients had: bone on bone arthritis in the medial compartment, retained full-thickness cartilage in the lateral compartment, functionally intact medial collateral ligament (MCL) and anterior cruciate ligament (ACL) and no evidence of bone loss and grooving to the lateral facet

[*] This chapter has been published as two papers "Fifteen-year survival and functional outcome of 1000 Oxford phase 3 UKR" Bone and Joint Journal (2015) and "The interaction of caseload and usage in determining outcomes of unicompartmental knee arthroplasty: A meta-analysis" Journal of Arthroplasty (2017) (**Appendix 1**).

of the patella. During the study period 70% of the developer surgeons' primary knee arthroplasty practice was OUKA highlighting the broad indications used for this procedure in this series.

All patients were independently followed up using a standard protocol of clinical review with functional and radiographic assessment and the ten-year functional and radiographic outcomes and fifteen-year implant survival have been reported.

2.1.2 Patients and methods

Between June 1998 and March 2009, 1000 consecutive OUKA were performed in 818 patients via a minimally invasive approach by the two developer surgeons, Professor DW Murray and Mr CAF Dodd.

Outcome assessment was performed by research physiotherapists independent of the surgical and clinical teams involved in the patients care. Functional outcomes were assessed using the: Oxford Knee Score (OKS), American Knee Society Objective Score (AKSS-O), American Knee Society Functional Score (AKSS-F), and the Tegner Activity Scale (TAS) (**Appendix 2**)[119-121]. In addition the AKSS-O was calculated without performing deductions for alignment, as unlike total knee arthroplasty (TKA), the OUKA aims to restore anatomical alignment not achieve neutral alignment[122]. Range of movement and alignment were measured using a long-arm goniometer using the standard method employed clinically. Patients were assessed clinically pre-operatively and at one, five, seven, ten, twelve and fifteen-years postoperatively. In addition the OKS, AKSS-F and TAS were administered annually via postal questionnaire.

At the time of surgery a detailed intra-operative record of the status of each of the compartments and structures within the knee was made on a paper pro forma (**Appendix 3**). The ACL was assessed and classified as: normal, synovial damage or longitudinal splits. ACL that were friable and

fragmented, absent or absent and reconstructed (simultaneously or staged) were excluded from this case series. The weight bearing articular surfaces of the involved tibia and femur, as well as uninvolved tibia and femur, medial and lateral patella facets and trochlea were graded for the presence and size and depth of any cartilage defect. These were defined as: normal, superficial damage, partial-thickness cartilage loss (PTCL), focal (≤2 cm^2) full-thickness cartilage loss (FTCL), extensive (>2 cm^2) FTCL, bone loss ≤5 mm or bone loss >5 mm[123].

Radiological assessment was performed at ten-years using aligned images. AP radiographs were performed supine, with the knee flexed to 20°, and the image aligned parallel to the undersurface, and the vertical wall, of the tibial component. True lateral radiographs were performed with the images aligned to the posterior facet of the femoral component. In order to assess intra- and inter-observer variability, repeated measurements in a subgroup of patients were made by myself and Professor HG Pandit.

The AP radiograph was assessed for the presence of radiolucency under the tibial component in Zone A (medial to keel), Zone B (surrounding the keel) and Zone C (lateral to the keel)[124]. The border of the lateral vertical wall of the tibial component was not assessed as the component is not fixed at this position and it is not filled with cement. Physiological radiolucency was defined as up to a maximum of 2 mm with a defined sclerotic border running parallel to the edge of the prosthesis. Pathological radiolucency was defined as 2 mm or greater with a poorly defined border. The lateral radiograph was assessed for the presence of radiolucencies running parallel to the posterior facet of the component. Due to the spherical geometry of the prosthesis, it is not possible to assess for radiolucencies along other aspects of the femoral prosthesis. Radiographs were also assessed for component subsidence, fracture and progression of arthritis in the retained compartments

All patients were contacted in the previous 18 months to ascertain the current functional status of their knee and incidence of re-operations. Where patients had died, information about the status

of their knee, and the presence of further operation was obtained via primary and secondary care records as well as via patient's relatives where appropriate. Data was extracted from our prospective database on 1st September 2014.

Ten-year functional outcomes were assessed. In addition categorical OKS outcomes were calculated using the method of Kalairajah *et al.* where an excellent outcome is defined as an OKS greater than 41, good an OKS score of 34 to 41, fair an OKS score of 27 to 33 and poor and OKS score of less than 27[125].

This study was approved by the local ethics committee chair person (Oxfordshire Research Ethics Committee C) who confirmed that the clinical and radiological follow-up of these patients formed part of routine assessment and therefore does not need formal ethical approval (**Appendix 4**).

2.1.3 Statistical methods

To assess for differences in functional outcome between subgroups, non-parametric tests (Mann-Whitney U, Kruskal–Wallis) were performed.

Throughout this thesis a broad definition of failure has been used with failure defined as any implant-related re-operation, which included any re-operations in which components were removed, changed, in which the mobile-bearings were replaced for dislocation, and any re-operations in which new components were inserted.

To assess survival, life-table analysis was performed using the following endpoints: (a) implant-related re-operations, which included any re-operations in which components were changed, in which the meniscal-bearings were replaced for dislocation, and any re-operations in which new components were inserted; (b) revision of the tibial or femoral components; (c) revision requiring revision TKA components. Confidence intervals (CI) were calculated using the method described by

Peto *et al*. [126]. In order to assess for differences in survival between subgroups, a Mantel log rank test was used.

Throughout this thesis, unless stated, all analyses were performed using SPSS, Version 22 (IBM Corporation, Armonk, New York) with a *p*-value of < 0.05 deemed statistically significant.

2.1.4 Results

Of the first consecutive 1000 medial OUKA, 636 were unilateral procedures and 182 bilateral. Of the bilateral cases 22 were performed simultaneously. The mean age at the time of operation was 66 years (range 32 to 88), 393 patients were men (48%) and 425 were women (52%). The underlying diagnosis was AMOA in 977 cases and SONK in 23 cases, 3 involving the tibia and 20 involving the femur.

All patients were followed up for a minimum of five-years with the exception of those who were lost to follow-up (4), died (44), underwent revision (23) or withdrew from the study due to poor health (58). Of those patients who withdrew from the study at any time point we are not aware of any revisions. The mean follow-up was 10.3 years (range 5.3 to 16.6) with 516 knees having a minimum ten-year follow-up and 60 knees a minimum fifteen-year follow-up.

The mean OKS by year following OUKA is displayed in **Figure 2.1**. At ten-years the mean OKS was 40 (SD 9) with 55% having an excellent outcome (score >41), 24% good outcome (34 to 41), 11% fair outcome (27 to 33) and 10% a poor outcome (<27).

The mean AKSS-O and AKSS-F by year following OUKA are displayed in **Figure 2.2**. At ten-years the mean AKSS-O was 80 (SD 15) and AKSS-F was 76 (SD 22). Overall, at ten-years 53% of knees had an excellent outcome according to AKSS-O criteria (score 85 to 100), 28% a good outcome (70 to 84), 9% fair outcome (60 to 69) and 10% a poor outcome (<60). When AKSS-O is calculated without

performing deductions for alignment, at ten-years the mean AKSS-O was 89 (SD 15) with 78% of knees had an excellent outcome according to AKSS-O criteria (score 85 to 100), 8% a good outcome (70 to 84), 8% fair outcome (60 to 69) and 6% a poor outcome (<60). The mean AKSS-O calculated without performing deductions for alignment by year following OUKA are displayed in **Figure 2.2**.

At ten-years the mean TAS was 2.7 (SD 1.3) and mean flexion 127° (range 65° to 155°), compared to a pre-operative flexion of 117° (range 25° to 145°).

At ten-years, aligned AP radiographs were available from 212 knees (182 patients) and true lateral radiographs from 210 knees (180 patients). The correlation coefficients for both intra- and inter-observer reliability were >0.95 ($p < 0.01$). Overall, 13.7% (29 knees) had evidence of physiological radiolucency under the tibial component with no pathological radiolucencies detected. Zone A radiolucency was seen in 7.5% (16 knees), Zone B in 9.0% (19 knees) and Zone C in 9.4% (20 knees). No significant difference in functional outcome in the presence or absence of physiological radiolucency under the tibial component, as assessed by OKS ($p = 0.10$), AKSS-O ($p = 0.09$) or AKSS-F ($p = 0.43$), was detected.

Radiolucency at the posterior facet of the femoral component was observed in 1.9% of knees (four knees). No significant difference in functional outcome was seen in those knees with evidence of posterior femoral facet radiolucency and those without (OKS, $p = 0.96$; AKSS-O, $p = 0.51$; AKSS-F, $p = 0.41$). Bone on bone arthritis was noted in three cases (1.4%) in the lateral compartment and in three cases (1.4%) in the patellofemoral compartment at ten-year follow-up.

Overall there were 52 implant-related reoperations at a mean of 5.5 years (range 0.2 to 14.7) (**Table 2.1**). Progression of arthritis in the retained lateral compartment (2.5%) followed by bearing dislocation (0.7%) and unexplained pain (0.7%) were the most common indications for revision. There were no cases of revision performed for wear, progression of PFJ osteoarthritis or for peri-prosthetic fracture. The distribution of failures is outlined in **Figure 2.3** and **Table 2.2**.

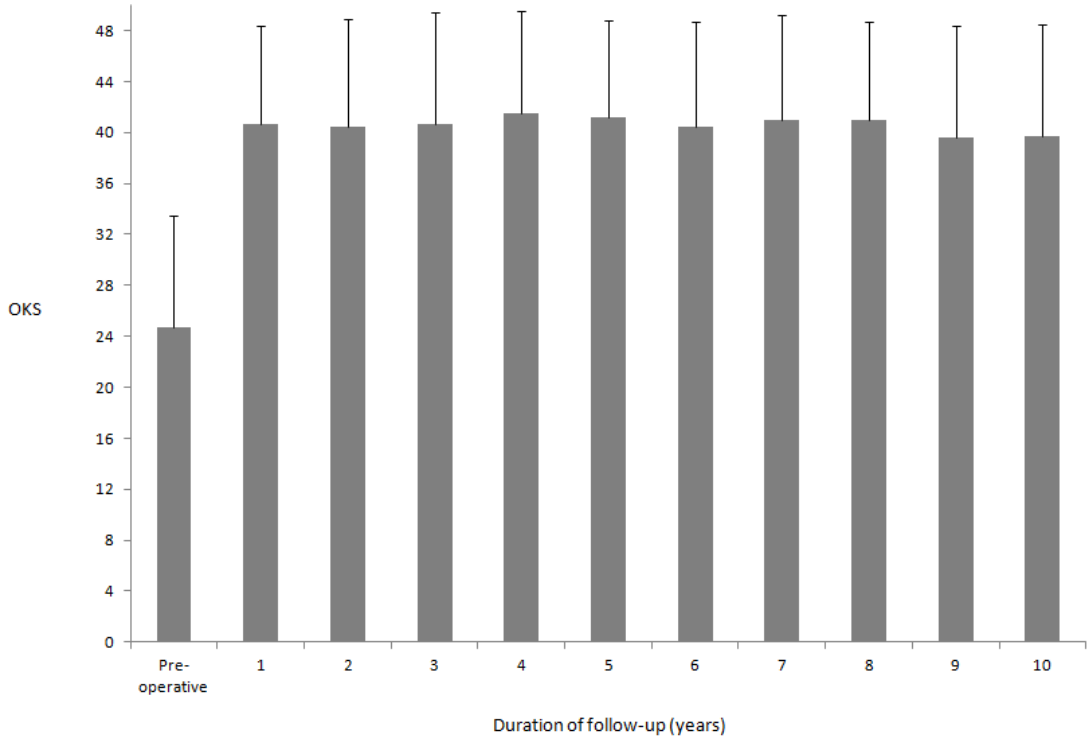


Figure 2.1: Bar chart showing the mean OKS and SD (error bars) for each year of follow-up for knees from the developer series of OUKA.

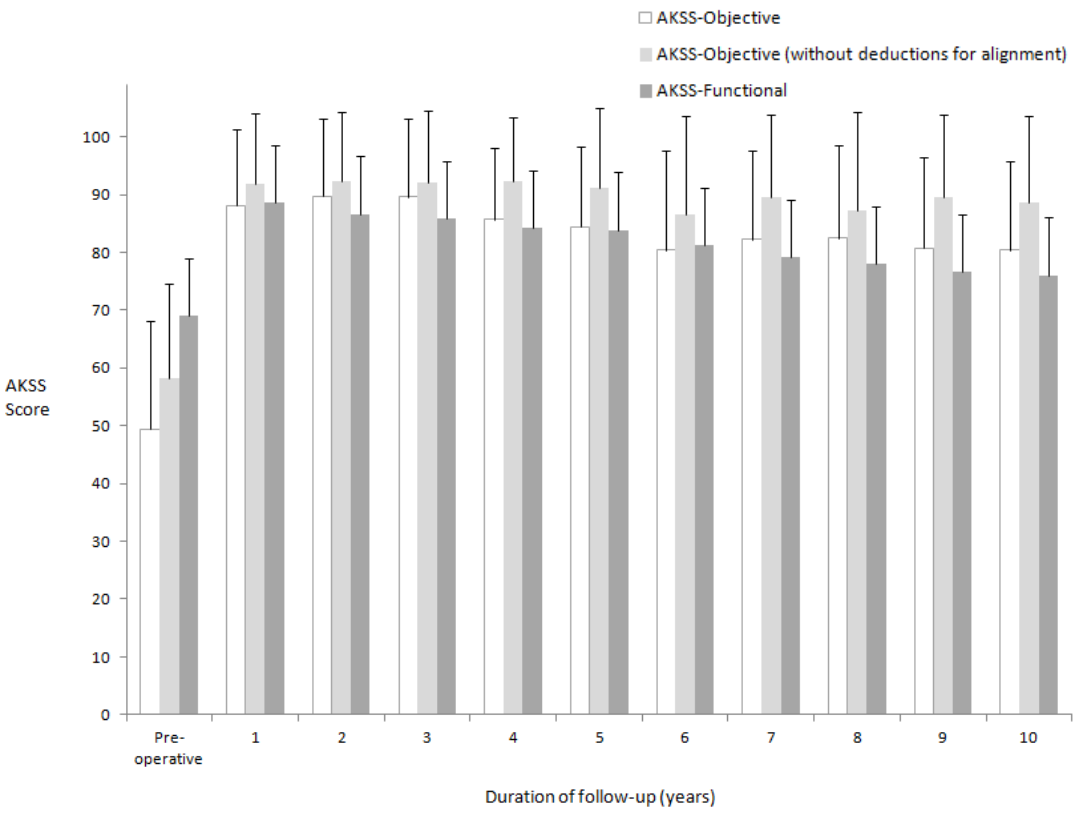


Figure 2.2: Bar chart showing the mean AKSS and SD (error bars) for each year of follow-up for knees from the developer series of OUKA.

Table 2.1: Details of revisions in the developer series of OUKA.

Case	Time to revision (years)	Indication	Operative Findings	Outcome
01	0.22	Dislocated bearing	Dislocated bearing	Bearing revised
02	0.43	Infection	Coagulase negative Staphylococcus	Two stage primary TKA
03	0.72	Unexplained pain	No cause found	Revised to primary TKA
04	0.75	Infection	Coagulase negative Staphylococcus	Two stage primary TKA
05	0.79	AVN lateral femur	AVN lateral femoral condyle	Revised to primary TKA
06	0.80	Dislocated bearing	Dislocated bearing	Bearing revised
07	0.84	Dislocated bearing	Dislocated bearing. Femoral component loosened whilst retrieving bearing	Bearing and femoral component revised
08	1.02	Dislocated bearing	Dislocated bearing	Bearing revised
09	1.03	Infection	Coagulase negative Staphylococcus	Two stage TKA with stemmed tibial component
10	1.57	Infection suspected	No organism grown. Synovitis with destruction of lateral compartment	Two stage primary TKA
11	1.80	Unexplained pain	No cause found	Revised to primary TKA
12	1.92	Tibial mal-position	Tibial overhang	Tibial component revised
13	1.94	Disease progression	Lateral compartment OA	Revised to primary TKA
14	2.12	Infection following ACL reconstruction trauma	Loosening of tibial component with destruction of lateral compartment	Two stage primary TKA
15	2.32	Disease progression	Lateral compartment OA	Revised to primary TKA
16	2.48	Unexplained pain	Revised overseas	Revised to primary TKA
17	2.49	Unexplained pain	No cause found	Revised to primary TKA
18	2.89	Infection	No organism grown. Synovitis with destruction of lateral compartment.	Two stage primary TKA
19	2.93	Disease progression	Lateral compartment OA	Lateral UKA
20	3.46	Dislocated bearing	Dislocated bearing	Bearing revised
21	3.68	Disease progression	Lateral compartment OA	Revised to primary TKA
22	3.81	Disease progression	Lateral compartment OA	Revised to primary TKA
23	4.64	Disease progression	Lateral compartment OA	Revised to primary TKA
24	5.16	Disease progression	Lateral compartment OA	Lateral UKA
25	5.21	Disease progression	Lateral compartment OA	Revised to primary TKA
26	5.56	Dislocated bearing	Dislocated bearing	Bearing revised
27	5.62	Unexplained pain	No cause identified	Revised to primary TKA
28	5.71	Disease progression	Lateral compartment OA	Revised to primary TKA
29	5.83	Disease progression	Lateral compartment OA	Revised to primary TKA
30	6.07	Disease progression	Lateral compartment OA	Lateral UKA
31	6.33	Disease progression	Lateral compartment OA	Lateral UKA
32	6.74	Disease progression	Lateral compartment OA	Revised to primary TKA
33	6.90	Disease progression	Lateral compartment OA	Revised to primary TKA
34	7.25	Disease progression	Lateral compartment OA	Lateral UKA
35	7.82	Dislocated bearing	Dislocated bearing	Bearing revised
36	8.35	Loose femur	Loose femoral component	Revised to primary TKA
37	8.75	Aseptic loosening tibia	Loose tibia and lateral compartment OA	Revised to primary TKA
38	8.97	Unexplained pain	Revised overseas	Revised to primary TKA
39	9.13	Disease progression	Lateral compartment OA	Revised to primary TKA
40	9.14	Instability	Medial compartment opening	Revised to hinged TKA
41	9.26	Disease progression	Lateral compartment OA	Revised to primary TKA
42	9.37	Unexplained pain	No cause identified	Revised to primary TKA
43	9.42	Disease progression	Lateral compartment OA	Lateral UKA
44	9.89	Disease progression	Lateral compartment OA	Lateral UKA
45	9.90	Disease progression	Lateral compartment OA	Revised to primary TKA
46	10.01	Disease progression	Lateral compartment OA	Lateral UKA
47	10.05	Disease progression	Lateral compartment OA	Revised to primary TKA
48	10.26	Disease progression	Lateral compartment OA	Lateral UKA
49	10.33	Disease progression	Lateral compartment OA	Revised to primary TKA
50	11.39	Disease progression	Lateral compartment OA	Lateral UKA
51	12.02	Unknown	Revised overseas	Revised to primary TKA
52	14.74	ACL Injury	Extensive synovitis. ACL rupture	Revised to primary TKA

Lateral progression was the most common cause of revision and occurred in 25 cases (2.5%) at a mean of 7.0 years (range 1.9 to 11.4). In ten cases the patient underwent lateral UKA and in fifteen cases primary TKA was performed. In our unit historically when a patient developed lateral osteoarthritis a primary TKA was performed, however it was noted that this was often unnecessary, particularly when the medial OUKA was well functioning and secure, and as such current surgical practice is to perform lateral UKA in these cases. In knees with lateral progression, at last follow-up prior to revision the mean OKS was 32 (SD8) with no significant difference seen between those revised to lateral UKA and primary TKA (p = 0.91). In this series if the ACL was intact at the time of revision a mobile-bearing lateral UKA (n = 9) was implanted and if the ACL was functionally not intact (friable and fragmented or absent) a fixed-bearing UKA (n = 1) was implanted.

Of the seven cases of bearing dislocation (0.7%), the dislocation was anterior in five cases and posterior in two cases. The mean time to bearing dislocation was 3.6 years (range 0.2 to 7.8), with three cases occurring within the first year following surgery. In four cases the dislocation was associated with trauma, typically a twisting injury to a flexed knee and in one case it was associated with bearing impingement. In the remaining two cases no cause was identified. In all cases open revision of the bearing was performed. In one case during retrieval of a posterior dislocated bearing the femoral component was loosened necessitating femoral component revision.

Infection occurred in six cases (0.6%) at a mean of 1.5 years (range 0.4 to 2.9). In all cases a two-stage revision was performed. With the exception of one case which required a stemmed tibial component, a primary TKA prosthesis was used in all other cases. In three cases the organism was isolated as a coagulase negative *Staphylococcus*. In two cases, in the same patient, infection was suspected and a two-stage revision was performed despite no organism being cultured. In one case infection followed ACL reconstruction for traumatic rupture 25 months after the index procedure.

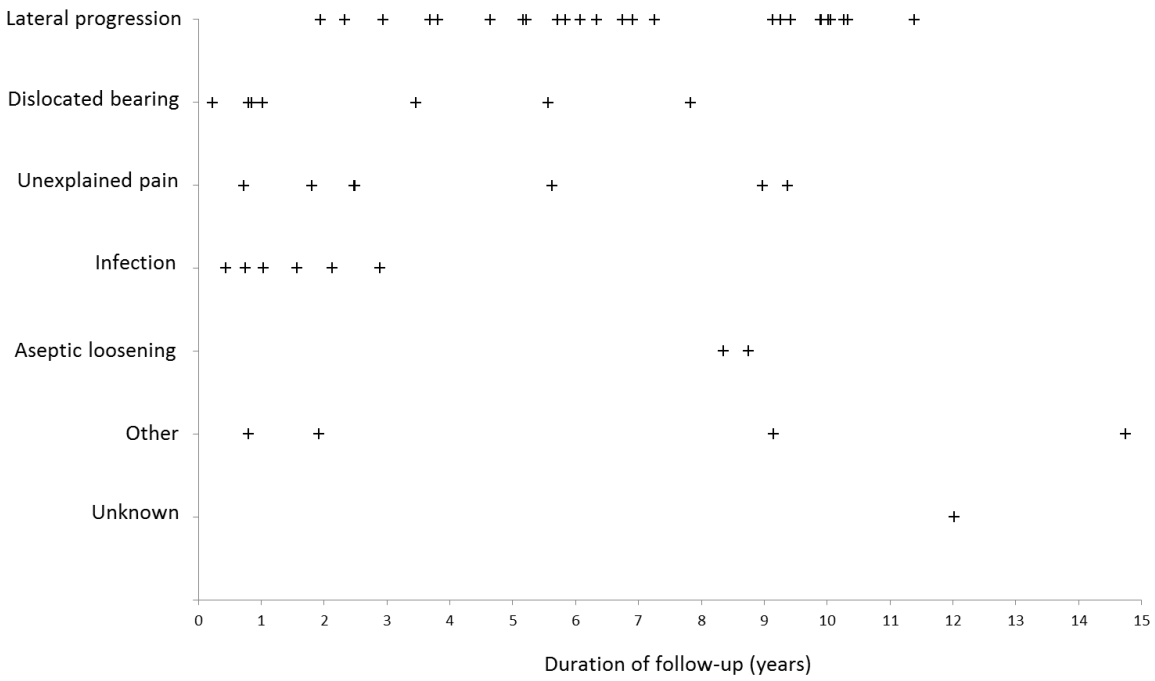


Figure 2.3: Graph showing the mechanism and timing of failures of OUKA in the developer series.

Table 2.2: Table showing the mechanism and timing of failures of OUKA in the developer series.

Failure mechanism	**Percent (number)**	**Mean years to failure (range)**
Lateral progression	2.5% (25)	7.0 (1.9 to 11.4)
Dislocated bearing	0.7% (7)	3.6 (0.2 to 7.8)
Unexplained pain	0.7% (7)	4.5 (0.7 to 9.4)
Infection	0.6% (6)	1.5 (0.4 to 2.9)
Aseptic loosening	0.2% (2)	8.6 (8.4 to 8.8)

Of the remaining revision cases the indications were: unexplained pain (7 cases), aseptic loosening (2 cases; 1 femur, 1 tibia), ACL rupture (1 case), lateral compartment SONK (1 case), mal-position of tibial component (1 case) and instability (1 case). The cause of one revision was unknown due to the operation being performed overseas at another centre. With the exception of the revision for instability, in which a hinged knee prosthesis was required, and in one case of infection where a stemmed tibial component was used as part of a two-stage revision procedure, all other cases were treated with a primary TKA prosthesis.

When implant-related re-operations are considered failures the fifteen-year survival rate was 90.5% (95%CI 83.0 to 97.9) (**Table 2.3**). When revisions of the tibial or femoral components are considered failures the fifteen-year survival rate was 93.0% (95%CI 86.4 to 99.5). When revision requiring revision TKA components are considered failures the fifteen-year survival rate was 99.7% (95%CI 98.2 to 100).

Table 2.3: Lifetable for 1000 OUKA from the developer series.

Follow-up (years)	Number at start	Revised	Withdrawn	FU ongoing	Lost to FU	Dead	At Risk	Annual Failure	Annual Success	Survival	95% CI	95% CI
0 to 1	1000	7	15	0	4	8	993	0.007	0.993	99.3	98.8	99.8
1 to 2	978	6	7	0	0	5	975	0.006	0.994	98.7	98.0	99.4
2 to 3	965	6	8	0	0	7	961	0.006	0.994	98.1	97.2	98.9
3 to 4	951	3	10	0	0	9	946	0.003	0.997	97.8	96.8	98.7
4 to 5	938	1	18	0	0	15	929	0.001	0.999	97.7	96.7	98.6
5 to 6	919	6	68	46	0	16	885	0.007	0.993	97.0	95.9	98.1
6 to 7	845	4	109	89	0	16	791	0.005	0.995	96.5	95.2	97.8
7 to 8	732	2	133	112	0	15	666	0.003	0.997	96.2	94.8	97.6
8 to 9	597	3	89	78	0	10	553	0.005	0.995	95.7	94.0	97.3
9 to 10	505	7	107	91	0	11	452	0.016	0.984	94.2	92.1	96.3
10 to 11	391	4	98	87	0	8	342	0.012	0.988	93.1	90.5	95.7
11 to 12	289	1	101	92	0	7	239	0.004	0.996	92.7	89.5	95.9
12 to 13	187	1	45	39	0	5	165	0.006	0.994	92.1	88.2	96.1
13 to 14	141	0	61	55	0	5	111	0.000	1.000	92.1	87.3	97.0
14 to 15	80	1	51	46	0	4	55	0.018	0.982	90.5	83.0	97.9

2.1.5 Discussion

This consecutive series of patients undergoing OUKA demonstrates that, in the hands of the developer surgeons, good long-term functional outcomes and implant-survival can be achieved with the minimally invasive approach. Assessed using OKS criteria 79% of knees had good or excellent outcome at ten-years and using AKSS criteria 82% had good or excellent outcomes with a mean knee flexion of 126° at this time-point. As the OUKA aims to achieve pre-disease, not neutral, alignment, it can be argued that there should not be deductions for alignment when scoring the AKSS. When no deductions are applied 86% of knees would be considered to have an excellent or good outcome at ten-years[122].

When implant-related re-operations were considered failures the fifteen-year survival of the cemented Phase 3 medial OUKA was 91% (95%CI 83 to 98) and when revision of the tibial or femoral components was considered a failure the fifteen-year survival was 93% (95%CI 86 to 100). In all but two cases, a stemmed tibial component following infection and a hinged TKA for instability, revision was performed with primary knee components highlighting that OUKA is a bone preserving procedure which permits further surgical options should they be required. As such the fifteen-year survival with the requirement for revision TKA components as an end point was 100% (95%CI 98 to 100). This contrasts to TKA where in the case of failure up to 85% of knees have been reported as requiring revision components[127].

In terms of radiological outcomes, whilst physiological radiolucency was observed under the tibial component in 14% of knees (4% complete, 10% partial) and around the posterior facet of the femoral component in 2% of knees, this study found no difference in functional outcomes in the presence or absence of physiological radiolucency even when they persisted until ten-year follow-up. Whilst the cause of physiological radiolucency remains unknown, they have been reported to form and consolidate during the first two-years, and thereafter remain stable[124,128]. The proportion

of knees with evidence of physiological radiolucency in this series was lower than previously reported at long-term follow-up[124,128]. The reasons for this may include improvements in surgical and cementing techniques, as well as improved instrumentation for the procedure, with previous long-term follow-up studies reporting the incidence of radiolucency with Phase 1 and 2 OUKA designs. Overall the results of this study confirm previous reports that physiological radiolucencies are of no clinical significance.

Of the 52 implant-related re-operations progression of arthritis in the retained lateral compartment (25 cases), followed by bearing dislocation (7 cases), and unexplained pain (7 cases) were the most common indications. There were low rates of revision due to aseptic loosening (2 cases) and no cases of revision due to wear or progression of PFJ arthritis.

Revision due to disease progression in the lateral compartment occurred in 2.5% of cases at a mean of 7.0 years (range 1.4 to 11.4). In this series lateral compartment disease progression occurred early, before five-years, in some patients (7 cases) and late, after ten-years, in others (5 cases). The wide range in timings of failure for this indication suggest that the reason for lateral compartment disease progression may be multifactorial. Whilst the aetiology of this mechanism of failure remains unknown several reasons for lateral compartment disease progression have been proposed.

One possible explanation is that the presence of pre-existing lateral compartment disease pre-disposes the knee to lateral compartment failure. A case-control study assessing the aetiology of disease progression in the lateral compartment following medial OUKA found the Kellgren-Lawrence grade of the lateral compartment on the aligned immediate postoperative radiographs to be a significant predictor of lateral progression (OR 2.63, $p = 0.02$)[75]. In this study of the 26 cases of disease progression 19% (5 knees) were identified as having Kellgren-Lawrence grade 2 or 3 arthritis in the lateral compartment on their aligned immediate postoperative radiographs compared to none of the 52 matched controls. In all cases, at the time of operation, the lateral

compartment was assessed as having full-thickness cartilage, highlighting that intra-operative assessment may not be able to detect all cases of lateral compartment disease, in part due to the difficulties with visualisation of this compartment when undertaking a minimally invasive approach. Taken into context this data would suggest that up to a fifth of cases of lateral compartment disease progression, the predominant cause of failure in the developer series, and third most common reason for failure in the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man (NJR), may be preventable if they were identified pre-operatively, or at the time of surgery[15]. As discussed in **Chapter 1** (**1.2.4.3 Assessment of the lateral compartment**) there is currently no consensus as to the optimum assessment of the lateral compartment and this will be discussed further in **Chapter 5.**

An alternative explanation is that lateral compartment disease progression may be due to other disease factors that predispose to this mechanism of failure, including ACL insufficiency and inflammatory arthritis[52]. Whilst a deficient ACL has been reported to be an absolute contraindication for OUKA due to the increased risk of aseptic loosening, it is also known that in the presence of functionally intact ligaments the disease is predominantly confined to the medial compartment, which progresses to involve the lateral compartment upon ACL rupture. Whether the incidence of lateral compartment disease increases with increasing macroscopic damage to the intact ACL is unknown. As in a large proportion of patients undergoing arthroplasty the ACL is macroscopically abnormal, but functionally intact, whether these patients are more prone to adverse outcomes, including lateral compartment disease progression will be investigated in **Chapter 4**.

A final consideration is that postoperative limb alignment may affect the risk of failure and in particular risk of lateral compartment progression. Whilst in fixed-bearing UKA limb alignment is related to the risk of lateral compartment progression, with a hip-knee-ankle angle of more than 180° being associated with progression of arthritis within the lateral compartment, this association

has not been demonstrated following OUKA[129]. OUKA aims to restore the patient's pre-disease alignment, by correcting intraarticular deformity, and whilst it is known that there is a wider range in postoperative alignment following OUKA, as compared to TKA, the extremes of alignment have not been found to be associated with adverse outcomes[122]. Whilst on a population level correction to pre-disease alignment does not appear to be associated with an increased risk of failure, the effect of overcorrection, which may occur with overstuffing the medial compartment in combination with MCL injury, may be a potential cause for lateral compartment disease in some cases.

Overall, in this series a very low incidence of failure secondary to aseptic loosening (2 cases, 0.2%) and an absence of cases with failure secondary to wear or progression of PFJ arthritis was noted compared to knee arthroplasty in general where these failure mechanisms make up around a third of cases of failure[130]. As discussed in **Chapter 1** (**1.2.1 Development of the Oxford Unicompartmental Knee Arthroplasty**) the design characteristics of the OUKA, with its full congruent bearing, reduce contact pressures by increasing the tibial contact area contributing to reduced micro-motion, stress and wear of the tibial component[131 18-20]. In addition, the inlay design of the femoral component on the OUKA appears to be PFJ conserving with no cases of revision secondary to PFJ pain or progression of disease seen, which is different to the experience with a fixed-bearing UKA where revision for PFJ problems is common[132].

This study provides evidence that in the hands of the developer surgeons minimally invasive OUKA can achieve similar long-term functional outcomes and implant survival compared to that reported by the designer surgeons using an open approach[30]. The strengths of this study are that it is a large, consecutive, series with a comprehensive, long-term clinical and radiological follow-up. A limitation is that we do not have the re-operation rate of these knees and that this is a developer series, and that the results might not be able to be replicated by other surgeons. A further limitation is the use of the Kalairajah classification in interpreting OKS. The Kalairajah classification, reported in 2005,

was developed in the total hip arthroplasty population anchoring the Oxford Hip Score to the Harris Hip Score with the cutoffs then applied to interpreting the OKS. Whilst this approach is widespread, and the Kalairajah classification has linked to risk of revision following TKA and UKA, the classification system has not been subject to formal validation in the knee arthroplasty population[133].

2.1.6 Conclusions

In the hands of the developer surgeons good outcomes, assessed via PROMS, objective clinical assessment, radiological assessment and implant survival can be achieved following OUKA. If the OUKA does fail progression of arthritis in the retained lateral compartment is the predominant failure mechanism, accounting for around half of all failures, followed by bearing dislocation, and unexplained pain. At long-term follow-up very low rates of revision due to aseptic loosening were seen and no cases of revision due to wear or progression of PFJ arthritis were identified.

2.2 Global Experience: Meta-analysis of published series of OUKA

2.2.1 Introduction

Whilst excellent results are achieved in the developer series, significant variation in outcomes of OUKA have been reported across the published literature[31]. To assess the global experience with OUKA a meta-analysis of all published series of cemented Phase 3 medial OUKA implanted via a minimally invasive approach was performed.

Variability in outcomes following OUKA may be due to patient, implant or surgeon factors. Whilst published case studies typically do not report individual patient data, thereby limiting the assessment of patient factors that affect outcomes, they do provide an insight as to implant factors, through analysis of failure mechanisms, as well as surgeon factors.

Surgeon factors associated with outcomes of OUKA include technical skills associated with the procedure itself as well as non-technical skills associated with decision making around patient selection. Technical skills have been hypothesised to improve as surgical volume increases and in TKA it has been demonstrated that high-volume surgeons have shorter procedure times, shorter length of stays, lower transfusion rates and lower infection rates which culminate in better patient reported outcomes[134]. Similar findings have been reported in UKA, albeit more marked than TKA, with a fourfold difference in revision rates seen between the lowest and highest-volume surgeons using NJR data suggesting that UKA may be more sensitive to technical errors[135].

Non-technical skills associated with decision making around patient selection are related to surgical indications. In severe osteoarthritis of the knee which fails to respond to non-operative treatments surgeons can choose between UKA and TKA. The decision as to which procedure to perform relates to an individual surgeon's indications, which is reflected by the relative proportions of a surgeon's primary knee practice that receive UKA and TKA. In UKA it has been demonstrated that, within

certain limits, surgeons who use UKA in a higher proportion of knees have significantly lower revision rates compared to surgeons who use UKA in a lower proportion of knees. With OUKA acceptable revision rates tend to be achieved by surgeons who use OUKA for 20% or more of their knee replacements and optimal results are achieved in those who perform between 40% and 60% of their knees as OUKA[136].

It has been reported that optimum outcomes following OUKA are achieved either when a surgeon operates on a high-volume of cases (high-caseload) or has a practice where a high proportion of primary knee arthroplasties are OUKA (high-usage) [135,136]. The relative importance of each of these factors on implant survival following OUKA has not been explored. At present it is unclear whether good outcomes can be achieved when a surgeon has a high-caseload but uses narrow indications such that they have low-usage, or vice versa where a surgeon has a low-caseload but implants OUKA in high proportion of cases (high-usage). This is relevant with regards to the provision of OUKA as a surgeon cannot change the volume of their practice but can change percentage of knees which can be OUKA.

The objective of this meta-analysis is review the results of the Phase 3 cemented OUKA to establish the overall outcomes and failure mechanisms for this implant, to determine the importance of caseload and usage of OUKA on implant survival, and to assess the interplay between these two factors.

2.2.2 Patients and methods

2.2.2.1 Search strategy and criteria

MEDLINE (Ovid), Embase (Ovid) and the Web of Science (ISI) were searched to identify studies reporting the outcomes of the cemented Phase 3 medial OUKA (Zimmer Biomet, Warsaw, Indiana) implanted through a minimally invasive approach between 1998, the year the Phase 3 was introduced, and 17 March 2016. The search strategy is outlined in **Appendix 5**. In addition reference lists of included publications, published reviews, conference abstracts and experts in the field were contacted to identify additional reports.

Studies were excluded if they did not report the outcomes of a consecutive series of knees or did not present implant survival data. Studies reporting the outcomes of comparative studies, including RCTs, were excluded if they did not report on consecutive patients due to the risk of selection bias. Registry studies were excluded due to the limitations in obtaining volume and proportion data for individual surgeons. The outcomes of bi-unicompartmental arthroplasty were excluded. There were no limits on language of publication, number of patients, duration of follow-up or indication for the procedure.

Searches were performed independently in duplicate by myself and Mr J Rizkalla with disagreement resolved by consensus. Where necessary the corresponding authors were contacted to confirm the data extraction was correct and to determine the surgical caseload and usage of OUKA in their published series. A flow diagram for study selection is outlined in **Figure 2.4**.

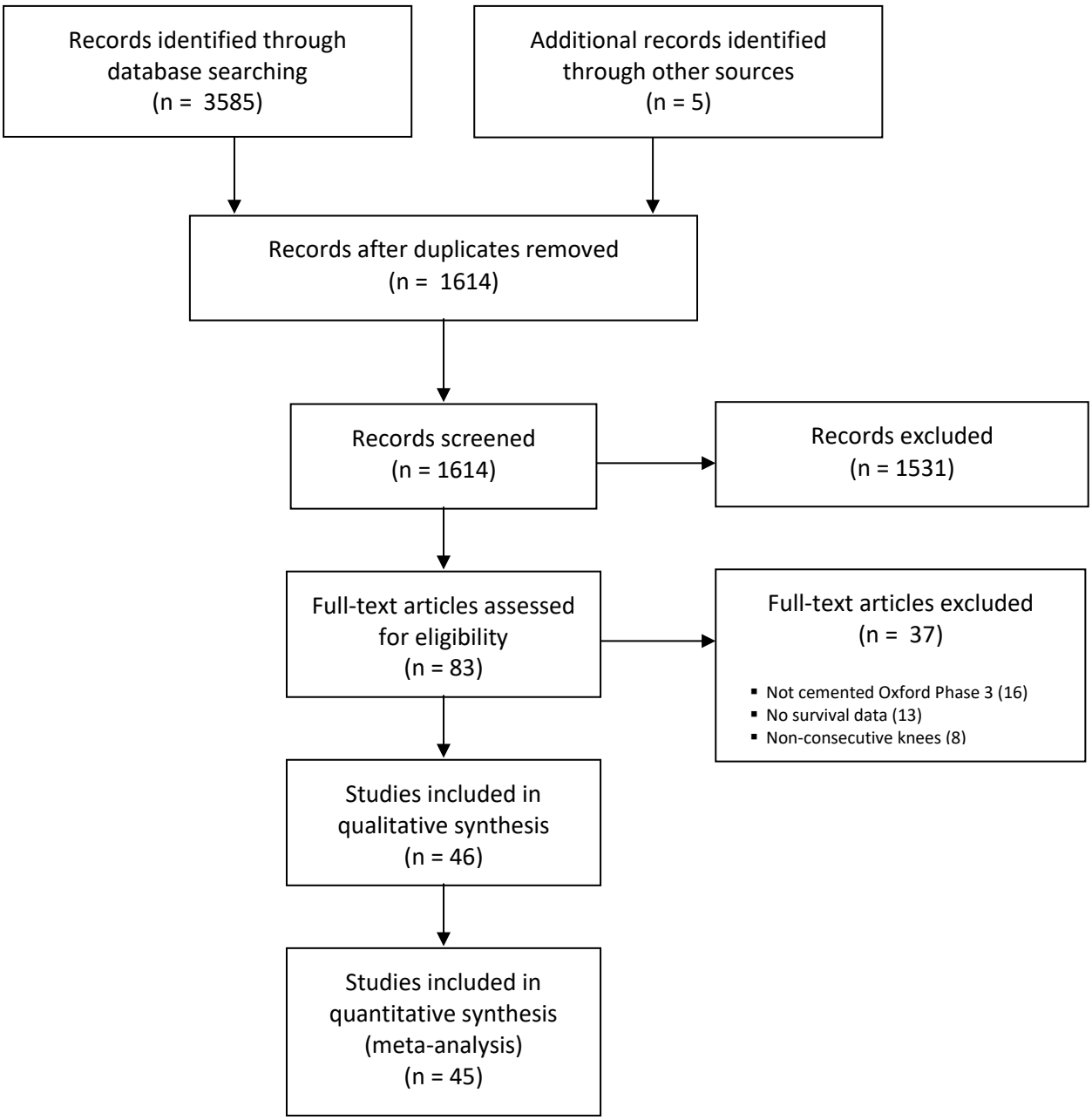


Figure 2.4: PRISMA flow diagram of studies included in the meta-analysis of OUKA.

2.2.2.2 Outcome measures assessed

For each study the number of OUKA, number of revisions, reason for revision, and mean follow-up were recorded independently in duplicate. In addition the caseload (number of OUKA performed per year per surgeon) and usage (proportion of OUKA, assessed as a percentage of all primary knee arthroplasty) was recorded where presented, and, as mentioned above, requested from authors where not presented. A broad definition of failure was used and we considered revisions in which components were removed or changed, including bearings in the case of dislocation, and any re-operations in which new components were inserted. The methodological quality of included studies was assessed using the Methodological Index for NOn-Randomised Studies (MINORS) score[137].

2.2.2.3 Caseload: OUKA per surgeon per year

Surgical caseload was divided based on clinically plausible cut-points *a priori*, based on the system employed by the New Zealand Joint Registry[138]. Surgeons performing under one OUKA every two months (≤6 OUKA per year) were considered very low-caseload, those performing more than one OUKA every two months, but not more than one per month (>6 and ≤12 OUKA per year) were considered low-caseload, those performing more than one OUKA every month, but not more than two per month (>12 and ≤24 OUKA per year) were considered medium-caseload and those performing more than two OUKA per month (>24 OUKA per year or more) were considered high-caseload.

2.2.2.4 Usage: OUKA as a proportion of all primary knee arthroplasty

Usage was defined as the proportion of all primary knee arthroplasty performed that were OUKA. Very low-usage was defined as surgeons who performed under 10% OUKA, low-usage as surgeons who performed at least 10% but under 20% OUKA, medium-usage as surgeons who performed at least 20% but under 30% OUKA and high-usage as surgeons who performed 30% or over OUKA.

2.2.2.5 Combined caseload and usage

To explore the interaction between caseload and usage four groups were created based on: low-caseload (≤12 OUKA per year) and high-usage (≥20% OUKA), high-caseload (>12 OUKA per year) and high-usage (≥20% OUKA), low-caseload (≤12 OUKA per year) and low-usage group (<20% OUKA), and high-caseload (>12 OUKA per year) and low-usage group (<20% OUKA).

2.2.3 Statistical methods

The primary outcome was the all cause revision rate per 100 observed component years, which is equal to the annual revision rate (%pa), and was calculated by dividing the number of revisions observed by the mean follow-up in years multiplied by 100. As revisions for bearing dislocation occur early after the primary operation, and as such may not have a constant annual revision rate the absolute revision rate was calculated. Confidence intervals were calculated using the Clopper-Pearson, exact, method[139]. As revision rates were expected to be low a Freeman-Tukey variance stabilising double arcsine transformation was used such that studies with zero rates would not be excluded[140]. Where a difference in the primary outcome was detected secondary outcomes were assessed: including the annual revision rate for lateral compartment disease progression, bearing dislocation, unexplained pain and aseptic loosening as these have been reported to be the

predominant failure mechanisms of OUKA[135]. In addition the rates of other potential causes of revision, including revision for disease progression in the PFJ, polyethylene wear and tibial fracture were assessed.

As revision rates follow a binomial distribution a meta-analysis of proportions was performed with summary annual revision rates pooled using a random effects model to minimise the effect of between study heterogeneity[141,142]. Statistical heterogeneity across studies was assessed using the I^2 statistic[143].

Analysis was performed overall and based on those studies with long-term, mean ten-years or greater, outcomes with sub-group analysis based on caseload, usage and the interaction between caseload and usage as defined above. Analysis was conducted using Stata Version 13 (Stata Corp, Texas, USA) with a $p < 0.05$ considered statistically significant.

2.2.4 Results

Searches identified a total of 3585 papers with an additional five studies identified through searches of references and conference abstracts (**Figure 2.4**). After screening, the full-texts of 83 studies were retrieved and assessed with 37 excluded (**Appendix 5**) leaving 46 studies (12,520 knees observed for 67,128 component years) meeting inclusion criteria (**Table 2.4**). The mean MINORS score of included studies was 12 (range 10-14) (**Table 2.4**).

After contacting authors, data on the caseload was available for 37 studies (80%) and on usage for 34 studies (74%) (**Table 2.5**). The smallest study, Palacios *et al.*, had 24 observed component years and reported no failures and was found to skew the revision estimate towards zero[144]. Therefore, as generally recommended, this study was excluded from the quantitative analysis[144]. The analysis was repeated including this study and this did not change the interpretation of the results.

The all cause revision rate was 1.21%pa (95%CI 0.97 to 1.47) (**Figure 2.5**). Revision indications are outlined in **Table 2.6**. Out of the 12,520 knees there were 121 (0.97%) dislocations, 20 (0.16%) tibial plateau fractures, 7 (0.06%) revisions for patello-femoral disease and 1 (0.01%) revision for polyethylene wear secondary to anterior impingement. In series with long-term outcomes, mean follow-up ten-years or greater, the all cause revision rate was 0.63%pa (95%CI 0.46 to 0.83) (**Table 2.7**).

Table 2.4: Demographic Information of included studies in the meta-analysis of OUKA.

Study	Country	Age	Age range	% male	BMI	BMI range	MINORS Score
Akan 2013[145]	Turkey	64	42 – 84	17	29.8	19 – 42	11
Amin 2006[146]	UK	68	40 – 91	50	29.2	21 – 43	13
Aslan 2007[147]	Turkey	57	47 – 73	11			11
Bergeson 2013[148]	USA	63	29 – 91	44	32.2	17 – 58	11
Bhattacharya 2012[149]	UK	69	50 - 83	50			12
Biau 2013[150]	Canada	60	55 - 65	33	32.0	29 – 34	11
Bottomley 2016[151]	UK	67		49			12
Bozkurt 2013[152]	Turkey	57					11
Burnett 2014[153]	Canada	69	40 - 88	44	29.7	18 – 49	14
Choy 2011[154]	South Korea	65	44 - 82	10			12
Cinar 2010[155]	Turkey	58	44 - 76	8			11
Clarius 2010[25]	Germany	63	45 - 78	49	29.0	20 – 42	13
Clark 2010[156]	Australia	64	45 - 81				11
Clement 2012[157]	UK	70		43			12
Cool 2006[158]	Belgium	66	45 - 90	29	27.5		12
Davidson 2013[159]	UK	65	41 - 87	51			10
Dervin 2011[160]	Canada	65	38 - 89	43	30.1	19 – 53	11
Edmondson 2011[161]	UK	67	57 - 86				11
Emerson 2016[162]	USA	67	38 - 89	55	29.9	17 – 62	12
Falcao 2014[163]	Portugal	64	49 - 78	15			11
Faour-Martin 2013[164]	Spain	59		29	27.1		12
Heller 2009[165]	Israel	63	45 - 80	32			11
Ingale 2013[58]	UK	67	42 - 92		29.3		12
Ji 2014[166]	South Korea	64	50 - 76	15			11
Keys 2013[167]	UK	69	40 - 87				13
Kim KT 2015[168]	South Korea	62	45 - 75				12
Kim SJ 2012[169]	South Korea	67	49 - 79	19			14
Kort 2007[170,171]	The Netherlands	66	43 - 93	34	30.7		11
Kuipers 2010[57]	The Netherlands	63	39 - 85	32			11
Lim 2012[172]	South Korea	69	48 - 82				13
Lisowski 2011[173]	The Netherlands	73	43 - 91		28.0	19 – 52	12
Luscombe 2007[174]	UK	63	41 - 79		28.4		11
Mallen 2014[175]	Mexico	71	57 - 81	16	28.1	19 – 36	11
Matharu 2012[59]	UK	63	35 - 87				11
Munk 2011[89]	Denmark	66		51			11
Nerhus 2012[176]	Norway	65	51 - 80	41			11
Palacios 2007[177]	Mexico		55 - 74	32			10
Pandit 2015[178]	UK	66	32 - 88	48			13
Parmaksızoglu 2012[179]	Turkey	67	56 - 75	26			10
Petersen 2013[180]	Germany	71	59 - 79				11
Schroer 2013[181]	USA	57	40 - 76	58			12
Smith 2012[182]	UK	67					11
Song 2009[183]	South Korea	66	57 - 82	7			11
Wagner-Kristensen 2013[56]	Denmark	64	30 - 94				12
Whittaker 2010[184]	Canada	63	49 - 87		30.7	19.3 - 43.1	10
Yoshida 2013[185]	Japan	77	47 - 94	18			13

Table 2.5: Details of included studies in the meta-analysis of OUKA.

Study	Number of knees	Number of patients	Mean follow-up (years)	Follow-up range (years)	Number of revisions	Caseload (OUKA/surgeon/year)	Usage (% OUKA)
Akan 2013[145]	141	120	3.5	2.0 - 4.3	10	21	
Amin 2006[146]	54	54	4.9	2.0 - 5.9	6		
Aslan 2007[147]	27	27	2.3	2.0 - 3.0	2		
Bergeson 2013[148]	839	688	3.7	0.1 - 6.5	40	111	22
Bhattacharya 2012[149]	49	44	5.6	2.0 - 9.9	1	15	5
Biau 2013[150]	37	33	5.3	4.9 - 6.3	1	12	8
Bottomley 2016[151]	1084	947	5.2		46	8	50
Bozkurt 2013[152]	53		1.2	0.5 - 3.3	1		15
Burnett 2014[153]	467	387	6.1	0.7 - 11.6	42	6	13
Choy 2011[154]	188	166	6.7	4.7 - 8.6	17	48	34
Cinar 2010[155]	41	40	1.6	0.8 - 3.5	1		8
Clarius 2010[25]	61	59	5.0	4.0 - 7.0	2	3	13
Clark 2010[156]	398	398	3.6	1.0 - 8.5	15	11	20
Clement 2012[157]	49	49	7.2		4	12	13
Cool 2006[158]	50	49	3.7	2.6 - 5.0	3		
Davidson 2013[159]	699	699	4.2		39	54	27
Dervin 2011[160]	545	545	3.8	2.3 - 7.4	32	18	17
Edmondson 2011[161]	48	48	4.5	3.0 - 6.0	4	6	6
Emerson 2016[162]	213	173	10.0	4.0 – 11.0	20	85	40
Falcao 2014[163]	29	27	3.9	0.8 - 6.9	2		
Faour-Martin 2013[164]	511	402	10.4		29	85	
Heller 2009[165]	59	59	2.7		7	7	5
Ingale 2013[58]	470		3.9		29	5	9
Ji 2014[166]	246	245	2.8	1.0 - 8.0	20	16	
Keys 2013[167]	107	NS	11.5		6	24	31
Kim KT 2015[168]	166	128	10.0		16	83	23
Kim SJ 2012[169]	124	104	6.7	4.2 - 9.1	3	40	
Kort 2007[170,171]	200	175	4.0	2.0 - 7.0	19	8	4
Kuipers 2010[57]	437	437	2.6	0.1 - 7.9	45	5	10
Lim 2012[172]	400	320	5.2	1.0 - 10.0	14	44	30
Lisowski 2011[173]	244	216	4.2	1.0 - 10.4	9	27	40
Luscombe 2007[174]	78	68	2.0		4	23	22
Mallen 2014[175]	30	25	6.1	1.1 - 11.5	3	3	
Matharu 2012[59]	459	392	4.4	0.5 - 11.2	23	8	18
Munk 2011[89]	268	268	1.0		3	19	15
Nerhus 2012[176]	99	96	2.0		6		
Palacios 2007[177]	24	22	1.0	0.7 - 3.0	0	6	33
Pandit 2015[178]	1000	818	10.3	5.3 - 16.6	52	50	70
Parmaksızoglu 2012[179]	38	38	2.0	1.5 - 2.7	0		
Petersen 2013[180]	50		5.0		3		
Schroer 2013[181]	83	77	3.6	0.3 - 7.1	13	28	7
Smith 2012[182]	230		7.3		21	19	23
Song 2009[183]	100	94	9.0		9	43	23
Wagner-Kristensen 2013[56]	695	579	4.6	0.0 - 10.7	51	24	22
Whittaker 2010 [184]	79	62	3.6	1.0 - 11.3	7	5	7
Yoshida 2013[185]	1251	990	5.2	1.0 – 10.5	25	114	70

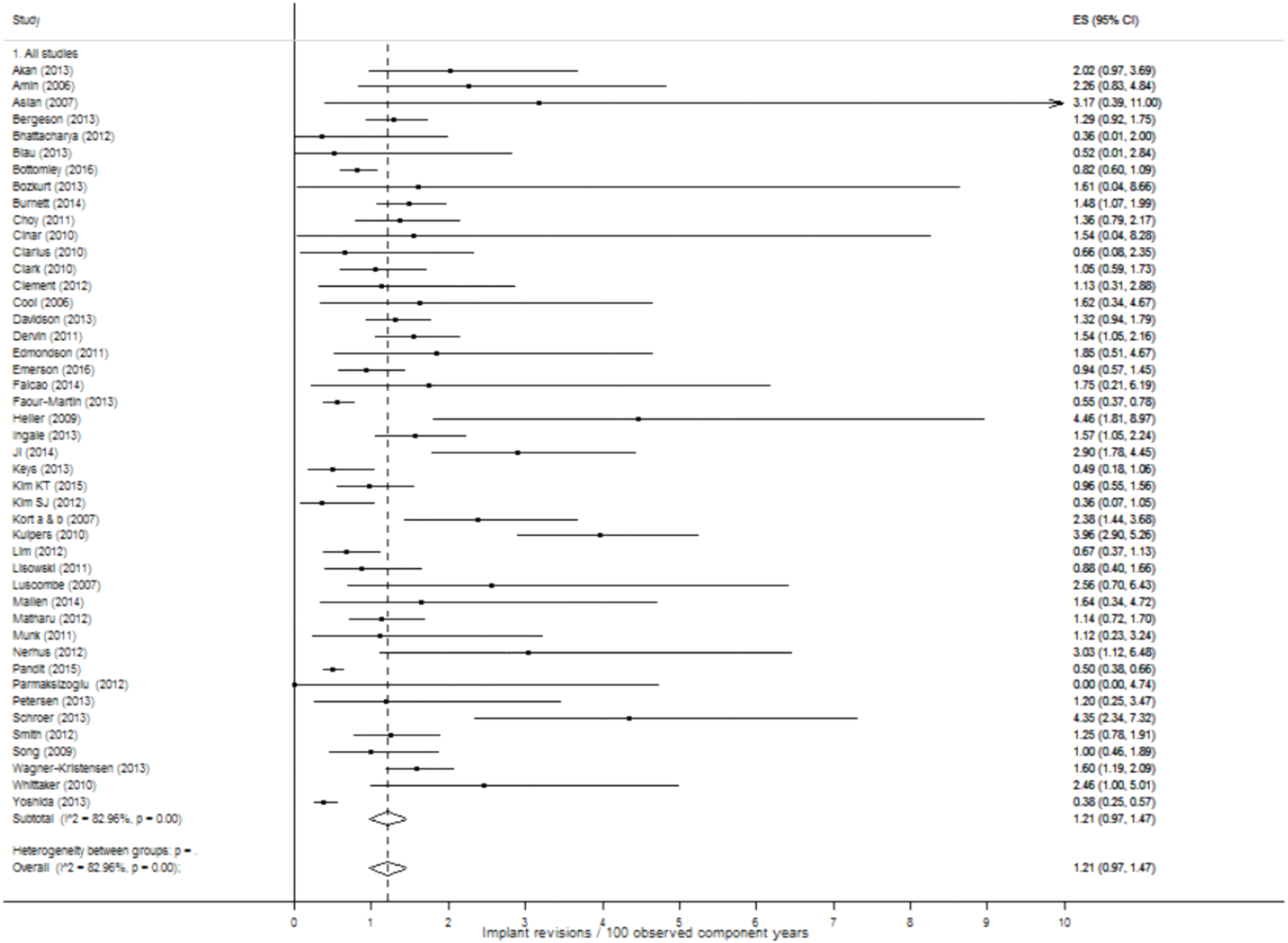


Figure 2.5: Outcomes of all published case series of Phase 3 OUKA.

Table 2.6: Indications for revision in included case studies in the meta-analysis of OUKA.

	All Cause %pa (95%CI)	**Aseptic Loosening** %pa (95%CI)	**Lateral Progression** %pa (95%CI)	**Bearing Dislocation** %pa (95%CI)	**Unexplained Pain** %pa (95%CI)
All series	1.21 (0.97 to 1.47)	0.19 (0.09 to 0.32)	0.10 (0.04 to 0.19)	0.10 (0.05 to 0.17)	0.05 (0.01 to 0.11)
Caseload					
≤6 OUKA pa	1.87 (1.14 to 2.76)	0.36 (0.15 to 0.64)	0.59 (0.35 to 0.87)	0.08 (0.01 to 0.19)	0.19 (0 to 0.60)
>24 OUKA pa	0.88 (0.63 to 1.61)	0.07 (0.01 to 0.19)	0.15 (0.04 to 0.32)	0.21 (0.10 to 0.35)	0.03 (0 to 0.09)
p-value	**0.02**	**0.03**	**0.005**	0.58	**0.02**
Usage					
<10%	1.89 (1.15 to 2.80)	0.65 (0.17 to 1.36)	0.19 (0.05 to 0.39)	0.04 (0 to 0.18)	0.22 (0.02 to 0.57)
≥30%	0.69 (0.50 to 0.90)	0.09 (0.01 to 0.22)	0.12 (0.03 to 0.26)	0.17 (0.07 to 0.15)	0.02 (0.01 to 0.12)
p-value	**<0.001**	**0.001**	0.10	0.94	**0.02**
Combined					
Low-caseload, Low-usage	1.76 (1.21 to 2.41)	0.56 (0.34 to 0.82)	0.23 (0.08 to 0.44)	0.08 (0.02 to 0.17)	0.28 (0.07 to 0.58)
High-caseload, Low-usage	1.58 (0.57 to 3.05)	0.62 (0 to 2.17)	0.58 (0.31 to 0.91)	0.06 (0 to 0.23)	0.09 (0 to 0.27)
Low-caseload, High-usage	0.85 (0.65 to 1.08)	0.23 (0.13 to 0.36)	0.24 (0.14 to 0.38)	0.12 (0.05 to 0.22)	0.06 (0.01 to 0.13)
High-caseload, High-usage	0.94 (0.69 to 1.23)	0.16 (0.05 to 0.31)	0.12 (0.04 to 0.25)	0.18 (0.08 to 0.30)	0.04 (0 to 0.11)
p-value	**0.004**	**0.001**	**0.002**	0.71	**0.01**

Table 2.7: Outcomes of published case series of Phase 3 OUKA with mean a follow-up of ten-years or greater.

Study	Number of knees	Annual revision rate (%pa)	Annual revision rate 95% CI (%pa)	10y survival (%)	10y survival (%) 95% CI	Caseload (OUKA/surgeon/year)	Usage (% OUKA)
Emerson 2016[162]	213	0.94	0.57 – 1.45	90.6	85.5 – 94.3	85	40
Faour-Martin 2013[164]	511	0.55	0.37 – 0.78	94.5	92.2 – 96.3	85	
Keys 2013[167]	107	0.49	0.18 – 1.06	95.1	89.4 – 98.2	24	31
Kim KT 2015[168]	166	0.96	0.55 – 1.56	90.4	84.4 – 94.5	83	23
Pandit 2015[178]	1000	0.50	0.38 – 0.66	95.0	93.4 – 96.2	50	70
OVERALL	1997	0.63	0.46 – 0.83	93.7	91.7 – 95.4		

2.2.4.1 Caseload: OUKA per surgeon per year

No difference in mean age (p = 0.69), gender (p = 0.71) or BMI (p = 0.38) was seen between groups based on caseload.

The revision rate decreased as the caseload increased (p = 0.02) (**Figure 2.6**). The revision rate where surgeons performed: ≤6 OUKA per year was 1.87%pa (95%CI 1.14 to 2.76), >6 but ≤12 OUKA per year was 1.25%pa (95%CI 0.77 to 1.83), >12 but under ≤24 OUKA per year was 1.37%pa (95%CI 0.93 to 1.89) and >24 OUKA per year was 0.88%pa (95%CI 0.63 to 1.61).The revision rate for lateral compartment disease progression (p = 0.005), unexplained pain (p = 0.02) and aseptic loosening (p = 0.003) decreased as caseload increased. No difference in annual revision rate (p = 0.58) or absolute revision rate (p = 0.17) for bearing dislocation was detected (**Table 2.6**).

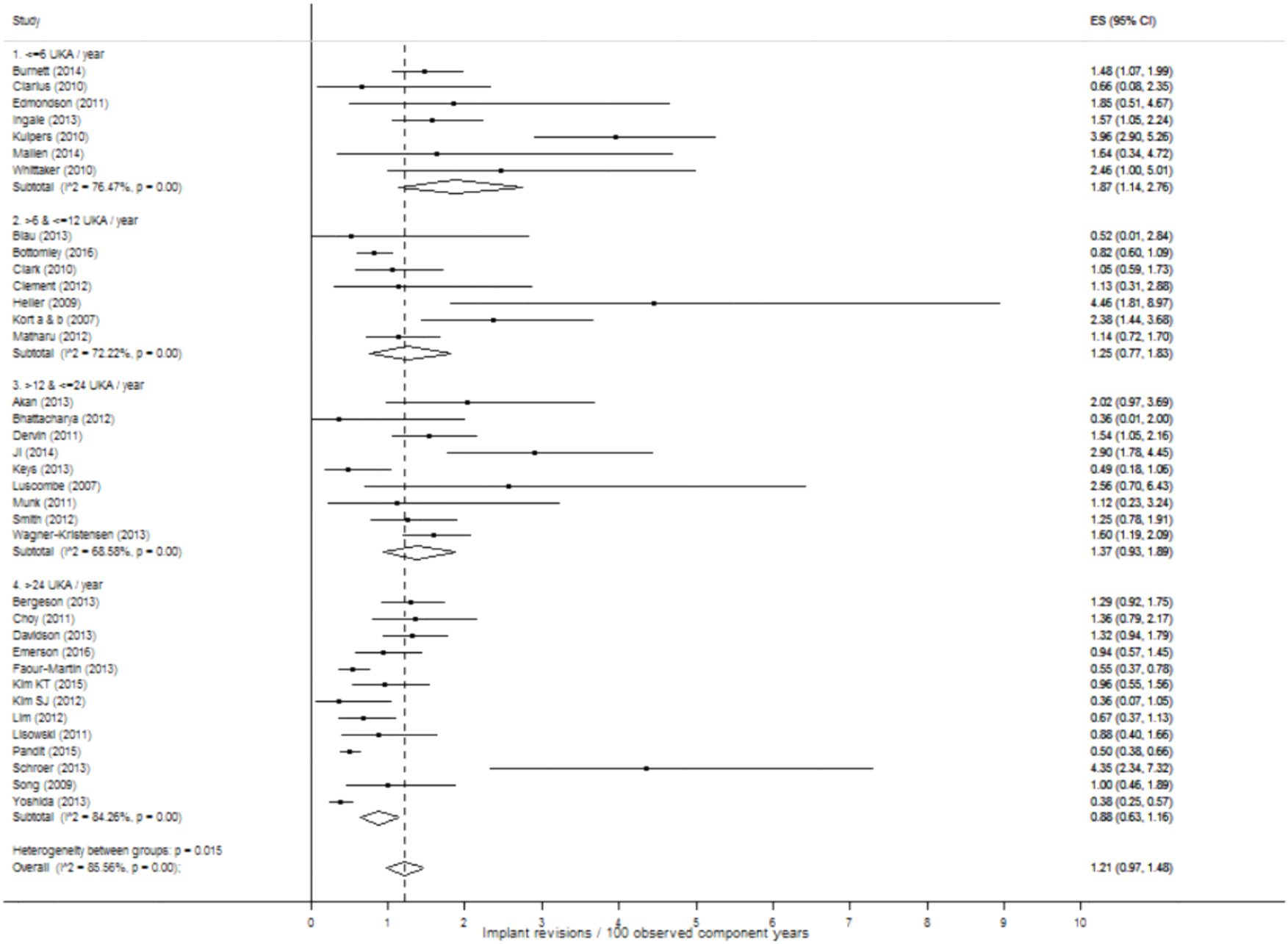


Figure 2.6: Outcomes by surgical caseload of Phase 3 OUKA (OUKA per surgeon per year).

2.2.4.2 Usage: OUKA as a proportion of all primary knee arthroplasty

As usage of OUKA increased the mean age increased (p = 0.04). The mean age of patients in surgeons who performed OUKA in <10% of cases was 63.4 years (SD4.2) increasing to 69.4 years (SD4.3) in surgeons who implanted OUKA in at ≥30% of cases. No difference in gender (p = 0.27) or BMI (p = 0.32) was seen.

The revision rate decreased as usage of OUKA increased (p < 0.001) (**Figure 2.7**). The revision rate in series where surgeons performed: <10% OUKA was 1.89%pa (95%CI 1.15 to 2.80), ≥10% but <20% OUKA was 1.48%pa (95%CI 0.91 to 2.18), ≥20% but <30% OUKA was 1.25%pa (95%CI 1.07 to 1.43) and ≥30% was 0.69%pa (95%CI 0.50 to 0.90).

The revision rate for unexplained pain (p = 0.02) and aseptic loosening (p = 0.001) decreased as the usage of OUKA increased. No difference in annual revision rate (p = 0.94) or absolute revision rate (p = 0.33) for bearing dislocation, or annual revision rate for lateral compartment disease progression (p = 0.10) was seen (**Table 2.6**).

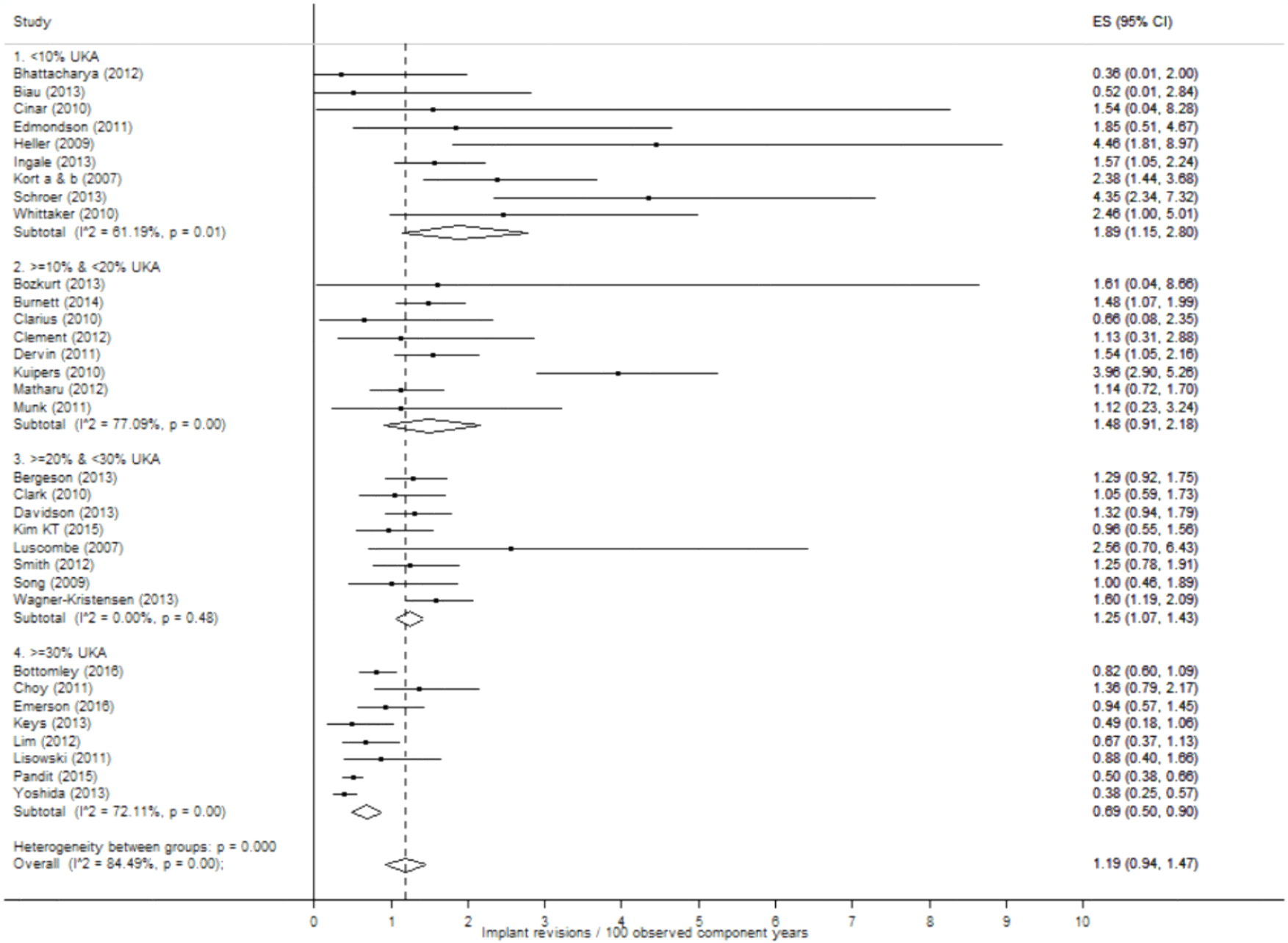


Figure 2.7: Outcomes by surgical usage of Phase 3 OUKA (OUKA as a percentage of all primary knee arthroplasty).

2.2.4.3 Combined caseload and usage

No difference in mean age (p = 0.84), gender (p = 0.73) or BMI (p = 0.19) was seen based on the combined caseload and usage of OUKA.

Significant differences in revision rate were seen between groups (p = 0.004) with lower revision rates seen where there was higher OUKA usage. The revision rate was 0.85%pa (95%CI 0.65 to 1.08) in the low-caseload (≤12 OUKA per year) and high-usage group (≥20% OUKA) and 0.94%pa (95%CI 0.69 to 1.23) in the high-caseload (>12 OUKA per year) and high-usage (≥20% OUKA) group compared to 1.76%pa (95%CI 1.21 to 2.41) in the low-caseload (≤12 OUKA per year) and low-usage group (<20% OUKA) and 1.58%pa (95%CI 0.57 to 3.05) in the high-caseload (>12 OUKA per year) and low-usage (<20% OUKA) group. (With the Palacios *et al.* study included the revision rate in the low-caseload, high-usage group was 0.32%pa (95%CI 0.16 to 0.52)) (**Figure 2.8**).

Significant differences in the revision rate for lateral compartment disease progression (p = 0.002), unexplained pain (p = 0.01) and aseptic loosening (p = 0.001) were observed with the lowest revision rates seen in the high-caseload high-usage series. No difference in annual revision rate (p = 0.71) or absolute risk of revision (p = 0.71) for bearing dislocation was detected (**Table 2.6**).

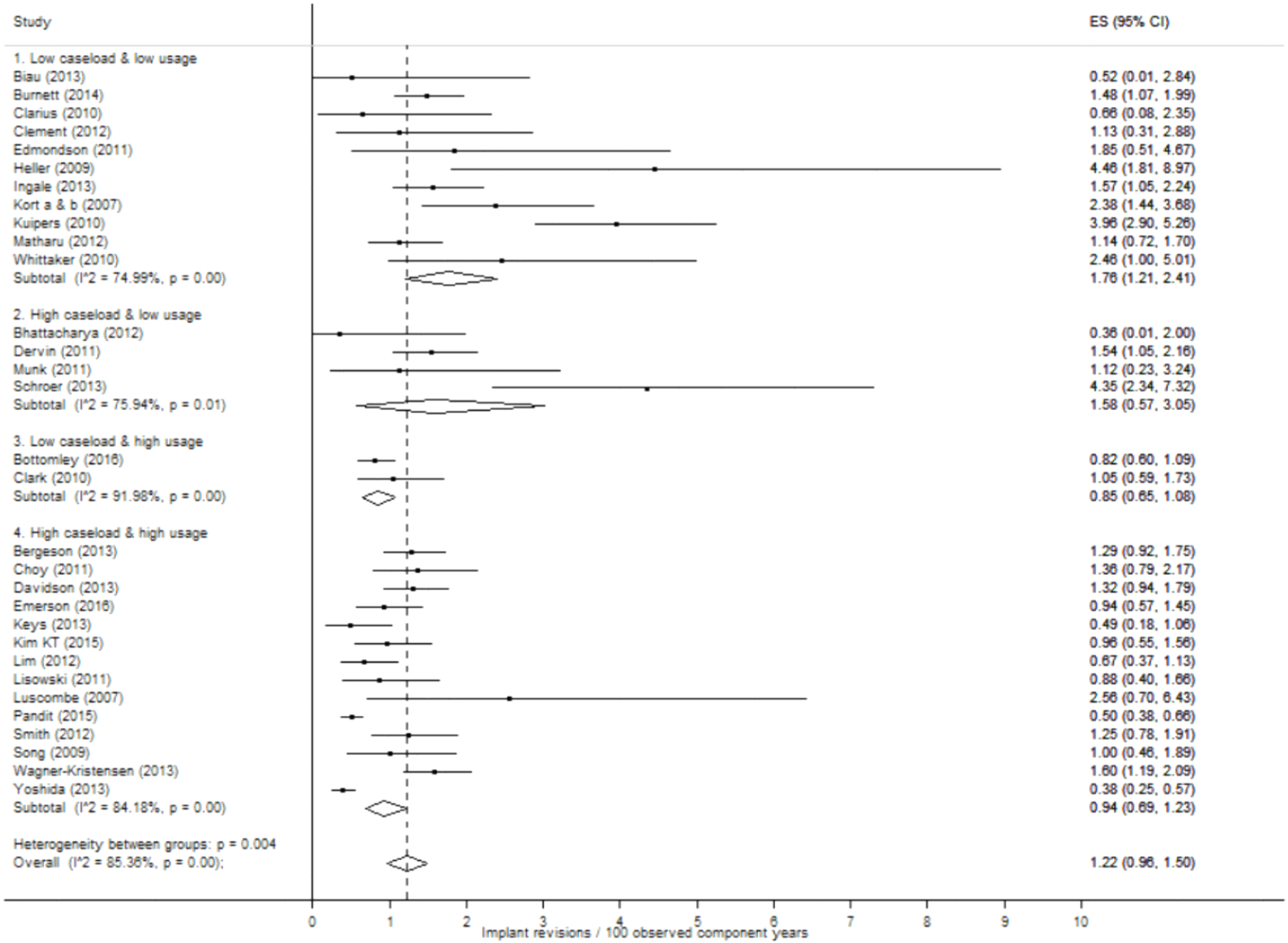


Figure 2.8: Outcomes by combined surgical caseload and surgical usage of Phase 3 OUKA.

2.2.5 Discussion

In published series of the cemented Phase 3 medial OUKA (46 studies, 12,520 knees followed-up for 67,128 observed component years) the all cause revision rate was 1.21%pa (95%CI 0.97 to 1.47) falling to 0.63%pa (95%CI 0.46 to 0.83) in series with a mean follow-up of ten-years or greater (**Table 2.7**). Aseptic loosening, progression of disease in the lateral compartment, bearing dislocation, and unexplained pain represented the predominant failure mechanisms with revisions for patello-femoral joint disease (7 cases) and polyethylene wear (1 case) being exceedingly rare (<0.1%).

Revision rates decreased with both increasing surgeon caseload (OUKA per surgeon per year) and usage (percentage of primary knee arthroplasty that are OUKA). It is well recognised, and expected, that revision rate should decrease with increasing caseload[135]. It is however counterintuitive that it should decrease with increasing usage. Kozinn & Scott described what they considered ideal indications for a UKA, and subsequent studies have suggested that these are satisfied in about 5% of knee arthroplasty[50,84,186]. Kozinn and Scott also suggested that with broader indications, and thus increased usage, the revision rate would increase. This meta-analysis is the first review of clinical studies that has shown that this is not the case, supporting analysis of NJR data, and concluding that the revision rate decreases with increased usage, at least for OUKA[136].

Overall usage was found to be more important than caseload. Whilst usage was found to be independent of caseload, with high-usage surgeons achieving equally good results regardless of their overall caseload, caseload was not found to be independent of usage. In low-usage surgeons the annual revision rate was almost double that of high-usage surgeons regardless of whether surgeons implanted a high number of OUKA (high-caseload) or not (low-caseload).

As low-usage surgeons have a high revision rate, regardless of whether they have a low or high-caseload, the reasons for this are likely related to their indications for OUKA, or possibly for revision of OUKA, rather than their surgical technique. As we have established, lateral compartment disease

progression remains the predominant failure mechanism for OUKA, even when implanted for correct indications, and as such surgeons may alter their practice to reduce the risk of this complication. Therefore surgeons, trying to mitigate the risk of lateral compartment disease progression may choose to only implant OUKA if the retained compartments are pristine, which usually only occurs if there is early arthritis with PTCL in the medial compartment. It is well known that patients with PTCL do not do well with TKA, so OUKA may seem to be an ideal solution, as these patients tend to be young and active. However, as discussed in **Chapter 1** (**1.2.3.4 Partial-thickness cartilage loss**), and will be further explored in **Chapter 4**, previous reports have suggested patients with PTCL also do badly with OUKA and have worse outcomes compared to those with bone on bone AMOA[53,68]. Whilst we can only speculate as to the reasons for failure, this study found that low-usage OUKA surgeons operated on younger patients, and had revision rates for unexplained pain that were ten-fold higher than high-usage surgeons, with both these features being associated with operating on knees with PTCL. Recent work has highlighted that around a quarter of young patients (<60 years) undergoing arthroplasty are not suitable for OUKA due to PTCL and it may be that low-usage surgeons are performing OUKA in these patients and achieving poor results as a consequence[187]. Further work is required to confirm this finding, as well as to clarify the results of registry studies which have reported higher failure rates of OUKA in young patients, a finding not observed in cases series performed for bone on bone arthritis[54,60,188].

A final consideration is that, the higher revision rate in low-usage surgeons may relate to their indications for revision. In this study low-usage surgeons had a higher revision rate due to aseptic loosening compared to high-usage surgeons. Aseptic loosening is typically identified radiographically by the presence of radiolucent lines around the prosthesis[189]. Following OUKA two types of tibial radiolucency are recognised: physiological and pathological. Physiological radiolucencies are common, occurring in two thirds of cases, and are non-progressive, narrow (<2 mm) with well-defined sclerotic margins. As we have established earlier in this Chapter they are not

related to worse outcomes, nor indicative or predictive of loosening, nor are they a source of pain[124,128,178]. In contrast pathological radiolucencies are rare, progressive and poorly-defined and are suggestive of loosening or infection. It is likely that surgeons who have not learnt the correct indications for OUKA, and are therefore low-usage surgeons, have also not understood the relevance of these radiolucencies, and may be doing unnecessary revisions for physiological radiolucencies[181].

Whilst this study found a relationship between caseload and implant survival it was only the high-usage surgeons, >24 OUKA per year, who appeared to have a lower failure rate (**Figure 2.6**). This result is different from previous studies which have reported a progressive decrease in failure rate with increasing caseload with revision rates in high-caseload series typically half to a quarter of that seen in low-caseload series[135,190,191]. One reason this relationship may not have been seen in this study is that in almost a quarter of the high-caseload studies included in this analysis were low-usage (4 of 17 studies), which we found to be associated with higher failure rate[89,149,160,181] . In cross-sectional studies, because of the relationship between caseload and usage, we would expect the number of high-volume and low-usage OUKA surgeons to be lower than seen in this series[135]. As such usage may be a confounding variable that has not been accounted for in previous reports.

In series reporting the long-term outcomes, mean follow-up of ten-years or greater, of OUKA the survival rate was 94% (95%CI 92 to 95) (**Table 2.7**). This result is better than the ten-year survival rate (88%; 95%CI 85 to 90) extrapolated from the annual revision rate for all series, which have, on average a shorter follow-up. One reason for this is that the annual revision rate tends to overestimate the long-term failure rate, particularly in studies with a high incidence of early failures and a short duration of follow-up. This is relevant to this study: firstly because with OUKA bearing dislocation occurs early, and secondly because many of the included studies represent the learning curve of the surgeons who may have more revisions during this period. However, the main reason why the revision rate of the ten-year series is lower than all series combined is that all the ten-year

series were from high-usage surgeons, whereas the other series came from a mixture of low and high-usage surgeons with low-usage surgeons tending to get worse results.

There are limitations of this study: firstly there may be publication bias where extremes of results, both positive and negative, are more likely to get published. Secondly surgeons may over or understate their OUKA caseload and usage representing a risk of recall bias. Thirdly, due to the low number of patients in the low caseload and low usage groups, and the low event rates in the high caseload and high usage groups, these results must be interpreted cautiously due to the methodological issues associated with meta-analysis in these scenarios. Finally, this study is based on revision rate as a marker of outcome, as, due to limited information provided in published series it was not possible to evaluate functional outcomes, nor radiological failures, which are equally critical in evaluating the outcomes of treatment.

2.2.6 Conclusions

The results of this meta-analysis demonstrate that globally the results of OUKA are variable with the annual revision rate varying from 0%pa to 4.35%pa, mean 1.21%pa (95%CI 0.97 to 1.47). Overall aseptic loosening, progression of arthritis in the retained lateral compartment, bearing dislocation, and unexplained pain were the predominant failure mechanisms with revision for PFJ problems and polyethylene wear exceedingly rare (<0.1%).

Both increasing caseload and usage were associated with decreasing revision rate with the lowest revision rates achieved with a caseload >24 OUKA/year (0.88%pa, 95%CI 0.63 to 1.61) and usage >30% (0.69%pa, 95%CI 0.50-0.90). Usage appeared more important than caseload as with high-usage (≥20%) the revision rate was low, whether the caseload was high (>12OUKA per year) or low (≤12OUKA per year), 0.94%pa (95%CI 0.69 to 1.23) and 0.85%pa (95%CI 0.65 to 1.08) respectively; whereas with low-usage (<20%) the revision rate was high, whether the caseload was high or low.

(1.58%pa, 95%CI 0.57 to 3.05 and 1.76%pa, 95%CI 1.21 to 2.41). This finding suggests that that indications for OUKA, which is reflected by usage, is likely a major determinant of outcomes following this procedure.

Where surgeons performed OUKA in a high-proportion of patients excellent long-term results were seen. In series with mean follow-up of ten-years or more the revision rate was 0.63%pa (95%CI 0.46 to 0.83), which equates to a ten-year survival of 94% (95%CI 92% to 95%).

The results of this study suggest that to achieve optimum outcomes OUKA should be performed in a high proportion of a surgeon's practice. Whilst there were no studies available for very low-caseload surgeons (<6 OUKA per year), and as such we cannot recommend that surgeons do such small numbers, the clinical relevance of this study is that it suggests that surgeons who perform a low number of knee arthroplasties can still achieve good results provided that OUKA is performed in an adequate proportion (≥20%). The results suggest that if they do this then they can expect to achieve results similar to those of the long-term series, which all had high-usage (>20%) and an average ten-year survival of 94%.

2.3 Summary

This chapter has demonstrated that the good results seen by the developer surgeons can be replicated at other centres provided broad indications, as reflected by high-usage of OUKA, are used. Differences in patient demographics (younger age at operation) and failure mechanism (unexplained pain and aseptic loosening) suggest that low-usage surgeons may be performing, or revising, OUKA for different indications compared to high-usage surgeons.

If OUKA fails it is predominantly due to progression of arthritis in the retained lateral compartment, bearing dislocation and unexplained pain and revision for PFJ problems. Failure due to polyethylene wear is exceedingly rare both in the developer series and through the global experience.

The next two chapters will explore in more detail patient factors (**Chapter 3**) and disease factors (**Chapter 4**) affecting the outcome of OUKA.

Chapter 3 Patient factors affecting outcome of OUKA

3.1 Introduction

As has been established in **Chapter 2** the global experience with OUKA (**2.2 Global Experience: Meta-analysis of published series of OUKA**) is more variable than that seen in the developer series (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**). To optimise outcomes following UKA, various authors have published evidence that certain patient demographic criteria are associated with superior outcomes[50,84,186]. The most well-known of these is the guidance by Kozinn and Scott who, aware of the more variable outcomes, advised that UKA should not be performed in patients aged younger than 60 years, who weigh 82kg (180lb) or more or who have high levels of activity. In particular Kozinn and Scott stated that UKA should not be performed in patients who meet all of these criteria, and are male, as their experience was that these patients had particularly poor outcomes[50,51].

Using the developer series, where patient selection criteria were standardised and the decision to perform OUKA based on the pathoanatomy of the disease this chapter will evaluate whether applying these previously published patient factor contraindications influences ten-year functional outcomes and fifteen-year implant survival.

[*] This chapter has been published as "Evidence-Based Indications for Mobile-Bearing Unicompartmental Knee Arthroplasty in a Consecutive Cohort of Thousand Knees" Journal of Arthroplasty (2016) (**Appendix 1**).

3.2 Patients and methods

Using the developer series of 1000 consecutive OUKA reported in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**) patients were classified into subgroups based on each of the previously proposed patient factor contraindications to OUKA: age younger than 60 years, weight 82kg (180lb) or greater and high levels of activity. High activity level was classified as a Tegner Activity Scale (TAS) of five or above at any stage after surgery as this incorporates: heavy labour (e.g. building/forestry) and/or competitive sports (e.g. cycling/cross-country skiing) and/or recreational sports (jogging on uneven ground at least twice a week). In addition, the outcomes of OUKA in young (age <60 years) males, weighing 82kg or more with a high activity level was compared to the outcomes of knees not in this group.

3.3 Statistical methods

A power calculation was performed using the minimally clinically important difference reported for OKS[192]. Using the Altman nomogram for a power of 80% at a significance level of 0.05 and using a standard deviation of 8, a sample size of 80 patients is required to detect a clinically important difference between groups[193]. Where there were imbalances between the numbers of knees in each group it was established that a minimum of 20 knees in the smaller cohort was required for the study to have adequate power[86].

Functional outcomes and implant survival were compared between groups based on the presence, or absence, of each of the individual published patient factor contraindications: age younger than 60 years, weight 82kg (180lb) or greater and high levels of activity. In addition a comparison was made between knees with any contraindication and those with none and between young (age <60 years) males, weighing 82kg or more with a high activity level and those not in this group.

Functional outcomes were compared at ten-years using non-parametric tests (Kruskal-Wallis). Differences in categorical functional outcomes were assessed using a Chi-Squared test. For Oxford Knee Score (OKS) a difference of four points or more was considered clinically relevant for differences between groups (minimal important difference (MID)) and individual improvements over time (minimal detectable change (MDC))[194]. Survival was assessed as outlined previously (**Chapter 2: 2.1.3 Statistical methods**). Statistical significance was defined as $p < 0.05$.

3.4 Results

3.4.1 Age

A quarter of the OUKA (25%, 245 knees) were implanted in patients aged under 60 years, with this group having a mean age of 54 years (range 33 to 60). Pre-operatively no difference in OKS ($p = 0.47$), American Knee Society Objective (AKSS-O) ($p = 0.31$), or Functional score (AKSS-F) ($p = 0.07$), or Tegner Activity Scale (TAS) ($p = 0.07$) was seen between those aged under 60 and those aged 60 years and older.

At ten-year follow-up patients aged under 60 years at the time of operation had significantly better OKS ($p = 0.03$), AKSS-F ($p < 0.001$) and TAS ($p < 0.001$) than those patients who did not meet these criteria (**Figure 3.1** and **Table 3.1**). No difference in AKSS-O ($p = 0.86$) was seen. No difference in OKS categorical functional outcomes was observed between groups ($p = 0.33$) with 82% of knees in patients aged under 60 obtaining good or excellent results, compared to 78% in patients aged 60 years or over. No difference in time to failure, mechanism of failure or fifteen-year implant survival was seen between groups (**Figure 3.2** and **Table 3.2**).

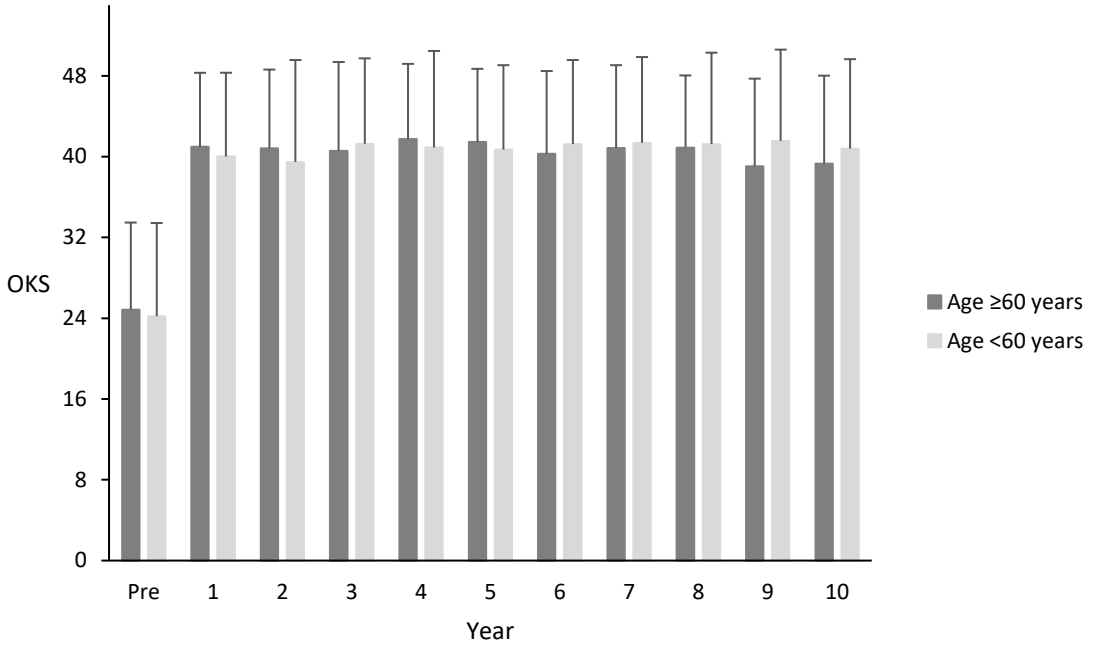


Figure 3.1: Bar Chart showing mean OKS by year (SD) of follow-up based on age ≥60 years versus age <60 years.

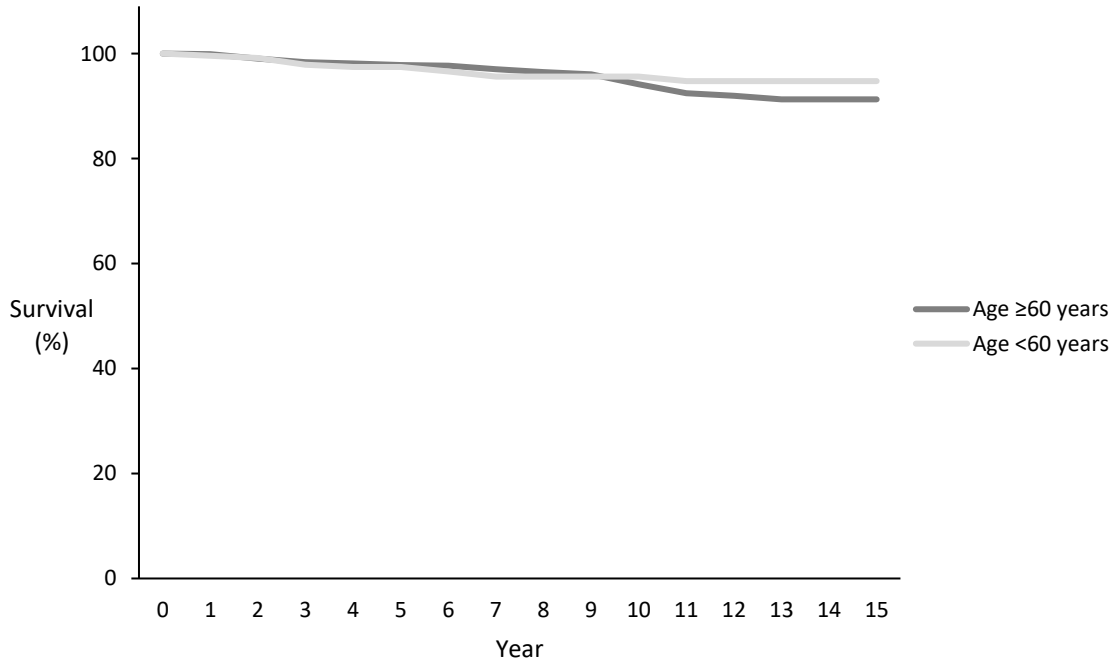


Figure 3.2: Survival analysis based on age ≥60 years versus age <60 years.

3.4.2 Weight

Almost half of the OUKA (45%, 449 knees) were implanted in patients who weighed 82kg or greater. The mean weight in this group was 95kg (range 82 to 185). Pre-operatively no difference in OKS (p = 0.74), AKSS-O (p = 0.73) or AKSS-F (p = 0.12) was seen between groups with the pre-operative TAS was found to be significantly higher in those who weighed 82kg or greater (2.5 (SD1) versus 2.2 (SD1), p = 0.01).

At ten-year follow-up no difference in OKS (p = 0.87), AKSS-O (p = 0.30) or AKSS-F (p = 0.13) was seen between those who weighed 82kg or greater and those that did not with the TAS (p < 0.001) remaining higher in those than those patients who weighed 82kg or greater (**Figure 3.3** and **Table 3.1**). No difference in OKS categorical functional outcomes between groups was observed at ten-years (p = 0.20) with 76% of knees in patients weighing 82kg or greater obtaining good or excellent results compared to 81% in those patients who weighed under 82kg.

No difference in time to failure, mechanism of failure or fifteen-year implant survival was seen between groups (**Figure 3.4** and **Table 3.1**).

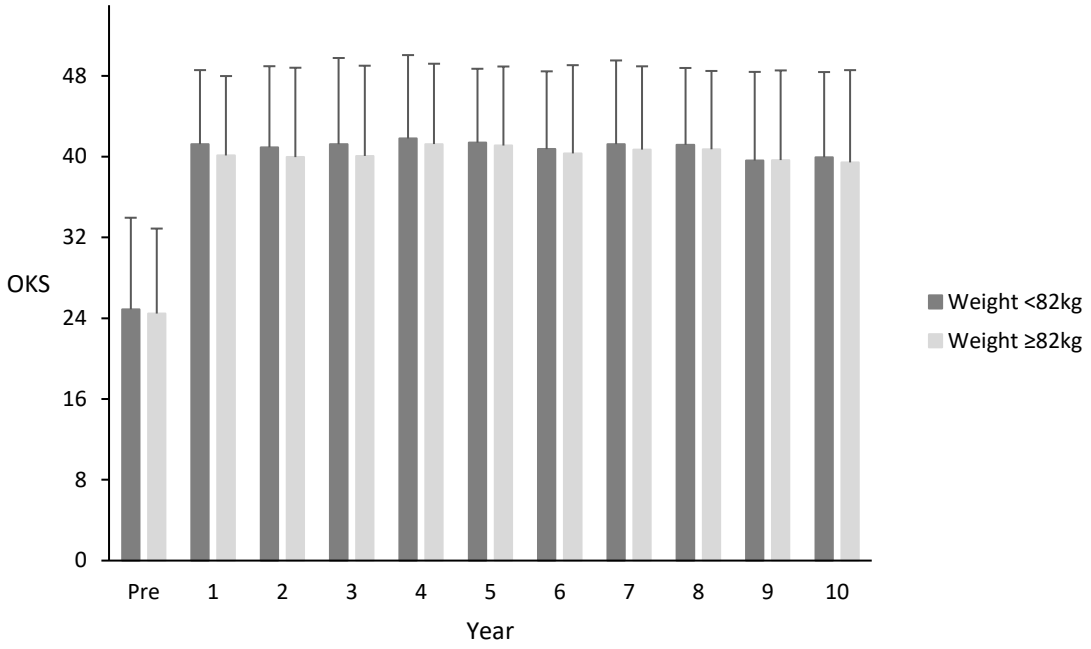


Figure 3.3: Bar Chart showing mean OKS by year (SD) of follow-up based on weight <82kg versus weight ≥82kg.

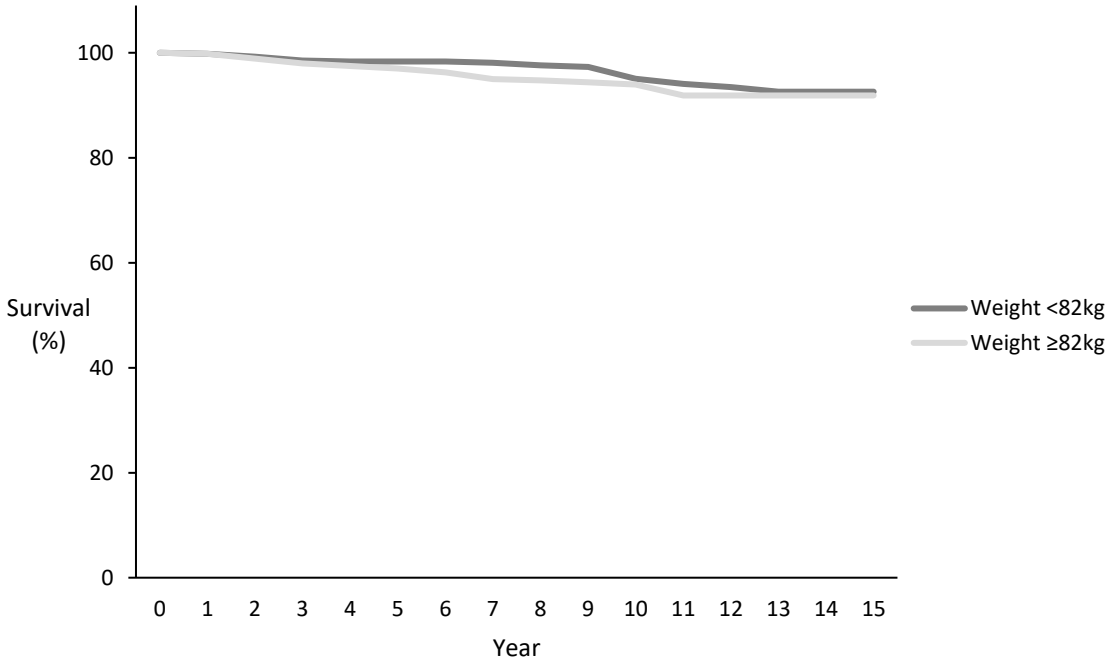


Figure 3.4: Survival analysis based on weight <82kg versus weight ≥82kg.

3.4.3 Activity Level

Ten-percent of the OUKA in this series (96 knees) were implanted in patients who reported high activity, a TAS of ≥5, postoperatively. The mean TAS in the high activity group was 5.4 (range 5 to 8) with pre-operatively the high activity group reporting significantly higher OKS (27.0 (SD8) versus 24.4 (SD9), $p = 0.02$), AKSS-F (75.8 (SD18) versus 68.5 (SD17), $p < 0.001$) and TAS (3.3 (SD1) versus 2.2 (SD1), $p < 0.001$) with no difference in AKSS-O ($p = 0.34$) between groups detected.

At ten-year follow-up the high activity group had better OKS ($p < 0.001$), AKSS-F ($p < 0.001$) and TAS ($p < 0.001$), however no difference in AKSS-O ($p = 0.37$) scores were seen compared to those patients that did not report high activity (**Figure 3.5** and **Table 3.1**). High activity patients reported significantly better OKS categorical functional outcomes at ten-years (p=0.01) with 93% of knees in high activity patients reporting good or excellent results compared to 77% in patients not in this group.

No difference in time to failure, mechanism of failure, or fifteen-year implant survival was seen between groups (**Figure 3.6** and **Table 3.1**).

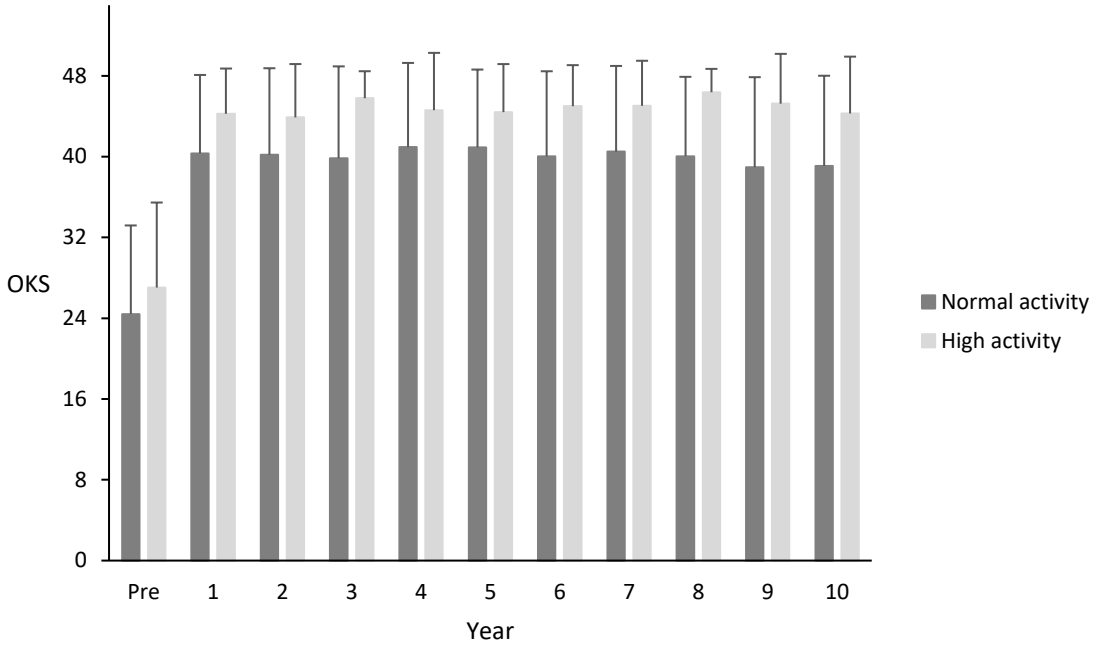


Figure 3.5: Bar Chart showing mean OKS by year (SD) of follow-up based on normal activity (TAS<5) versus high activity (TAS≥5).

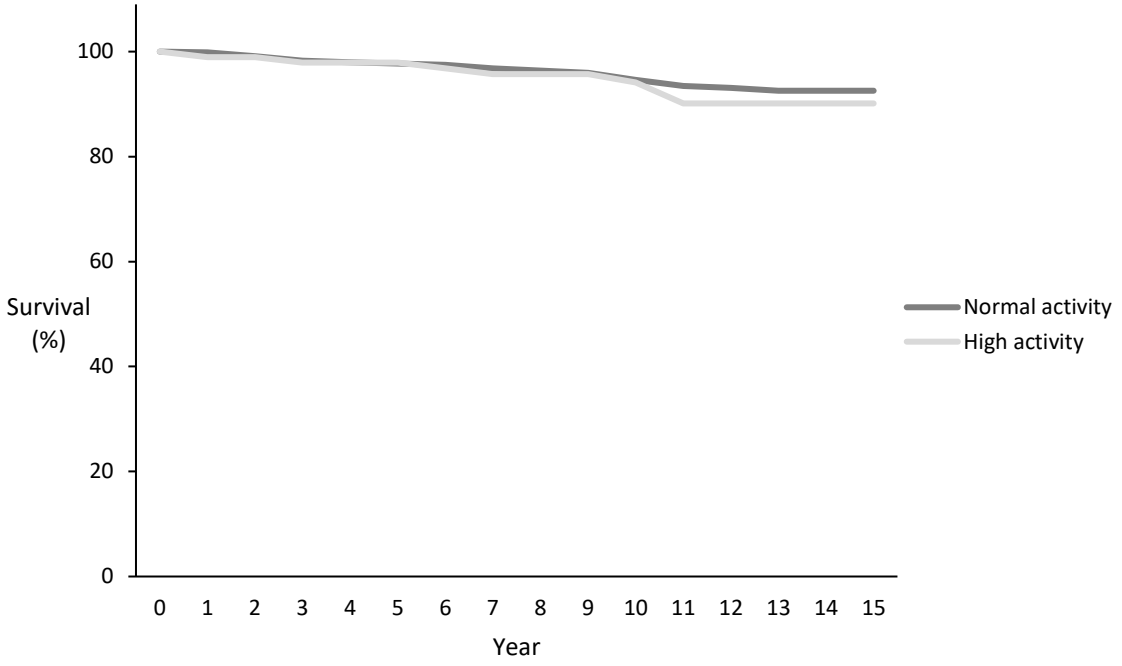


Figure 3.6: Survival analysis based on normal activity (TAS<5) versus high activity (TAS≥5).

3.4.4 Any contraindication

Almost 60% of OUKA in this series (57%, 565 knees) had one or more patient contraindication (age <60 years, weight ≥82kg, high activity (TAS≥5). 370 knees (37%) had one patient contraindication, 167 (17%) had two patient contraindications and 28 (3%) had all three patient contraindications. Pre-operatively no difference was seen in OKS ($p = 0.57$) and AKSS-O ($p = 0.82$) compared to knees not in this group however knees with patient contraindications had significantly higher pre-operative AKSS-F (70.8 (SD18) versus 67.2 (SD17), $p = 0.008$) and TAS (2.5 (SD1) versus 2.1 (SD1), $p < 0.001$).

At ten-years no difference was seen in OKS ($p = 0.12$) or AKSS-O ($p = 0.06$) between groups. Knees with patient contraindications reported significantly higher AKSS-F ($p < 0.001$), and TAS ($p < 0.001$) compared to knees not in this group (**Figure 3.7** and **Table 3.1**). No difference in OKS categorical functional outcomes was seen at ten-years between groups ($p = 0.79$) with 79% of knees with any of the patient contraindications obtaining good or excellent results, compared to 80% of knees without any patient contraindications.

No difference in time to failure, mechanism of failure, or fifteen-year implant survival was seen between groups (**Figure 3.8** and **Table 3.1**).

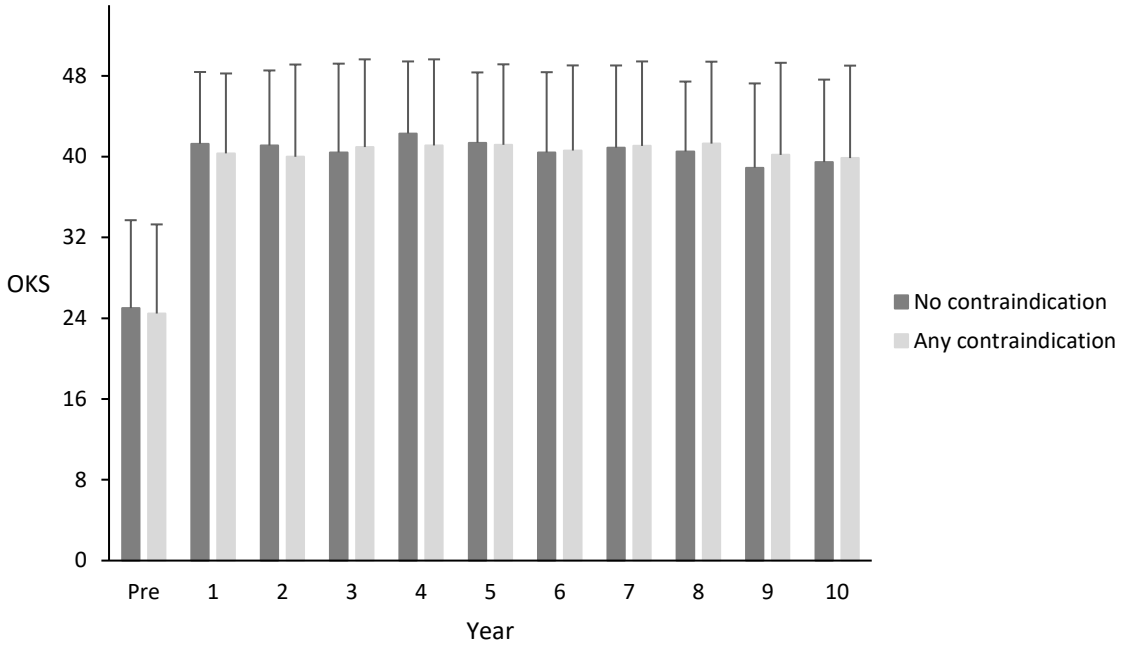


Figure 3.7: Bar Chart showing mean OKS by year (SD) of follow-up based on any patient factor contraindication.

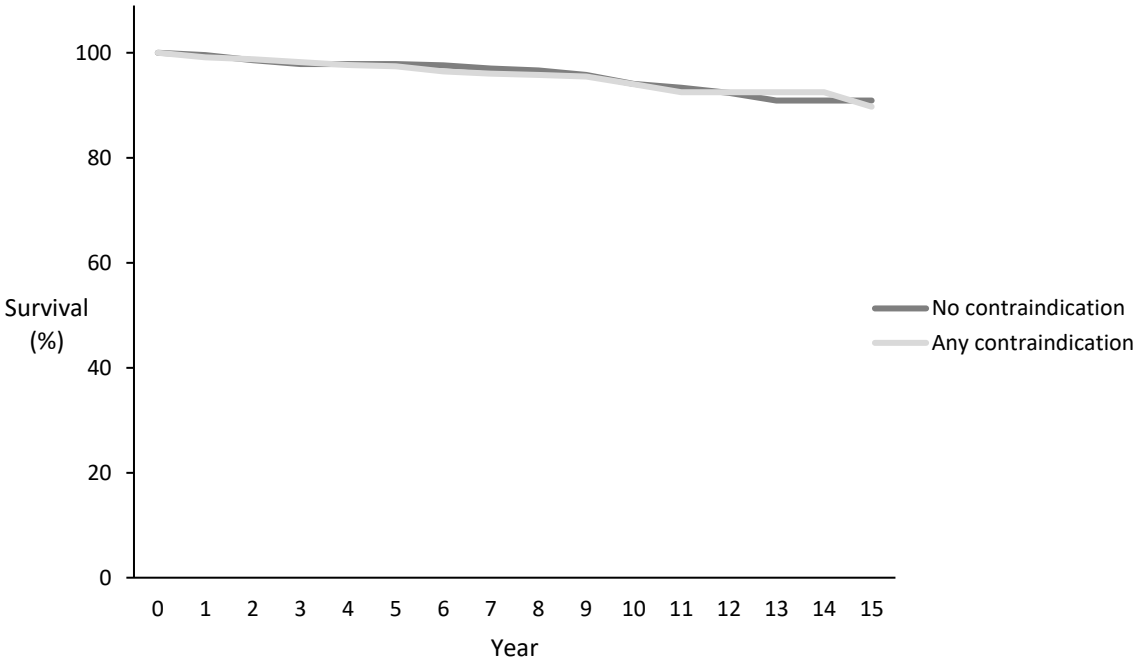


Figure 3.8: Survival analysis based on any patient factor contraindication.

3.4.5 Compound Assessment: Young, heavy, males with high activity levels

Three-percent of OUKA in this series (28 knees) were performed in young males (age <60) weighing 82kg or more with high activity levels. Pre-operatively this group reported higher OKS (29.7 (SD7) versus 24.5 (SD9), $p = 0.003$), AKSS-F (78.6 (SD15) versus 68.9 (SD18), $p = 0.02$), and TAS (3.4 (SD1) versus 2.3 (SD1), $p = 0.001$) than knees not in this group with no difference in AKSS-O ($p = 0.06$).

At ten-years young males weighing more than 82kg with high activity level reported significantly higher OKS ($p < 0.001$), AKSS-F ($p < 0.001$), and TAS ($p < 0.001$) compared to knees not in this group with no difference in AKSS-O ($p = 0.54$) seen (**Figure 3.9** and **Table 3.1**). No difference in OKS categorical functional outcomes was seen at ten-years between groups ($p = 0.29$) with 89% of knees in young males weighing more than 180lb with high activity level obtaining good or excellent results, compared to 79% of knees not in this group.

No difference in time to failure, mechanism of failure, or fifteen-year implant survival was seen between groups (**Figure 3.10** and **Table 3.1**).

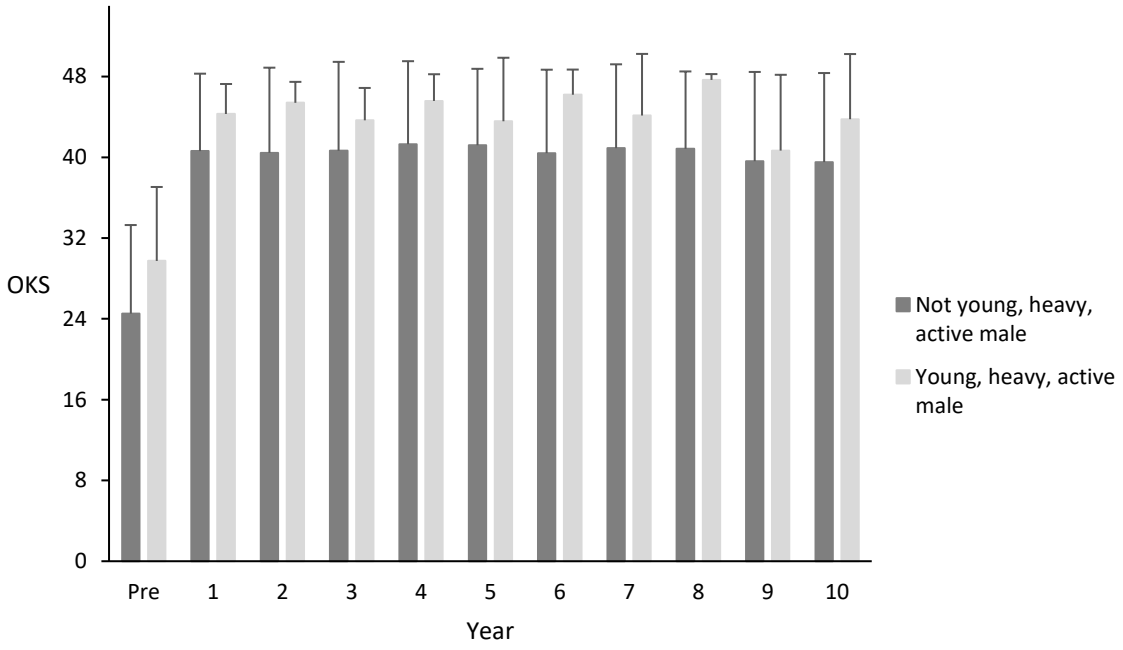


Figure 3.9: Bar Chart showing mean OKS by year (SD) of follow-up based on young, heavy, active males.

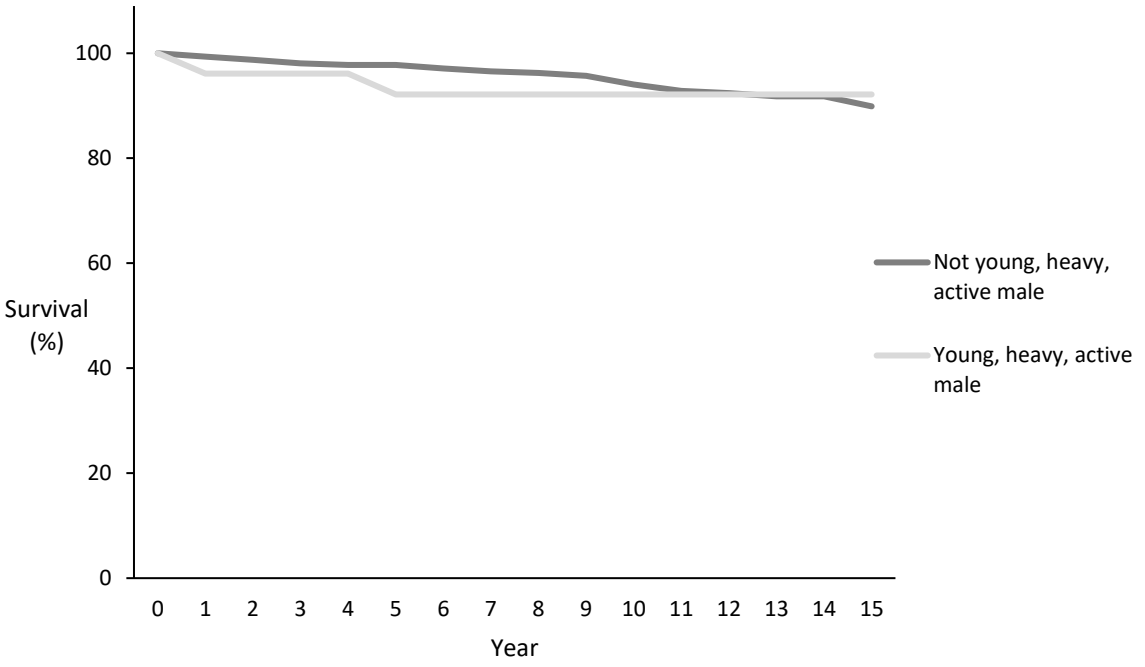


Figure 3.10: Survival analysis based on young, heavy, active males.

Table 3.1: Mean (SD) clinical outcome scores at ten-years and fifteen-year survival for the different subgroups.

Group	Number*	Follow-up Years (SD)	OKS (SD)	AKSS-O (SD)	AKSS-F (SD)	TAS (SD)	15 year survival % (95% CI)
Age (years)							
< 60	245	10.1 (3)	40.8 (9)	80.5 (15)	86.9 (18)	3.1 (1)	94.8 (85.8 – 100)
≥ 60	755	10.4 (3)	39.3 (9)	80.3 (15)	71.9 (22)	2.3 (1)	91.3 (84.4 – 98.2)
			***p*=0.03**	*p*=0.86	***p*<0.001**	***p*<0.001**	*p*=0.70
Weight (kg)							
≥ 82	449	10.4 (3)	39.4 (9)	81.3 (15)	77.4 (22)	2.7 (1)	91.9 (83.7 – 100)
< 82	551	10.2 (3)	39.9 (8)	79.3 (16)	74.6 (22)	2.3 (1)	92.6 (84.9 – 100)
			p=0.87	*p*=0.30	*p*=0.13	***p*<0.001**	*p*=0.16
Activity (TAS)							
≥ 5 (High)	96	10.5 (3)	44.3 (6)	78.2 (17)	95.0 (10)	3.9 (1)	90.1 (72.1 – 100)
< 5 (Normal)	904	10.3 (3)	39.1 (9)	80.7 (15)	73.4 (22)	2.3 (1)	92.5 (86.7 – 98.4)
			***p*<0.001**	*p*=0.37	*p*<**0.001**	***p*<0.001**	*p*=0.51
Any contraindication							
Present	565	10.3 (3)	39.9 (8)	81.5 (15)	79.5 (22)	2.8 (1)	89.7 (80.3 – 99.1)
Absent	435	10.3 (3)	39.5 (9)	78.2 (15)	70.6 (21)	2.1 (1)	90.9 (78.4 – 100)
			p=0.12	*p*=0.06	*p*<**0.001**	*p*<**0.001**	*p*=0.09
Compound Assessment							
Male, <60y, ≥82kg, high activity	28	10.7 (3)	44.2 (6)	79.9 (12)	96.3 (8)	4.1 (1)	92.2 (50.8 - 100)
Not male or >60y or <82kg or not high activity	972	10.3 (2)	39.5 (9)	80.4 (16)	75.0 (22)	2.4 (1)	89.9 (82.2 – 97.6)
			***p*<0.001**	*p*=0.54	*p*<**0.001**	***p*<0.001**	*p*=0.75

* Number at start

3.5 Discussion

Almost 60% (57%, 565 knees) of knees had one or more patient factor contraindications (age <60 years, weight ≥82kg, high activity (TAS≥5) to UKA according to the previously published literature. However, there was no evidence that these published patient factor contraindications should be applied to OUKA as at ten-year follow-up knees that would be considered contraindicated to UKA based on patient factors reported had significantly better AKSS-F and TAS scores compared to those knees considered ideal candidates. Furthermore, no difference in time to failure, mechanism of failure, or implant survival at fifteen-years was observed between the groups.

For each of the previously published patient factor contraindications to UKA the ten-year functional outcomes were equal, or superior, in those knees considered contraindicated compared to those knees considered ideal. Additionally for each of the contraindications no difference in implant survival at fifteen-years was seen compared to ideal candidates providing strong evidence that OUKA should not be restricted based on these patient factors.

One of the reasons that patient selection guidelines were introduced was that, based on the experience with fixed-bearing UKA, it was noted that some patient groups had poor outcomes[51]. One such group is young (age<60) males weighing 82kg or greater with a high activity level. In this series of OUKA we found this group to have better results than those of knees not in this group with no difference in implant survival at fifteen-years. These results suggest that OUKA should not be restricted in the same way as fixed-bearing designs and that OUKA may be preferable in this patient group.

As discussed in **Chapter 1** (**1.2.3 Patient Selection for Oxford Unicompartmental Knee Arthroplasty**) previous shorter term studies have also shown that patients treated with the OUKA that have these proposed patient factor contraindications have similar functional outcomes and

survival as those considered ideal[54,60]. This study has however shown that, when disease factors are standardised, patients with contraindications may have better results. Therefore applying the contraindications will worsen outcomes overall as OUKA will not be carried out in the patients who have the potential to attain best results from it.

During the study period around 70% of all primary knee arthroplasty performed were OUKA. This would have been reduced to around 30% if the previously described patient contraindications were used[84,186]. Additionally, further reductions in OUKA utilisation would be seen if patients were considered contraindicated based on other factors such as exposed bone at the PFJ and presence of anterior knee pain which have also been reported to affect outcomes and will be explored further in **Chapter 4**[87]. These findings may, in part as identified in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**), explain why low-usage surgeons have significantly worse outcomes compared to high-usage surgeons, however the differences in outcomes between groups are relatively minor, and unlikely to be of clinical significance. Additionally no difference in implant survival was seen between any of the groups examined meaning that it is likely that there are other factors responsible for the differences in outcomes seen between high and low-usage surgeons which was identified in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**).

There are some limitations to this work. Firstly the results presented are those of the developer surgeons and as such may not be achieved elsewhere. Secondly, as many patients achieved excellent scores following arthroplasty the outcome measures used may exhibit a ceiling effect preventing the detection of differences between groups at the higher end of function. To accommodate this additional scoring systems such as the OKS – Activity Participation Questionnaire (APQ), High-Activity Arthroplasty Score (HAAS) or Forgotten Joint Score could be used[195-197].

3.6 Summary

This chapter has identified that in OUKA implanted based on the pathoanatomy of disease using the recommended indications as described by Goodfellow *et al.* the previously published patient factor contraindications based on the patient age (<60 years), weight (≥82kg) and activity level (high activity) do not influence outcomes and as such they should not be used for patient selection[52]. Based on long-term evidence knees implanted in patients with these previously reported patient factor contraindications often actually did better than those without these factors and as such the contraindications proposed by Kozinn and Scott and others should not be applied to OUKA[50,52,84,186].

If patient factor contraindications were applied to the developer surgeon's series then there would be a decrease in the caseload, from 47 OUKA per surgeon per year to 20 OUKA per surgeon per year, and a decrease in usage, from 70% OUKA to 30% OUKA with both of these factors being identified in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**) as being associated with poor outcomes.

Chapter 4 Disease factors affecting outcome of OUKA

4.1 Introduction

In addition to the patient factors which were explored in **Chapter 3**, various disease factors have been reported to influence the outcomes of UKA. These include partial-thickness cartilage loss (PTCL) in the medial compartment, macroscopic anterior cruciate ligament (ACL) disease, lateral osteophytes and patellofemoral joint (PFJ) disease. This chapter explores whether these disease factors affect the outcomes of OUKA.

To evaluate whether PTCL influences functional outcomes and risk of reoperation and revision following OUKA a propensity score matched cohort study was performed comparing outcomes of OUKA in knees with PTCL matched with knees with full-thickness cartilage loss (FTCL) which were reported in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**). To evaluate whether macroscopic ACL damage, lateral osteophytes and PFJ disease influences functional outcomes and implant survival following OUKA the results of the developer series of 1000 consecutive Phase 3 OUKA reported in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**), where these factors were not considered a contraindication, were analysed based on the presence of these findings on pre-operative radiographs or at the time of surgery.

[*] This chapter has been published as four papers. "Unsatisfactory outcomes following unicompartmental knee replacement for partial thickness cartilage loss: a medium-term follow-up" Bone and Joint Journal (2017). "Unicompartmental Knee Replacement: Does the macroscopic status of the anterior cruciate ligament affect outcome?" Knee (2016). "Lateral osteophytes do not represent a contraindication to medial unicompartmental knee arthroplasty: a 15-year follow-up" Knee Surgery, Sports Traumatology, Arthroscopy (2017). "Pre-operative anterior knee pain and evidence of patellofemoral degeneration should not be considered contraindications to mobile-bearing UKR: a 15-year follow-up" Bone and Joint Journal (2017) (**Appendix 1**).

4.2 Patients and methods

4.2.1 Partial-thickness cartilage loss in the medial compartment

Our prospective database of consecutive patients undergoing medial Phase 3 OUKA via a minimally invasive approach by the developer surgeons was examined to identify knees that were found to have PTCL in the medial compartment at the time of operation (**Figure 4.1**). OUKA implanted for spontaneous osteonecrosis of the knee (SONK), based on radiological or histological diagnosis, or that did not fulfil other criteria for OUKA as stated by Goodfellow *et al.* were excluded from the analysis[52]. Between November 2002 and November 2014, 94 OUKA (90 patients) were identified with PTCL on the femur (18 knees), tibia (63 knees) or both femur and tibia (13 knees) in the medial compartment at the time of operation.

This cohort of patients was matched, 1:2, using propensity score matching based on age, gender and pre-operative OKS to knees with FTCL AMOA identified from the 1000 OUKA cohort reported in **Chapter 2**[178]. Independent follow-up was as described previously (**Chapter 2**: **2.1.2 Patients and methods**).

Functional outcomes were assessed in knees with FTCL and PTCL pre-operatively and at one, two and five-years postoperatively using absolute, improvement from baseline and categorical functional outcome measures as outlined in **Chapter 2: 2.1.2 Patients and methods.** Subgroup analysis was performed based on the location of the partial-thickness disease. To assess for the impact of time from surgery on functional outcome following OUKA in knees with FTCL and PTCL a Friedman Test was performed. Survival analysis, based on reoperation and implant revision was performed as previously (**Chapter 2: 2.1.2 Patients and methods**).

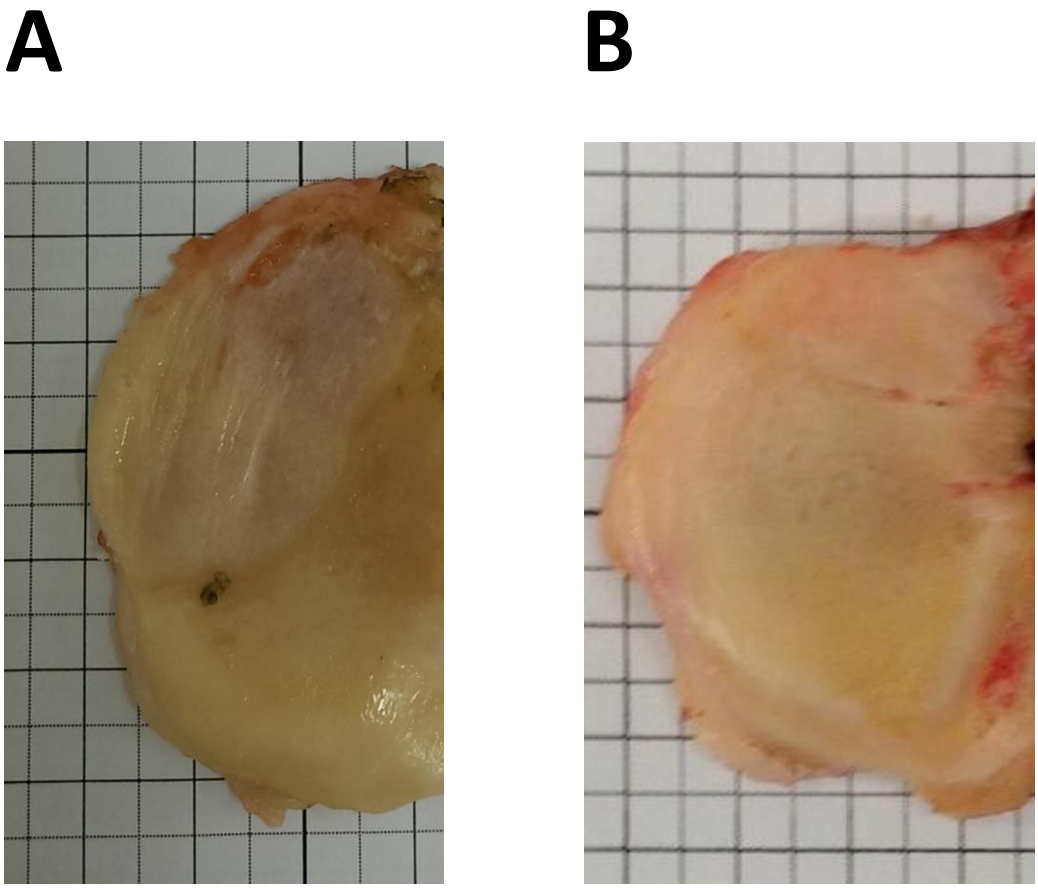


Figure 4.1: Tibial plateau with (A) full-thickness cartilage loss anteromedial osteoarthritis at operation and tibial plateau with (B) partial-thickness cartilage loss at operation.

4.2.1.1 MRI sub-study of patients with partial-thickness medial compartment disease

As MRI is increasingly being used in the workup for patients with radiographic PTCL in the medial compartment an MRI sub-study was performed on knees with PTCL. Of the 94 OUKA identified with PTCL 36 knees (36 patients) had undergone MRI prior to OUKA.

MRI scans were assessed for evidence of FTCL in the medial compartment, the presence of bone-marrow oedema, which has been associated with FTCL, in the medial compartment, evidence of synovitis and the presence of a moderate to large suprapatellar effusion using the methodology and criteria outlined by Hunter *et al.* [198,199]. MRI scans were assessed by an experienced musculoskeletal radiology consultant who was blinded and given no clinical information about the patients.

4.2.2 Macroscopic status of the anterior cruciate ligament

The macroscopic status of the ACL was recorded in the first 1000 consecutive cemented medial Phase 3 OUKA presented in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**). In this series OUKA was performed where the ACL was considered functionally normal, and not friable and fragmented or absent. The macroscopic status of the ACL was classified as, normal, or having synovial damage or longitudinal splits[200]. Data on the ACL status was available in 820 knees.

Data was assessed to see if there was a relationship between macroscopic ACL status and patient demographics. A correlation analysis was performed to assess whether there was an association between macroscopic ACL status and size of medial compartment tibial lesion as well as functional outcomes at ten-years and implant survival at fifteen-years.

4.2.3 Lateral osteophytes

Our prospective database of the first 1000 consecutive cemented Phase 3 medial OUKA presented in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**) was searched to identify knees with available pre-operative radiographs. In this series lateral osteophytes were not considered a contraindication[8,52,201].

Lateral osteophytes were assessed using the Osteoarthritis Research Society International (OARSI) Classification system by an assessor blinded to the outcome of treatment. The OARSI classification system is an atlas-based grading system ranging from Grade 0 (no osteophyte) to Grade 3 (large osteophyte)[202]. The lateral compartment was scored based on the largest osteophytes observed, be that on the tibia or femur. Radiographs were scored by myself with 20% of randomly chosen radiographs scored by Mr R Choudhary to allow for assessment of inter and intraobserver reliability.

The primary analysis compared outcomes in knees with no lateral osteophytes (OARSI Grade 0), with knees with lateral osteophytes (OARSI Grades 1 to 3). Subgroup analysis was used to compare the outcomes of those in those knees with no lateral osteophytes and those with OARSI Grade 3 osteophytes. Patient demographics, disease pattern, baseline functional performance, ten-year functional performance and improvement from baseline to ten-year functional performance were assessed. Implant survival was assessed at fifteen-years.

4.2.4 Patellofemoral joint disease

The influence of PFJ disease on the outcomes of OUKA was assessed with respect to intra-operative, radiological and clinical findings.

4.2.4.1 Intra-operative assessment

The status of PFJ and trochlea was assessed intra-operatively in the first 1000 consecutive cemented Phase 3 medial OUKA presented in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**). In this series OUKA was performed independent of the status of the PFJ. With the exception of cases of bone loss with grooving to the lateral patella facet, which was considered a contraindicated for OUKA, the location of pre-operative knee pain and/or presence of anterior knee pain was not considered a contraindication[52].

Scoring of the PFJ was performed intra-operatively with the medial and lateral patella facets as well as trochlea scored according to the size and depth of damage: No damage, superficial, focal (≤2cm^2) FTCL and extensive (>2cm^2) FTCL[186]. Independent follow-up was as described previously (**Chapter 2: 2.1.2 Patients and Methods**).

A correlation analysis was performed to assess whether there was an association between degree of cartilage loss at operation at the medial and lateral patella facets and trochlea and functional outcomes at ten-years. To assess the impact of full-thickness cartilage loss at different sites within the PFJ knees were grouped into those with full-thickness cartilage loss and those without full-thickness cartilage loss based on the following groupings: any site within the PFJ, medial facet, lateral facet and trochlea.

In addition to the standard assessments of functional outcome and implant survival outlined in **Chapter 2: 2.1.2 Patients and Methods** independent analysis of Q12 of the OKS, 'In the last four

weeks could you walk down a flight of stairs', was performed as it provides further information on the function of the PFJ.

4.2.4.2 Radiographic assessment

In a subgroup of 100 knees (91 patients, January 2000 to September 2003) a detailed pre-operative radiographic and pain assessment was performed.

For the radiographic assessment skyline radiographs, with the knee flexed to 30 degrees, were graded by an independent Consultant Musculoskeletal Radiologist, Dr SJ Ostlere, blinded to intra-operative findings and clinical outcome. The medial and lateral patella facets were scored using the Altman scoring system, which scores a range of arthritic characteristics, and the Ahlback grade, which assesses degrees of cartilage and bone loss. The Altman score assesses osteophytes, joint space narrowing, subchondral sclerosis and bone destruction, scoring each from 0 to 3, giving a maximum score of 12, with a higher score indicating increasing severity[203]. The Ahlback grade measures the severity of cartilage and bone loss: 0 normal, I joint space narrowing, II joint space obliteration, III bone destruction < 5 mm and IV bone destruction > 5 mm[204].

A correlation analysis was performed to assess whether there was an association between Altman score and functional outcomes at last follow-up. To assess the impact of radiographic changes on outcome knees were sub-divided into groups divided based on their Altman and Ahlback scores. Using a broad definition of radiographic degenerative change within the PFJ knees were divided into those with an Altman score ≥2, considered to have evidence of degenerative change, and compared with those with an Altman Score of 0 or 1, considered to have no evidence of degenerative change. To assess the impact of radiographic structural changes within the PFJ, knees were divided into knees with evidence of cartilage and bone loss (joint space narrowing including joint space obliteration; Altman score ≥2) and compared to knees without these features. The

medial and lateral PFJ were considered separately with outcomes assessed using absolute functional outcomes at last follow-up as well improvement from baseline to last follow-up. Implant survival at ten-years was assessed.

4.2.4.3 Clinical assessment

In the same subgroup of 100 knees the presence and location of pre-operative pain was assessed by a physiotherapist, independent of the clinical team, who was blinded to radiographic findings. Pain was classified as medial, anterior, lateral or generalised with patients were grouped based on the presence or absence of anterior knee pain.

4.2.5 Statistical methods

To assess for differences in functional outcomes between groups non-parametric tests (Mann–Whitney U, Kruskal-Wallis) were performed. Categorical data was assessed using a Chi Squared Test and correlation analysis performed using a Spearman's Rank Test. Functional outcomes were assessed at ten-years and survival analysis performed at fifteen-year as previously stated (**Chapter 2: 2.1.2 Patients and methods**).

4.3 Results

4.3.1 Partial-thickness cartilage loss in the medial compartment

Overall patients with medial compartment PTCL (94 knees, 90 patients) were younger than patients with FTCL (64.1 years (SD 11) versus 67.0 years (SD 10); $p = 0.02$). No difference in gender ($p = 0.11$),

BMI (p = 0.23), macroscopic ACL status (p = 0.09) or pre-operative function assessed by OKS (p = 0.43), AKSS-O (p = 0.16), AKSS-F (p = 0.69) or TAS (p = 0.28) was seen between groups.

Following 1:2 matching based on age, gender and pre-operative OKS no differences in baseline patient characteristics was seen between groups (**Table 4.1**). With the exception of pre-operative TAS, which was higher in knees with partial-thickness lesions of the tibia compared to knees with partial-thickness lesions on both the femur and tibia (p = 0.02), no differences in pre-operative demographics were seen based on the location of the PTCL (femur, tibia or femur and tibia).

Follow-up data for the primary outcome measure, OKS, was available for 86% of knees at year one, 65% of knees at year two and 94% of knees at year five. No difference in patient demographics (age (p = 0.939), gender (p = 0.430), BMI (p = 0.915) or year one outcome scores (OKS (p = 0.86), AKSS-O (p = 0.96), AKSS-F (p = 0.99), TAS (p = 0.62)) was seen between those scores between those patients reporting five-year functional outcomes and those that did not.

Table 4.1: Pre-operative patient demographics and functional scores in matched knees with PTCL.

	Control Group (*n* = 188)	**All PTCL (*n* = 94)**	***p*-value**	**PTCL femur only (*n* = 18)**	**PTCL tibia only (*n* = 63)**	**PTCL both femur and tibia (*n* = 13)**	***p*-value**
Age (years) Mean (SD)	63.6 (10)	64.2 (11)	0.87	64.2 (14)	63.6 (11)	66.9 (10)	0.67
% female *n* (%)	104 (55%)	54 (57%)	0.73	10 (56%)	37 (59%)	7 (54%)	0.93
BMI Mean (SD)	29.7 (5)	29.1 (5)	0.58	29.4 (7)	29.2 (5)	28.6 (6)	0.66
ACL status *n* (%)							
Normal	116 (62%)	63 (67%)	0.74	9 (50%)	48 (76%)	6 (46%)	0.27
Synovial Damage	19 (10%)	8 (9%)		3 (17%)	4 (6%)	1 (8%)	
Longitudinal splits	18 (10%)	7 (7%)		1 (6%)	4 (6%)	2 (15%)	
Unknown	35 (18%)	16 (17%)		5 (28%)	7 (11%)	4 (31%)	
OKS (SD)	24.6 (8)	23.9 (8)	0.34	23.3 (5)	23.9 (7)	24.8 (7)	0.77
AKSS-O (SD)	52.2 (18)	45.3 (24)	0.16	38.0 (117)	47.6 (25)	45.3 (24)	0.24
AKSS-F (SD)	69.3 (18)	70.1 (16)	0.69	70.5 (14)	71.7 (17)	63.3 (17)	0.19
TAS (SD)	2.5 (1)	2.1 (1)	0.12	1.8 (0.4)	2.4 (1)	1.4 (1)	**0.03***

*post-hoc testing revealed that knees with partial-thickness lesions of the tibia had significantly better pre-operative TAS compared to knees with partial-thickness lesions on both the femur and tibia ($p = 0.02$). No difference was seen between other groups.

4.3.1.1 Year 1

At year one knees with PTCL in the medial compartment had significantly lower OKS (mean 37 (SD9) v 41 (SD8), $p < 0.001$) and AKSS-O (mean 80 (SD20) v 89 (SD11), $p = 0.007$) scores compared to those with medial compartment FTCL (**Table 4.2**). No difference in AKSS-F ($p = 0.08$) or TAS ($p=0.38$) was seen between groups. No difference in outcomes was detected based on the location of the PTCL (**Table 4.2**).

Compared to knees with FTCL the outcomes of knees with PTCL were more variable (**Figure 4.2**). Using OKS criteria at year one 25% (19 of 77 knees) of knees with PTCL reported poor or fair outcomes, almost double that of knees with FTCL (14%; 22 of 156 knees; $p = 0.049$) (**Figure 4.3**).

Compared to baseline score 22% (11 of 50 knees) of knees with PTCL failed to achieve clinically meaningful improvements in OKS of four points at one year compared to knees with FTCL in which 10% (12 of 115 knees; $p = 0.049$) failed to achieve clinically meaningful improvements in OKS.

Compared to patients with PTCL in the medial compartment who achieved good or excellent outcomes in the first year postoperatively, patients with PTCL who reported poor or fair outcomes were significantly younger (mean 59.2 years (SD14) v 65.9 years (SD10), $p = 0.04$) and had significantly worse pre-operative knee function, as assessed by a lower pre-operative OKS (mean 18.8 (SD8) v 25.2 (SD8), $p = 0.04$) and AKSS-F score (mean 60.0 (SD19) v 72.0 (SD16), $p = 0.05$). No difference in gender ($p = 0.87$), BMI ($p = 0.74$), ACL status ($p = 0.45$), location of PTCL ($p = 0.73$), AKSS-O ($p = 0.99$) or TAS ($p = 0.45$) was seen between groups.

Table 4.2: Functional outcomes following OUKA in knees with PTCL.

	Control Group (*n* = 188)	**All PTCL (*n* = 94)**	***p*-value**	**PTCL femur only (*n* = 18)**	**PTCL tibia only (*n* = 63)**	**PTCL both femur and tibia (*n* = 13)**	***p*-value**
Year 1							
OKS (SD)	40.9 (8)	37.0 (9)	**<0.001**	38.9 (8)	36.1 (10)	38.5 (8)	0.57
AKSS-O (SD)	88.8 (11)	79.7 (20)	**0.007**	84.2 (15)	78.0 (23)	82.1 (16)	0.94
AKSS-F (SD)	88.9 (15)	85.2 (17)	0.08	90.7 (15)	84.3 (18)	82.0 (11)	0.23
TAS (SD)	2.9 (1)	2.9 (1)	0.38	3.3 (1)	2.9 (1)	2.3 (1)	0.10
Year 2							
OKS (SD)	41.2 (8)	37.1 (11)	**0.02**	42.8 (3)	36.4 (11)	34.9 (12)	0.52
AKSS-O (SD)	88.2 (15)	76.7 (23)	**0.002**	90.0 (8)	73.5 (25)	82.6 (10)	0.29
AKSS-F (SD)	88.6 (15)	82.8 (19)	0.09	88.8 (16)	82.3 (20)	79.4 (17)	0.48
TAS (SD)	2.9 (1)	2.9 (1)	0.69	2.8 (1)	3.0 (1)	2.6 (1)	0.81
Year 5							
OKS (SD)	41.9 (6)	39.3 (8)	**0.05**	41.8 (6)	38.5 (8)	38.9 (10)	0.45
AKSS-O (SD)	83.7 (13)	78.2 (13)	**0.02**	82.9 (13.5)	77.2 (13)	76.4 (15)	0.44
AKSS-F (SD)	87.0 (16)	80.9 (16)	**0.01**	85.5 (13)	79.5 (15)	80.0 (23)	0.54
TAS (SD)	2.9 (1)	2.8 (1)	0.81	3.4 (1)	2.8 (1)	2.4 (1)	0.12

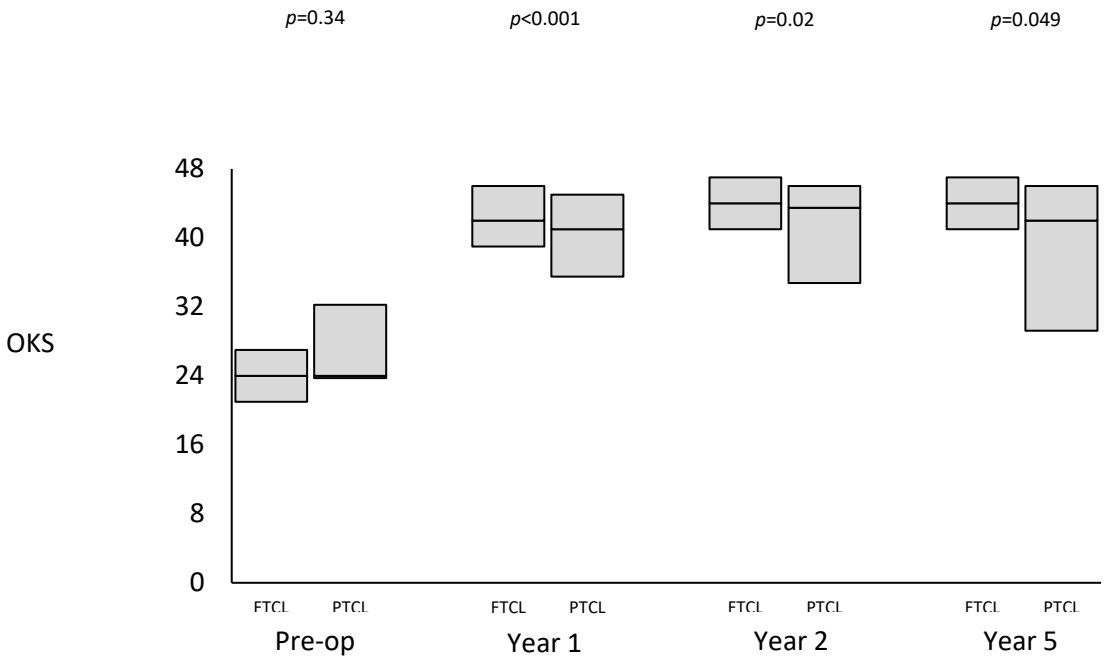
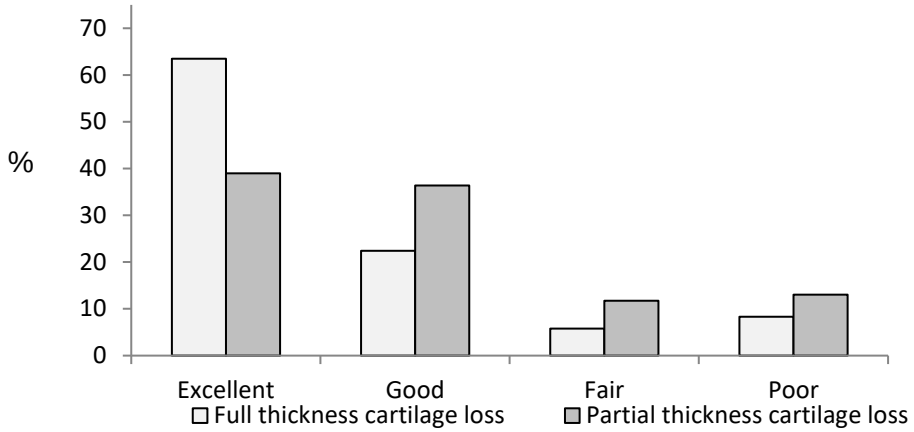
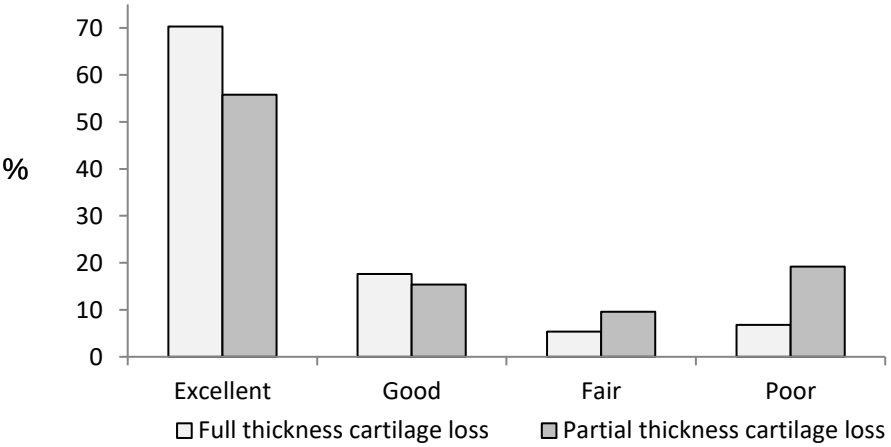


Figure 4.2: Box plot of OKS by year following OUKA in the setting of FTCL and PTCL in the medial compartment.

A: Year One



B: Year Two



C: Year Five

Figure 4.3: Categorical outcomes using OKS criteria at one (A), two (B) and five-years (C) following OUKA in the setting of FTCL and PTCL in the medial compartment. Significantly fewer patients with FTCL achieved fair or poor results at one (p = 0.049), two (p = 0.02) and five (p = 0.04) years.

4.3.1.2 Year 2

At year two postoperatively knees with PTCL in the medial compartment had significantly lower OKS (mean 37 (SD11) v 41 (SD8), p = 0.02) and AKSS-O (mean 77 (SD23) v 88 (SD15), p = 0.002) scores compared to those with medial compartment FTCL (**Table 4.2** and **Figure 4.2**). No difference in AKSS-F (p = 0.09) or TAS (p = 0.69) was seen between groups. No difference in outcomes was detected based on the location of the PTCL (**Table 4.3**).

Using OKS criteria at year two 29% (15 of 52 knees) of knees with PTCL reported poor or fair outcomes, double that of knees with FTCL (12%; 9 of 74 knees; p = 0.02) (**Figure 4.3**).

4.3.1.3 Year 5

At year five postoperatively knees with PTCL in the medial compartment had significantly lower OKS (mean 39 (SD8) v 42 (SD6), p = 0.049), AKSS-O (mean 78 (SD13) v 84 (SD13), p = 0.02) and AKSS-F (mean 81 (SD16) v 87 (SD16), p = 0.01) scores compared to those with medial compartment FTCL (**Table 4.2** and **Figure 4.2**). No difference in TAS (p = 0.81) was seen between groups. No difference in outcomes was detected based on the location of the PTCL (**Table 4.2**).

Using OKS criteria at year five 25% (13 of 51 knees) of knees with PTCL reported poor or fair outcomes, double that of knees with FTCL (12%; 17 of 139 knees; p = 0.04) (**Figure 4.3**).

A Friedman test, performed to see whether there was any change in functional scores between years one, two and five post-OUKA in the setting of PTCL, demonstrated no improvement in OKS (p = 0.10), AKSS-O (p = 0.68) or TAS (p = 0.78) and a significant worsening of AKSS-F (p = 0.004) during this period.

4.3.1.4 Implant survival and reoperations

In knees with PTCL in the medial compartment there were four revisions cases at a mean of 5.9 years (range 0.9 to 10.3). There were two cases of disease progression, one treated with lateral UKA (6.3 years) and one treated with TKA (10.3 years), one case of femoral component loosening secondary to bearing impingement (7.2 years) and one revision for unexplained pain (0.9 years). Two cases occurred in knees with partial-thickness femoral cartilage loss and two cases in partial-thickness tibial cartilage loss. No difference in implant survival was seen between knees with PTCL compared to those with FTCL in the medial compartment ($p = 0.06$).

In addition to the four revision cases, in knees with PTCL in the medial compartment there were 9 reoperations at a mean of 3.4 years (range 3 days to 9.9 years). There were seven arthroscopies performed for pain at a mean of 4.1 years (range 1.2 to 9.9 years) and two arthroscopic debridement's performed for suspected infection at a mean of 1 year (3 days and 2 years). One case occurred in a knee with partial-thickness femoral cartilage loss, six cases in knees with partial-thickness tibial cartilage loss and two cases in knees with both PTCL of the femur and tibia. At five-years the reoperation rate of knees with PTCL was 10.9% (95% CI 1.4 to 20.4%), almost three times that of knees with FTCL (3.9% (95% CI 1.1 to 6.7%); $p < 0.001$) (**Figure 4.4**).

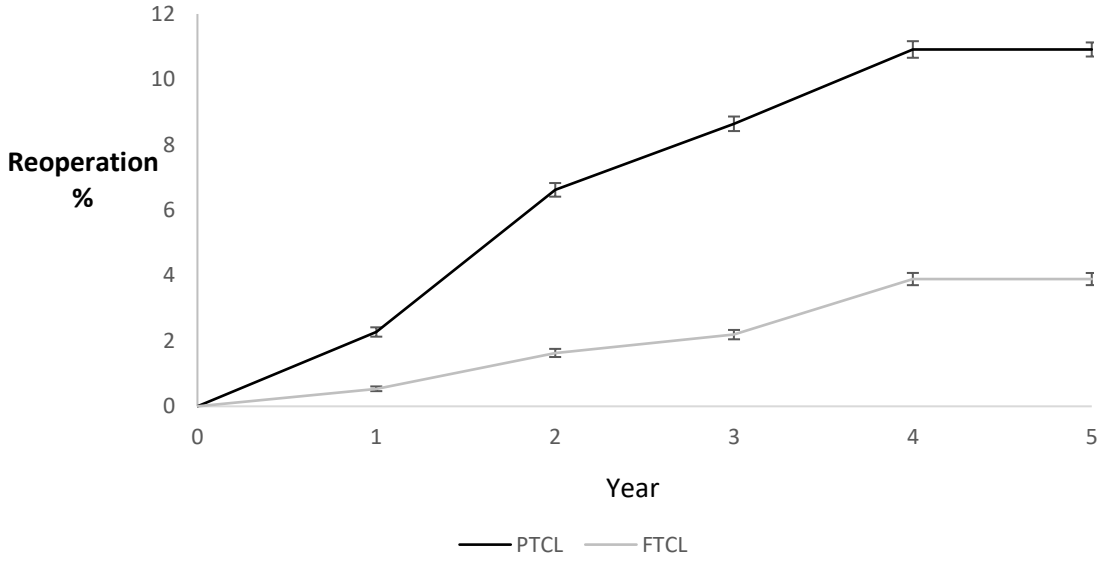


Figure 4.4: Cumulative reoperation rate by year following OUKA in the setting of PTCL (SD).

4.3.1.5 MRI sub-study of patients with partial-thickness medial compartment disease

In this cohort of patients with medial compartment PTCL on the femur, tibia or femur and tibia, the sensitivity and specificity of MRI at detecting FTCL was 68% and 80% for the medial femoral condyle plateau and 67% and 55% for the medial tibial plateau.

In knees with PTCL no difference in functional outcomes (OKS, AKSS-O and AKSS-F) at one-year were seen between knees with MRI evidence of: FTCL on both the femur and tibia within the medial compartment, bone marrow oedema on both the femur and tibia within the medial compartment, suprapatellar effusion or evidence or synovitis and those without these findings (**Table 4.3**). Knees with MRI evidence of bone marrow oedema of both the femur and tibia within the medial compartment were found to have a higher year one TAS (p = 0.003) than knees without bone marrow oedema. No difference TAS was seen between other groups.

Table 4.3: Year-one outcomes of OUKA in the setting of PTCL based on MRI findings.

1. MRI evidence of FTCL on both the femur and tibia within the medial compartment

	Present (*n* = 12)	Absent (*n* = 24)	*P* value
OKS (SD)	35.8 (13)	38.3 (9)	0.70
AKSS-O (SD)	68.5 (38)	73.2 (20)	0.45
AKSS-F (SD)	79.6 (26)	86.5 (15)	0.70
TAS (SD)	3.9 (2)	2.7 (2)	0.13

2. MRI bone marrow oedema on both femur and tibia within the medial compartment

	Present (*n* = 5)	Absent (*n* = 31)	*P* value
OKS (SD)	32.4 (15)	38.1 (10)	0.39
AKSS-O (SD)	65.6 (44)	72.4 (26)	0.54
AKSS-F (SD)	84.0 (26)	83.8 (19)	0.75
TAS (SD)	6.7 (1)	2.8 (4)	**0.003**

3. MRI evidence of medium or large suprapatellar effusion (12 medium, 3 large)

	Present (*n* = 15)	Absent (*n* = 21)	*P* value
OKS (SD)	40.1 (6.3)	34.9 (12.7)	0.44
AKSS-O (SD)	80.2 (20)	63.8 (34)	0.19
AKSS-F (SD)	87.3 (17)	80.8 (22)	0.44
TAS (SD)	3.6 (1)	2.8 (1)	0.50

4. MRI evidence of synovitis (7 mild, 4 moderate)

	Present (*n* = 11)	Absent (*n* = 25)	*P* value
OKS (SD)	37.5 (11)	37.1 (10)	0.69
AKSS-O (SD)	70.7 (26)	71.0 (32)	0.82
AKSS-F (SD)	86.8 (16)	82.3 (22)	0.72
TAS (SD)	3.2 (2)	3.2 (1)	0.62

4.3.2 Anterior cruciate ligament

Of the 820 cases where the status of the ACL was recorded, 540 were unilateral procedures and 140 bilateral. In 565 cases the ACL was normal, 116 cases it had synovial damage and 139 cases it had longitudinal splits. Baseline demographics are outlined in **Table 4.4**. Those knees with longitudinal splits were in patients who were significantly older (p = 0.004), more likely to be male (p = 0.007), and who had lower pre-operative AKSS-O scores (p = 0.03) compared to those patients with a macroscopically normal ACL.

The size of the anteromedial tibia medial defect increased as the degree of macroscopic damage to the ACL increased (p < 0.01). In patients with a macroscopically normal ACL a tibial defect involving bone loss of > 5 mm was observed in 25% of cases compared to in almost 50% of cases in those patients with longitudinal splits to the ACL (**Figure 4.5**).

All patients were followed up for a minimum of five-years with the exception of those who were lost to follow-up (4), died (31), underwent revision (15) or withdrew from the study due to poor health (5). Of those patients who withdrew from the study at any time point, all due to medical co-morbidities not associated with their knee, we are not aware of any revisions. The mean follow-up was 10.4 years (range 5.3 to 16.6) with 460 knees having a minimum ten-year follow-up and 54 knees a minimum fifteen-year follow-up.

The mean OKS by year following OUKA for each of the three groups is displayed in **Figure 4.6**. At ten-years there was no significant difference in OKS scores between groups (p = 0.94) with an overall mean score of 40 (SD9) and 79% of knees having good or excellent outcomes[125].

The mean AKSS-O and AKSS-F by year following OUKA are displayed in **Figure 4.7**. At ten-years no significant difference in AKSS-O (p=0.15), AKSS-F (p=0.96) or TAS (p=0.97) were detected between groups (**Table 4.5**).

Table 4.4: Baseline demographics by macroscopic ACL status.

	Normal (565)	**Synovial damage (116)**	**Longitudinal splits (139)**	***p*-value**
Age (SD)	66.1 (9.7)	67.1 (9.3)	69.1 (9.2)	**0.004***
% Male	48.0 (*n*=271)	54.3 (*n*=63)	62.6 (*n*=87)	**0.007**
OKS (SD)	24.5 (8.8)	23.3 (9.0)	26.5 (8.6)	0.05
AKSS-O (SD)	51.3 (19.2)	48.5 (17.8)	45.0 (16.2)	**0.03***
AKSS-F (SD)	69.6 (18.3)	66.3 (14.7)	69.0 (18.4)	0.19
TAS (SD)	2.3 (1.1)	2.3 (1.5)	2.4 (1.2)	0.49

*post-hoc test revealing that there are significant differences in age and AKSS-O between those patients with a normal ACL and those with longitudinal splits.

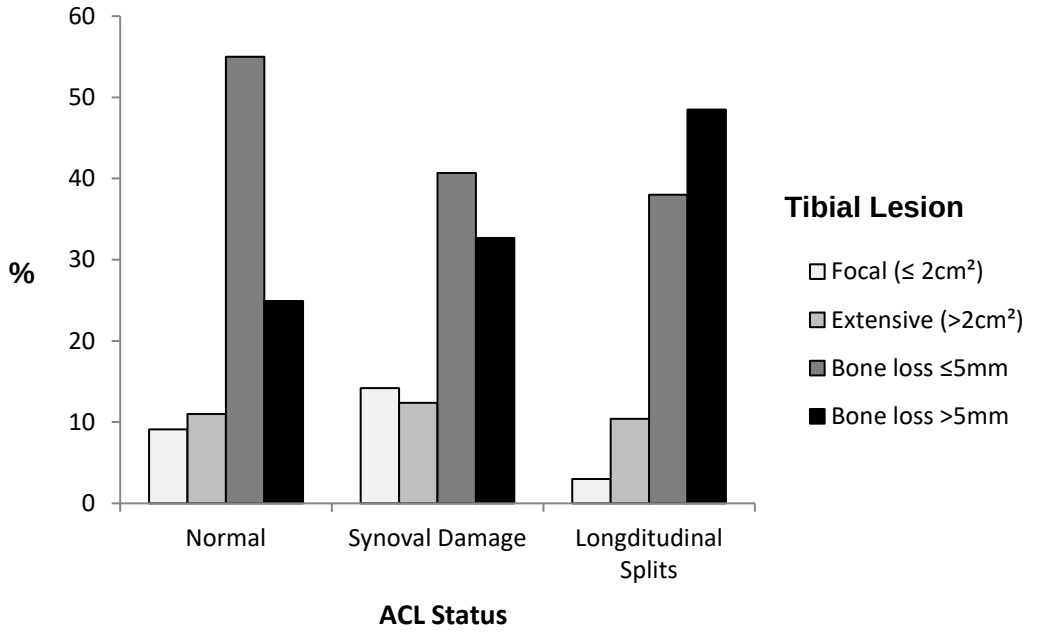


Figure 4.5: Anteromedial tibial lesion size by macroscopic status of ACL

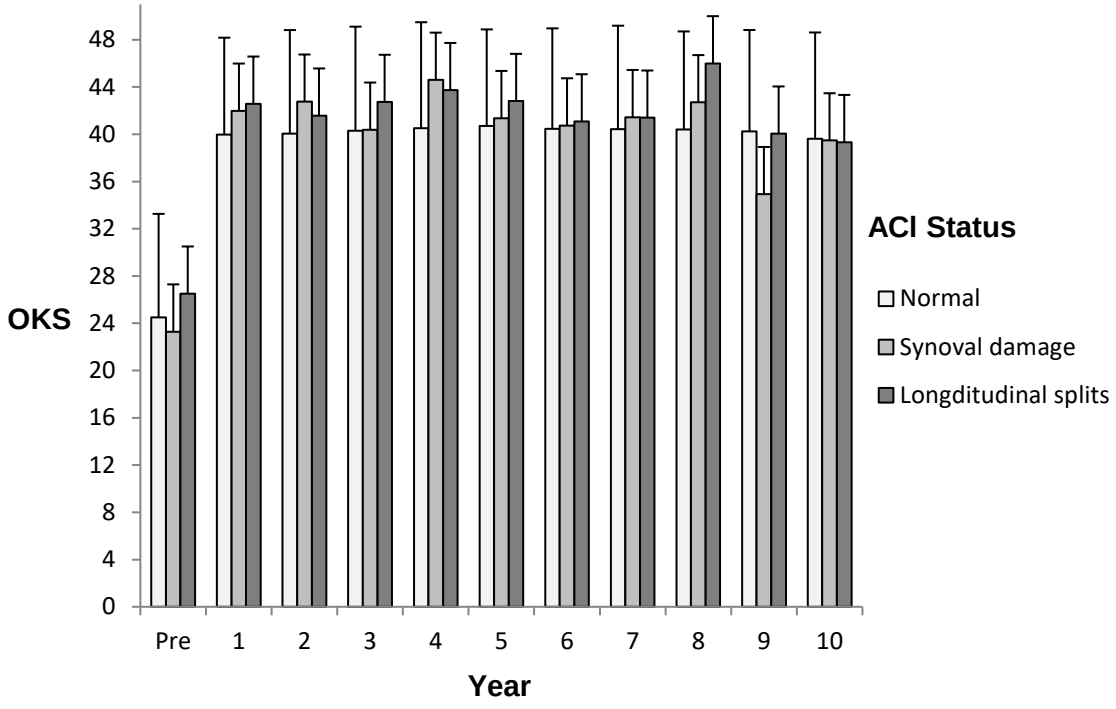


Figure 4.6: Mean OKS by year following surgery (SD) based on ACL status.

Table 4.5: Ten-year functional outcomes based on ACL status.

	Normal	**Synovial damage**	**Longitudinal splits**	***p*-value**
OKS (SD)	39.6 (9.0)	39.5 (9.4)	39.3 (8.3)	0.94
AKSS-O (SD)	82.1 (13.4)	80.3 (12.1)	75.6 (19.0)	0.15
AKSS-O (excluding deductions for alignment) (SD)	90.1 (12.9)	89.2 (13.9)	84.8 (20.5)	0.30
AKSS-F (SD)	75.5 (22.8)	76.9 (18.9)	76.3 (23.7)	0.96
TAS (SD)	2.5 (1.2)	2.5 (1.0)	2.6 (1.4)	0.97

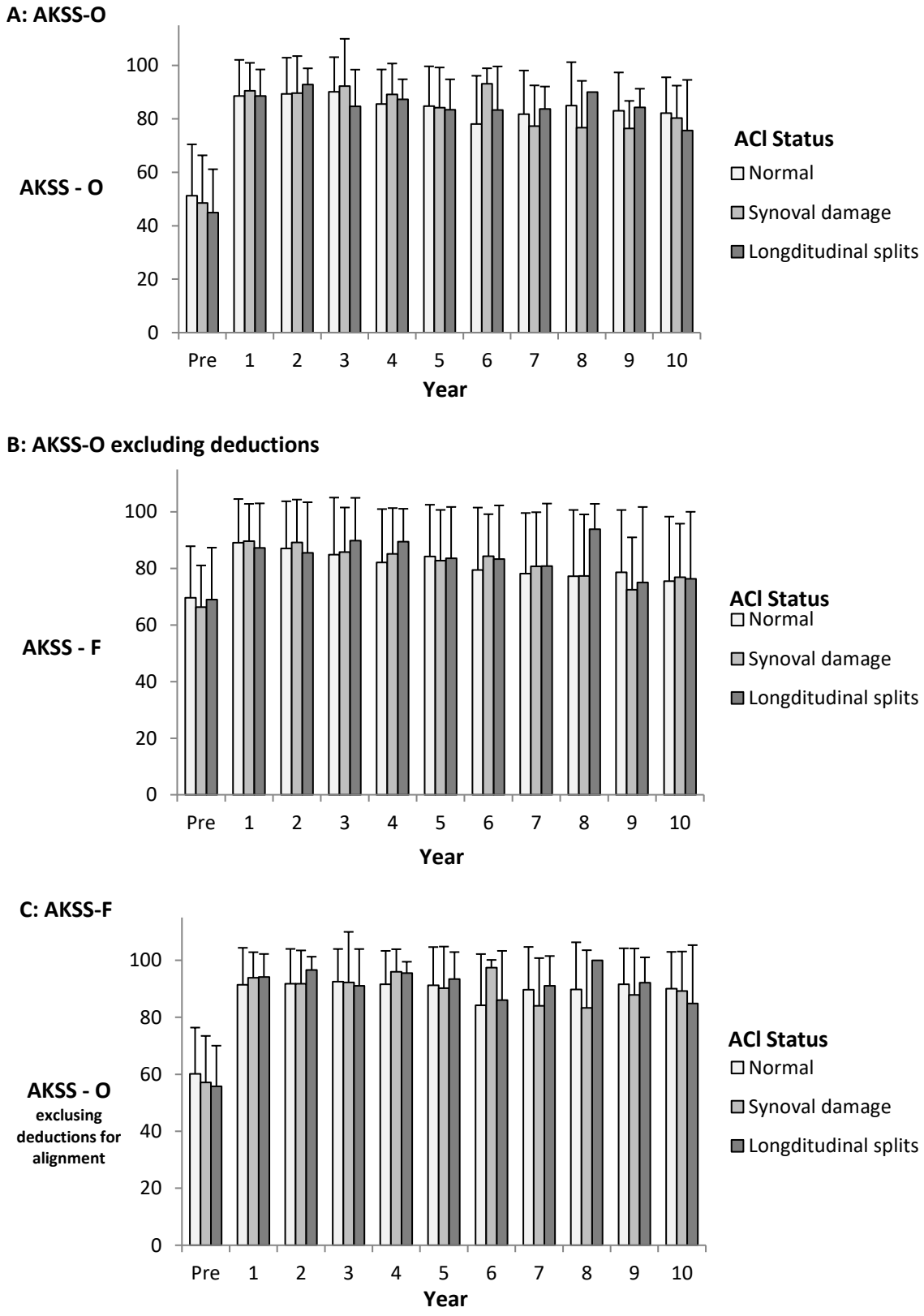


Figure 4.7: Mean AKSS-O (A), AKSS-O not including deductions for alignment (B) and AKSS-F (C) by year following surgery (SD) based on ACL status.

A significantly greater increase in OKS (p = 0.04) and AKSS-O (p = 0.03) from baseline score to ten-year score, indicating greater improvement in function, was observed in knees with macroscopic damage to the ACL, synovial damage or longitudinal splits, compared to those knees with a macroscopically normal ACL at the time of operation. No significant difference in improvement from baseline at ten-years was seen when assessing AKSS-F or TAS (**Table 4.6**).

Overall there were 39 implant related reoperations. In the cohort with normal ACL there were 29 reoperations (5.5%) at a mean of 6.0 years (range 0.4 to 14.7). Progression of arthritis in the retained lateral compartment (2.1%) followed by unexplained pain (0.9%) and bearing dislocation (0.6%) were the most common indications for revision. In the cohort with synovial damage to the ACL there were two reoperations (1.8%), one for lateral compartment disease progression and one with an unknown indication (operation performed overseas), at a mean of 9.4 years (6.7 and 12.0). In the cohort with longitudinal splits to the ACL there were eight reoperations (6.0%) at a mean of 4.5 years (range 0.2 to 10.3). Progression of arthritis in the retained lateral compartment (3.0%) followed by bearing dislocation (1.5%) and infection (1.5%) were the most common indications for revision.

There were two cases of ACL rupture with both knees having macroscopically normal ACL at the time of operation. One case was associated with trauma and initially treated with ACL reconstruction at another hospital but subsequently the knee joint became infected and two-stage revision TKA was performed at 2.1 years. In the second case the ACL rupture was associated with extensive synovitis and the patient underwent TKA at 14.7 years. In both cases primary knee arthroplasty prostheses were used.

When implant-related re-operations are considered failures the fifteen-year survival rate was 90% (95%CI 72 to 100) in those patients with a normal ACL, 96% (95%CI 68 to 100) in those patients with

synovial damage to the ACL and 90% (95%CI 50 to 100) in those knees with longitudinal splits (**Figure 4.8**)**.** Overall no significant difference in survival existed between groups (p = 0.15).

Table 4.6: Improvement in function from baseline to ten-years based on ACL status.

	Normal	**Synovial damage**	**Longitudinal splits**	***p*-value**
OKS (SD)	15.7 (10.4)	20.2 (10.7)	17.0 (8.9)	**0.04**
AKSS-O (SD)	25.3 (22.6)	40.1 (17.6)	31.3 (19.2)	**0.03**
AKSS-O (excluding deductions for alignment) (SD)	26.3 (21.4)	38.5 (17.2)	27.5 (16.2)	**0.05**
AKSS-F (SD)	7.0 (22.2)	11.9 (18.9)	11.9 (20.1)	0.47
TAS (SD)	0.3 (1.2)	-0.4 (2.2)	0.5 (1.6)	0.41

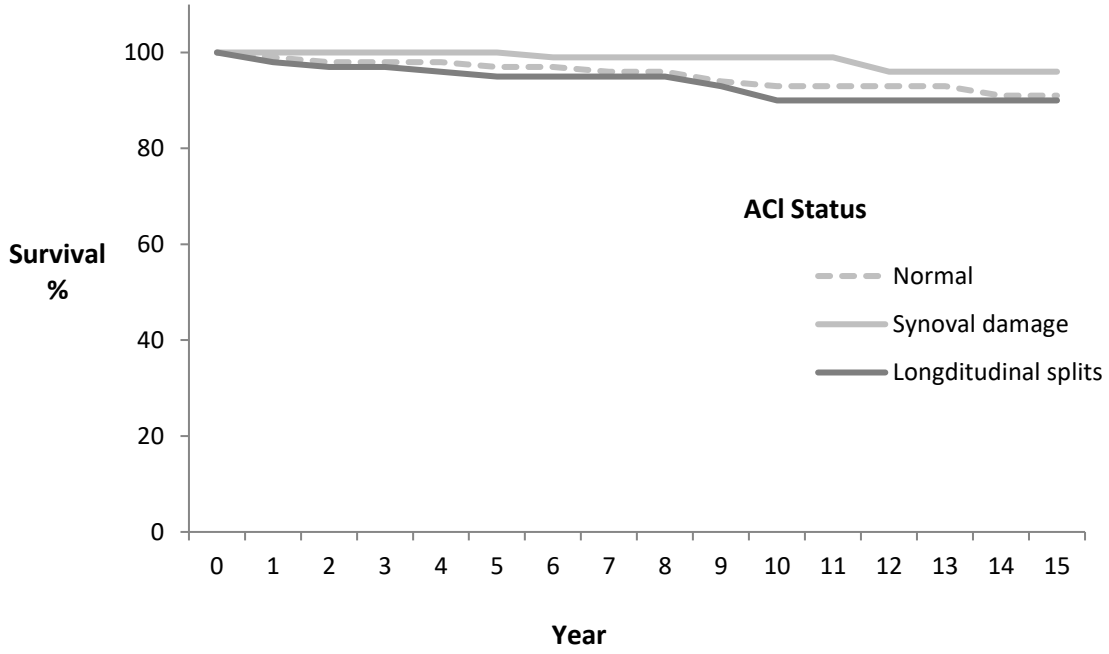


Figure 4.8: Survival analysis based on ACL status.

4.3.3 Lateral osteophytes

Radiographs of 458 knees (392 patients) were identified consisting of 326 unilateral procedures and 66 sequential staged bilateral procedures (**Figure 4.9**). Inter (kappa=0.70) and intra-observer (kappa=0.70) reliability was good.

Lateral osteophytes were identified in 62% (285) of knees. Of these, Grade 1 osteophytes were seen in 48% (137 knees), Grade 2 in 34% (98 knees) and Grade 3 in 18% (50 knees). Where lateral osteophytes were present they were seen on the tibia only in 47% (134 knees), femur only in 16% (46 knees) and both the tibia and femur in 37% (105 knees).

Baseline demographics are outlined in **Table 4.7**. Lateral osteophytes were associated with younger age at joint arthroplasty (p = 0.01) and higher BMI (p = 0.01). There was no association seen between the presence and location of lateral osteophytes and pre-operative function as assessed by OKS (p = 0.96), AKSS-O (p = 0.22) or TAS (p = 0.53), however AKSS-F was found to be lower in knees with both lateral tibial and femoral osteophytes compared to knees with no osteophytes (p = 0.02) and compared to knees with lateral tibial osteophytes only (p < 0.01).

Overall there was no association between the size of the medial tibial lesion in those knees without lateral osteophytes and those knees with lateral osteophytes (Grade 1-3; p = 0.40)) or those knees with Grade 3 lateral osteophytes (p = 0.17) (**Figure 4.10**). Similarly there was no association seen between the macroscopic status of the ACL in those knees with and without lateral osteophytes (Grade 1-3; (p = 0.32) however subgroup analysis revealed those knees with Grade 3 lateral osteophytes were significantly more likely to have a greater degree of macroscopic damage of the ACL than those without osteophytes (p = 0.04) (**Figure 4.11**).

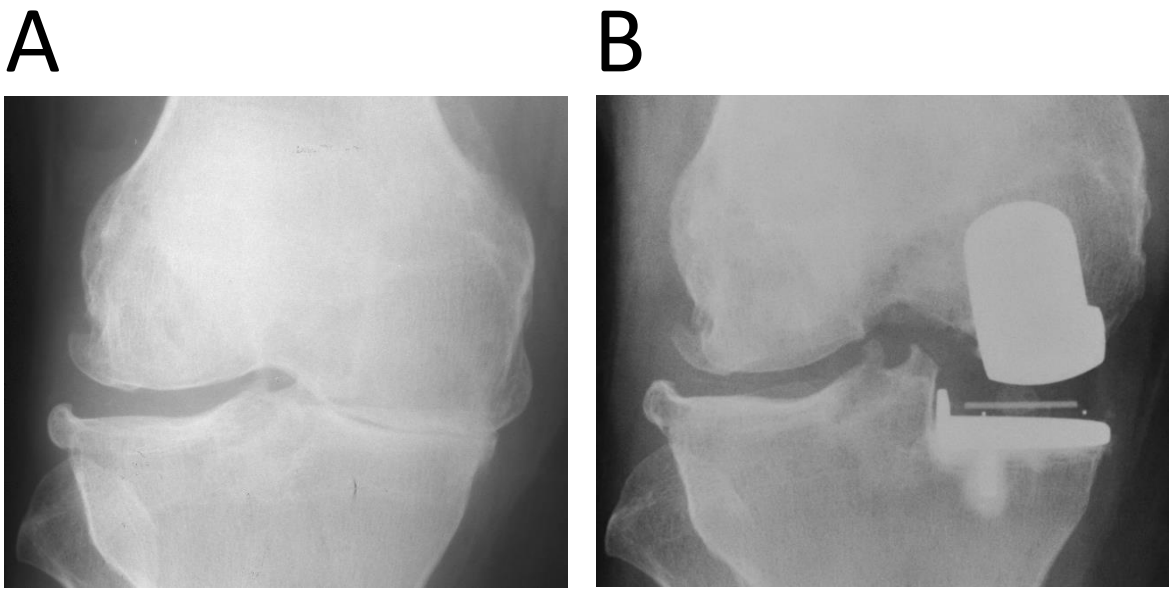


Figure 4.9: Pre-operative (A) and fifteen-year (B) radiographs of a knee with lateral tibial and femoral osteophytes managed with OUKA.

Table 4.7: Pre-operative demographics based on the presence of lateral osteophytes.

	No osteophytes (Grade 0)	**Lateral osteophytes (Grade 1 – 3)**	***p*-value**	**Lateral osteophytes (Grade 3)**	***p*-value**
Mean Age (range)	69.0 (38 - 87)	66.5 (40 - 88)	0.007	64.2 (41 – 83)	**0.002**
% Male (*n*)	51 (89)	53 (151)	0.75	48 (24)	0.56
Mean BMI (range)	27.5 (15 - 52)	28.9 (18 - 47)	0.008	30.5 (22 - 46)	**0.001**
Mean OKS (range)	23.6 (9 - 47)	23.9 (7 - 47)	0.71	24.1 (7 -38)	0.72
Mean AKSS-O (range)	49.1 (0 - 95)	45.5 (6 - 80)	0.16	44.5 (8 - 70)	0.28
Mean AKSS-F (range)	70.1 (35 - 100)	68.5 (30 - 100)	0.42	63.8 (35 - 100)	0.11
Mean TAS (range)	2.4 (1 - 6)	2.5 (1 - 7)	0.99	1.9 (1 - 4)	0.10

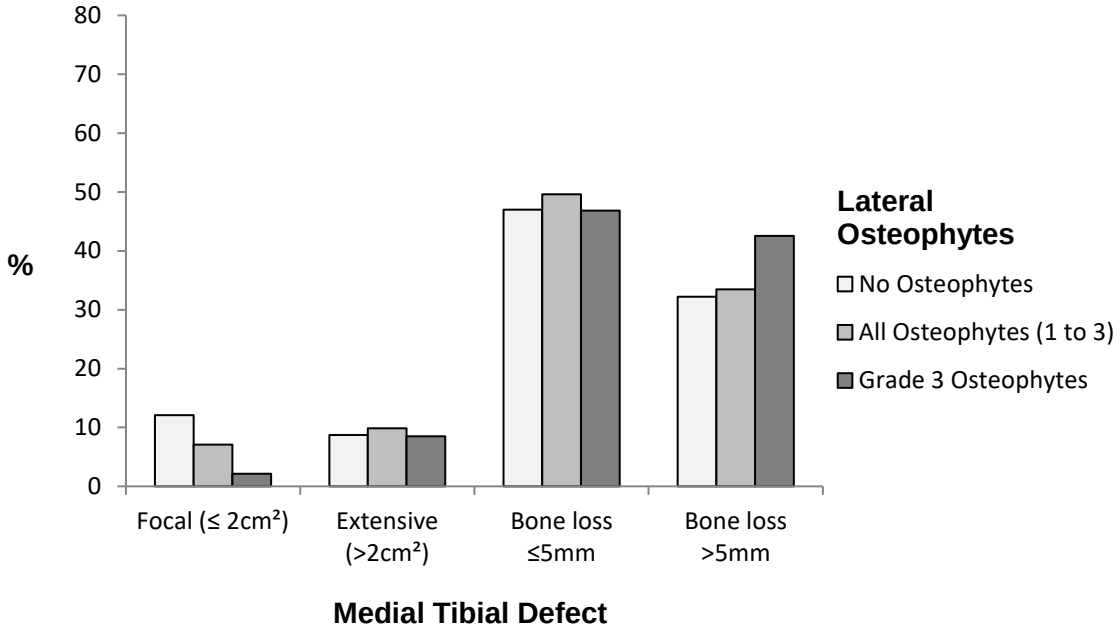


Figure 4.10: Size of medial tibial defect in the presence and absence of lateral osteophytes. No association was seen between the size of the medial tibial defect and the size of lateral osteophytes.

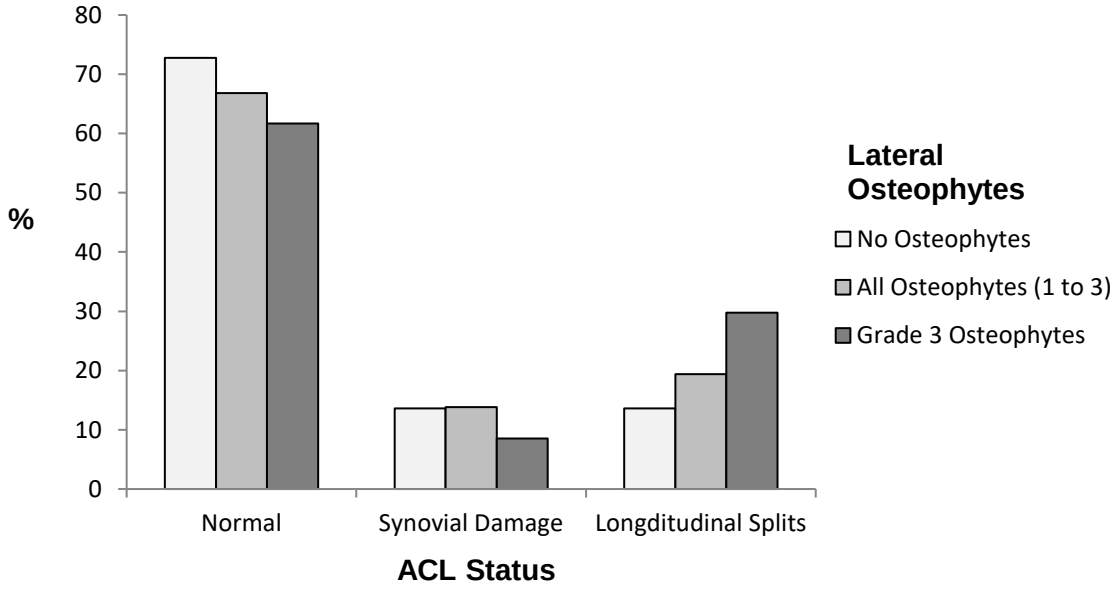


Figure 4.11: Anterior Cruciate Ligament Status. Grade 3 osteophytes were associated with increasing macroscopic damage to the ACL ($p = 0.04$).

All patients were followed up for a minimum of five-years with the exception of those who underwent revision (8 prior to 5 years), died (19) or withdrew from the study due to poor health (1). No patients were lost to follow-up. In the patients who died or withdrew from the study at any time point, all due to medical co-morbidities not associated with their knee, we are not aware of any revisions. The mean follow-up was 10.3 years (range 5.3 to 16.6) with 198 knees having a minimum ten-year follow.

The mean OKS by year following OUKA for each of the groups is displayed in **Figure 4.12**. At ten-years no significant difference in absolute or improvement from baseline OKS (p = 0.91; p = 0.52), AKSS-O (p = 0.68; p = 0.33), AKSS-F (p = 0.68; p = 0.76) or TAS (p = 0.36; p = 0.82) was detected between groups or on subgroup analysis of knees with large lateral osteophytes (Grade 3) (**Table 4.8**).

At ten-years no difference in functional outcome was seen between groups based on location of lateral osteophytes as assessed by OKS (p = 0.05), AKSS-F (p = 0.45) or TAS (p = 0.07) however AKSS-O was found to be significantly lower in knees with lateral femoral osteophytes compared to other groups (no osteophytes (p = 0.008), lateral tibial osteophytes only (p = 0.003), both lateral tibial and femoral osteophytes (p = 0.002)). Overall, no difference in improvement from baseline across all functional scores was seen between groups.

Overall there were 20 implant related reoperations. In knees without lateral osteophytes there were five reoperations (3%) at a mean of 6.3 years (range 0.8 to 11.4), two of which were for progression of arthritis in the lateral compartment (1%). In knees with lateral osteophytes (Grade 1-3) there were 15 reoperations (5%) at a mean of 6.2 years (range 0.7 to 14.7), six of which were for progression of arthritis in the lateral compartment (2%). In knees with Grade 3 lateral osteophytes there was one reoperation (2%) at 4.6 years for progression of arthritis in the retained

lateral compartment (2%). No difference was seen in the timing or mechanism of failure between groups.

When implant-related re-operations are considered failures the fifteen-year survival rate was 94% (95%CI 82 to 100) in those patients without lateral osteophytes, 88% (95%CI 76 to 100) in those patients with lateral osteophytes (Grade 1 – 3) and 98% (95%CI 83 to 100) in those knees with Grade 3 lateral osteophytes (**Figure 4.13**). Overall no significant difference in survival existed between knee without lateral osteophytes and those with lateral osteophytes (Grade 1 – 3; $p = 0.28$) or between knees without lateral osteophytes and those with Grade 3 lateral osteophytes ($p = 0.71$). No difference in implant survival was seen based on the location of lateral osteophytes ($p = 0.43$).

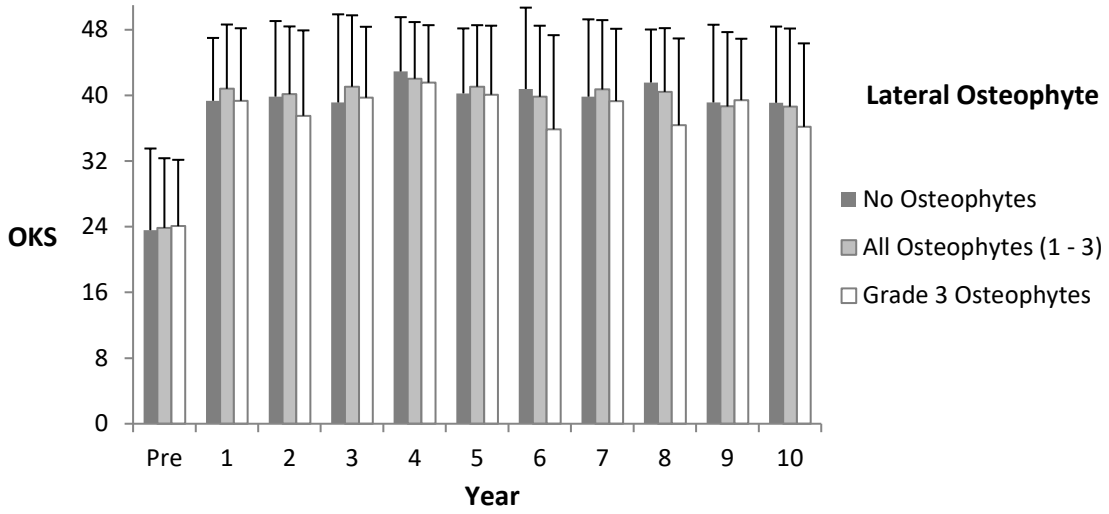


Figure 4.12: Functional outcomes by year. No difference in OKS at ten-years was seen between knees with (Grade 1-3) or without osteophytes, or on subgroup analysis of knees with Grade 3 osteophytes, at ten-years.

Table 4.8: Improvement from baseline function to ten-year function base on the presence of lateral osteophytes.

	No osteophytes (Grade 0)	**Lateral osteophytes (Grade 1 – 3)**	***p*-value**	**Lateral osteophytes (Grade 3)**	***p*-value**
Mean Improvement OKS (Range)	18.4 (0 to 29)	17.3 (1 to 27)	0.52	14.3 (4 to 18)	0.17
Mean Improvement AKSS-O (Range)	27.4 (-25 to 52)	36.1 (-12 to 90)	0.33	24.8 (-12 to 40)	0.92
Mean Improvement AKSS-F (Range)	5 (-30 to 40)	5.8 (-10 to 40)	0.76	11.7 (-30 to 40)	0.45
Mean Improvement TAS (Range)	0 (-2 to 2)	0.1 (-2 to 4)	0.82	0.2 (0 to 1)	0.50

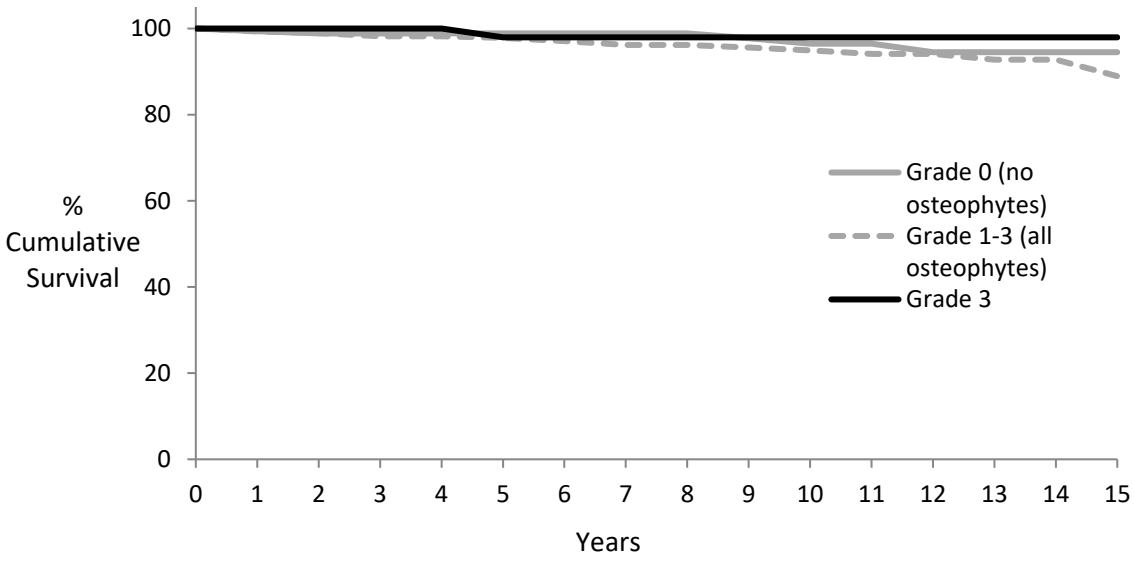


Figure 4.13: Cumulative implant survival of knees with and without lateral osteophytes. No difference in cumulative implant survival out to fifteen-years was seen between knees with (Grade 1-3) or without osteophytes, or on subgroup analysis of knees with Grade 3 osteophytes.

4.3.4 Patellofemoral joint disease

4.3.4.1 Intra-operative assessment of the PFJ

Detailed intra-operative data on the status of the PFJ was available for 805 knees (677 patients). A flow chart outlining the study is provided in **Figure 4.14**.

Knees with FTCL at the medial facet were significantly older and had better pre-operative OKS compared with knees without FTCL at the medial facet. No difference in baseline characteristics or function were detected between knees with or without FTCL at the lateral facet, trochlea or any site within the PFJ (**Table 4.9**).

All patients were followed up for a minimum of five-years with the exception of those who died (31), underwent revision (14 prior to 5 years), withdrew from the study due to poor health (5) or were lost to follow-up (4). In the patients who died, withdrew from the study at any time point, all due to medical co-morbidities not associated with their knee, or were lost to follow-up we are not aware of any revisions. The mean follow-up was ten-years (range 5 to 17) with 347 knees having a minimum ten-year follow.

The functional outcomes at ten-years are outlined in **Table 4.10**. No difference in absolute functional scores at ten-years or improvement from baseline to ten-years assessed by OKS, AKSS-O, AKSS-F or TAS was detected between groups. Analysis of Q12 of the OKS revealed that, compared to knees without exposed bone, knees with FTCL at the lateral patella facet had a lower ten-year Q12 score (p = 0.01) and lower improvement from baseline to ten-year score (p = 0.01). Additionally, knees with FTCL at the trochlea had a higher improvement from baseline to ten-year score (p = 0.01). In all cases the difference was under one point and as such this is regarded to be unlikely to be clinically relevant.

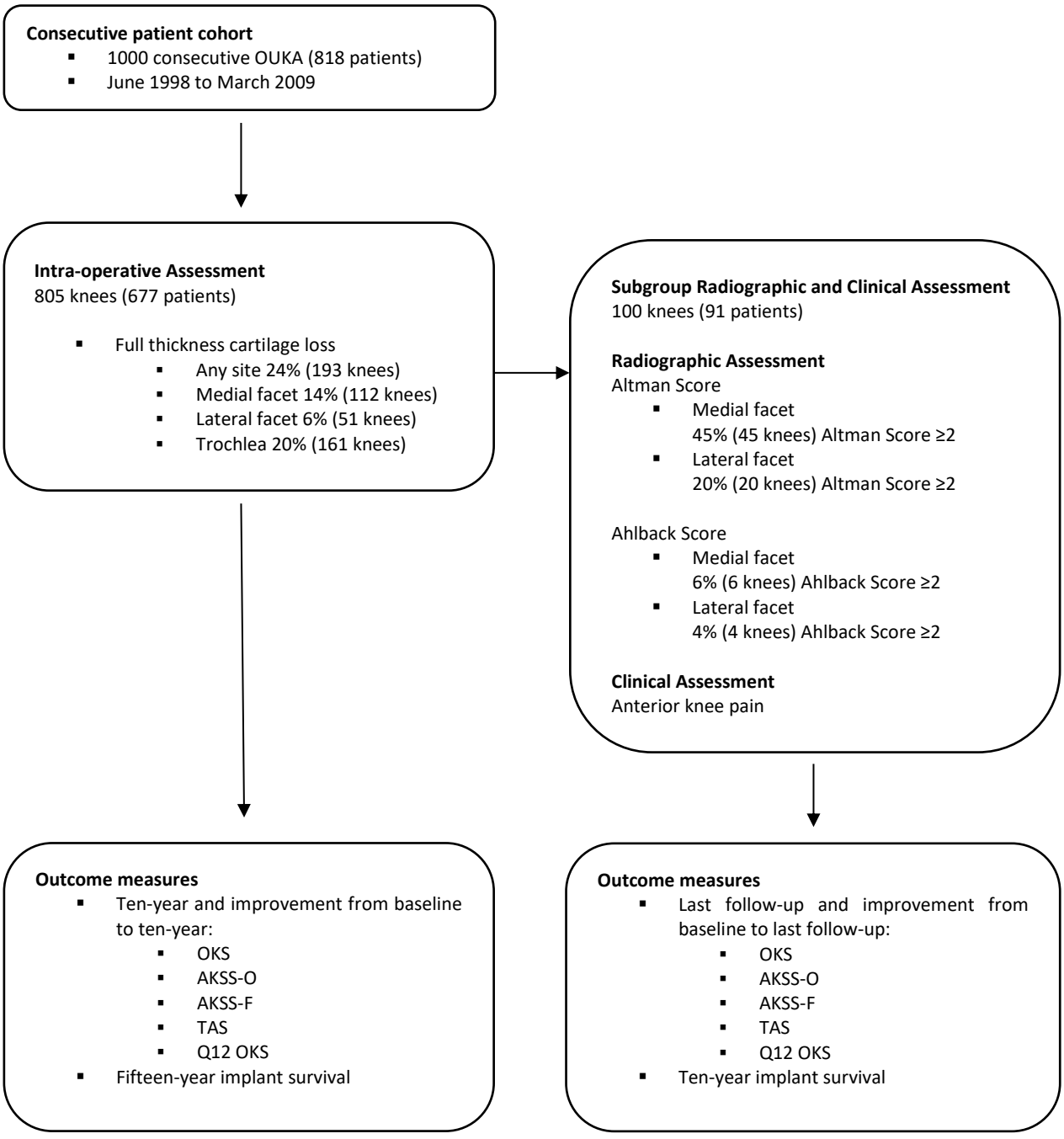


Figure 4.14: Flow chart outlining subgroups of radiographic and clinical assessment for PFJ disease.

Table 4.9: Pre-operative demographics and functional performance of knees with and without full-thickness cartilage loss in the PFJ.

	Anywhere in PFJ			Medial Facet			Lateral Facet			Trochlear Surface		
	Absent (615)	**Present (190)**	***p-value***	**Absent (693)**	**Present (112)**	***p-value***	**Absent (754)**	**Present (51)**	***p-value***	**Absent (644)**	**Present (161)**	***p-value***
Mean Age (SD)	66.6 (10)	67.6 (9)	0.20	66.5 (10)	68.8 (9)	**0.01**	66.8 (10)	66.9 (9.5)	0.87	66.7 (10)	67.2 (9)	0.52
% Male (*n*)	51% (314)	54% (102)	0.35	52% (358)	47% (53)	0.09	50% (378)	59% (30)	0.73	50% (324)	56% (90)	0.20
Mean OKS (SD)	24.5 (9)	25.7 (8)	0.18	24.4 (9)	26.9 (8)	**0.01**	24.6 (9)	26.6 (7)	0.13	24.5 (9)	25.5 (8)	0.20
Mean AKSS-O (SD)	49.1 (19)	51.7 (17)	0.18	49.4 (19)	51.2 (16)	0.41	49.8 (19)	50.4 (16)	0.67	49.1 (19)	51.8 (18)	0.19
Mean AKSS-F (SD)	69.1 (18.3)	69.1 (16.4)	0.78	68.9 (18)	69.5 (16.7)	0.85	68.9 (18)	69.2 (17)	0.99	68.9 (18)	69.3 (17)	0.97
Mean TAS (SD)	2.3 (1)	2.3 (1)	0.70	2.3 (1)	2.3 (1)	0.99	2.3 (1)	2.4 (1)	0.62	2.3 (1)	2.4 (1)	0.34
Mean Q12 OKS (SD)	2.4 (1)	2.4 (1)	0.73	2.3 (1)	2.5 (1)	0.13	2.4 (1)	2.5 (1)	0.62	2.4 (1)	2.4 (1)	0.91

Table 4.10: Ten-year functional outcomes and fifteen-year implant survival of knees with and without full-thickness cartilage loss in the PFJ.

	Anywhere in PFJ			Medial Facet			Lateral Facet			Trochlear Surface		
	Absent	**Present**	***p-value***	**Absent**	**Present**	***p-value***	**Absent**	**Present**	***p-value***	**Absent**	**Present**	***p-value***
Mean OKS (SD)	39.7 (9)	38.9 (10)	0.86	39.6 (9)	38.8 (10)	0.99	39.8 (9)	35.0 (11)	0.14	39.6 (9)	39.6 (9)	0.54
Mean AKSS-O (SD)	81.0 (14)	81.6 (15)	0.57	81.3 (13)	79.0 (18)	0.97	81.2 (14)	79.0 (23)	0.70	80.7 (14)	84.0 (14)	0.15
Mean AKSS-F (SD)	76.1 (22)	75.0 (21)	0.58	76.2 (22)	72.4 (21)	0.23	76.3 (22)	66.8 (26)	0.11	75.7 (22)	77.1 (20)	0.75
Mean TAS (SD)	2.5 (1)	2.5 (1)	0.94	2.6 (1)	2.2 (1)	0.11	2.5 (1)	2.7 (2)	0.75	2.5 (1)	2.6 (1)	0.25
Mean Q12 OKS (SD)	3.3 (1)	3.1 (1)	0.30	3.2 (1)	3.0 (1)	0.17	3.3 (1)	2.5 (1.3)	**0.01**	3.2 (1)	3.2 (1)	0.74
15year survival (%) (95%CI)	92.6 (85 - 100)	94.2 (78 - 100)	0.68	92.6 (85 - 100)	95.2 (62 - 100)	0.99	92.7 (85 - 100)	97.9 (58 - 100)	0.54	92.4 (84 - 100)	95.0 (79 - 100)	0.96

There was no correlation between functional outcome at ten-years and the degree of intra-operative cartilage damage at the medial facet (OKS p = *0*.27, AKSS-O p = 0.66, AKSS-F p = 0.67), lateral facet (OKS p = 0.99, AKSS-O p = 0.92, AKSS-F p = 0.49) or trochlea (OKS p = 0.32, AKSS-O p = 0.14, AKSS-F p = 0.95).

Overall there were 32 implant related reoperations, with none performed due to progression of arthritis within the PFJ or due to PFJ symptoms. In one patient who underwent revision to primary TKA for lateral progression at 6.9 years progression of PFJ degeneration was noted, however this was not considered to be symptomatic and the patella was not resurfaced with the patient subsequently progressing to a full recovery with no further surgery at three years post-revision. At fifteen-years no difference in implant survival was seen based on the presence, or location of FTCL in the PFJ (**Table 4.10** and **Figure 4.15**).

4.3.4.2 Radiographic assessment of the PFJ (Altman score)

Details of the subgroup of 100 knees (91 patients) which underwent a detailed radiographic (Altman and Ahlback Scoring) as well as pain assessment have been reported previously[88]. The mean follow-up was ten-years (range 1 to 13) with 77 knees having a minimum five-year follow.

No correlation between Altman Scores and functional outcomes in the medial facet (OKS p = 0.91, AKSS-O p = 0.99, AKSS-F p = 0.97) or lateral facet (OKS p = 0.77, AKSS-O p = 0.78, AKSS-F p = 0.65) was seen.

At last follow-up no difference in absolute functional outcome score or implant survival was seen between knees with radiographic degenerative disease of the PFJ (Altman Score ≥2) at either the medial or lateral facet. Aside from a lower improvement from baseline OKS to OKS at last follow-up no difference in improvement was seen between groups (**Table 4.11**).

Figure 4.15: Implant survival of knees with and without full-thickness cartilage loss in the PFJ (all sites).

Table 4.11: Functional outcomes at last follow-up, improvement from baseline function to function at last follow-up and ten-year implant survival of knees with and without radiographic disease of the PFJ as assessed by Altman Score ≥2.

	Medial Facet			**Lateral Facet**		
	Normal (*n*=55)	**Altman≥2 (*n*=45)**	***p-value***	**Normal (*n*=80)**	**Altman≥2 (*n*=20)**	***p-value***
Mean OKS (SD)	36.1 (12)	37.5 (9)	0.72	37.5 (10)	33.5 (12)	0.25
Mean AKSS-O (SD)	74.5 (22)	78.2 (12)	0.95	78.2 (16)	59.8 (28)	0.15
Mean AKSS-F (SD)	67.4 (32)	70.0 (23)	0.90	69.0 (29)	61.5 (13)	0.66
Mean TAS (SD)	2.4 (1)	2.4 (1)	0.65	2.4 (1)	2.4 (2)	0.43
Mean Q12 OKS (SD)	2.9 (1)	3.1 (1)	0.80	3.0 (1)	2.9 (1)	0.60
Mean improvement OKS (SD)	12.8 (10)	13.8 (10)	0.82	14.3 (10)	9.1 (9)	**0.02**
Mean improvement AKSS-O (SD)	24.2 (23)	25.4 (23)	0.67	26.4 (23)	11 (16)	0.20
Mean improvement AKSS-F (SD)	6.3 (26)	7.8 (28)	0.59	7.5 (27)	5 (25)	0.67
Mean improvement TAS (SD)	0.6 (1)	0.8 (1)	0.37	0.6 (1)	0.9 (1)	0.47
Mean improvement Q12 OKS (SD)	0.7 (1)	0.9 (1)	0.44	0.9 (1)	0.5 (1)	0.19
15year survival (%) (95%CI)	91.9 (83 - 100)	96.9 (91 - 100)	0.41	92.7 (86 - 100)	100	0.92

4.3.4.3 Radiographic assessment of the PFJ (Ahlback score)

No difference in absolute functional outcome score, improvement from baseline or implant survival was seen between knees with evidence of radiographic joint space obliteration (Ahlback Score ≥2) and those without (**Table 4.12**).

4.3.4.4 Clinical Assessment

No significant difference was found in absolute functional outcome score, improvement from baseline or implant survival between knees with and knees without anterior knee pain (**Table 4.13**).

Table 4.12: Functional outcomes at last follow-up, improvement from baseline function to function at last follow-up and ten-year implant survival of knees with and without radiographic disease of the PFJ as assessed by Ahlback Score ≥2. Data was not available for the American Knee Society Score in this cohort.

	Medial Facet			**Lateral Facet**		
	Normal (*n*=91)	**Ahlback≥ 2 (*n*=6)**	***p-value***	**Normal (*n*=93)**	**Ahlback ≥2 (*n*=4)**	***p-value***
Mean OKS (SD)	36.5 (11)	40.3 (4)	0.74	36.8 (11)	34.3 (14)	0.62
Mean TAS (SD)	2.4 (1)	1.8 (1)	0.21	2.4 (1)	1.5 (1)	0.28
Mean Q12 OKS (SD)	3.0 (1)	3.2 (1)	0.64	3.0 (1)	3.0 (1)	0.84
Mean improvement OKS (SD)	13.0 (10)	16.3 (6.5)	0.53	13.5 (10)	7.3 (9)	0.18
Mean improvement TAS	0.7 (1)	0.6 (1)	0.91	0.7 (1)	0.5 (1)	0.84
Mean improvement Q12 OKS (SD)	0.8 (1)	0.8 (1)	0.62	0.8 (1)	0.5 (1)	0.66
15year survival (%) (95%CI)	94.0 (88 - 100)	100	0.60	94.1 (88 - 100)	100	0.69

Table 4.13: Functional outcomes at last follow-up, improvement from baseline function to function at last follow-up and ten-year implant survival of knees with and without anterior knee pain.

	Anterior knee pain		
	Absent (*n*=46)	**Present (*n*=54)**	***p-value***
Mean OKS (SD)	37.8 (10.2)	35.7 (11)	0.28
Mean AKSS-O (SD)	80.3 (16)	73.1 (19)	0.37
Mean AKSS-F (SD)	74.2 (25)	64.0 (29)	0.11
Mean TAS (SD)	2.6 (1)	2.3 (1)	0.18
Mean Q12 OKS (SD)	3.2 (1)	2.8 (1)	0.10
Mean improvement OKS (SD)	13.3 (10)	13.2 (10)	0.79
Mean improvement AKSS-O (SD)	20.3 (25)	28.1 (21)	0.19
Mean improvement AKSS-F (SD)	9.2 (24)	5.0 (30)	0.82
Mean improvement TAS (SD)	0.7 (1)	0.6 (1)	0.56
Mean improvement Q12 OKS (SD)	0.9 (1)	0.7 (1)	0.63
10year survival (%) (95%CI)	90 (80 - 100)	98 (93 - 100)	0.84

4.4 Discussion

4.4.1 Partial-thickness cartilage loss in the medial compartment

Following medial OUKA, knees with PTCL in the medial compartment at operation had significantly worse functional outcomes than knees with FTCL bone on bone arthritis, with no evidence of improvement seen over time and this difference maintained to at least five-years postoperatively. A quarter of knees with PTCL reported fair or poor results and a fifth failed to achieve a clinically significant improvement from baseline of four points or more on the OKS, double that seen in knees with FTCL bone on bone arthritis. Whilst no difference in implant survival was detected between groups, knees with PTCL had three times the reoperation rate with the majority, three-quarters, being arthroscopies for unexplained pain.

Knees with PTCL that achieved fair or poor outcomes were significantly younger with worse pre-operative function, compared to those knees with PTCL who did not achieve fair or poor outcomes, however no other differences in baseline demographics were seen. An MRI sub-study in knees with PTCL did not identify any prognostic MRI features. Whilst it must be acknowledged that the sample size in this analysis was small the results are in line with previous studies that have reported that, once disease severity is accounted for, the presence, or absence, of bone marrow oedema within the medial compartment is not associated with outcome following OUKA[205]. Whilst some knees do well, overall knees with PTCL in the medial compartment report significantly worse results, with a higher incidence of reoperations, compared to knees with FTCL in the medial compartment. As, based on patient demographics, or MRI findings we cannot identify which knees with PTCL will do well, knees with PTCL cannot be regarded as optimal for OUKA.

It is not the developer surgeons' practice, as reflected by the low number of cases, to perform OUKA in the setting of PTCL due to previous reported worse functional outcomes. Therefore, the results

of this study represent a highly selected population who, it was believed, would achieve good results. As such the results seen in this study may not be representative of all patients with PTCL who undergo OUKA, and on a population level it is likely that the outcomes of patients with PTCL may well be worse than seen here. As such the results of this study do not support the use of OUKA in the setting of PTCL.

In knees with PTCL in the medial compartment higher variability in functional outcomes has been previously reported, with fewer patients achieving good or excellent results at a mean of two-years (range 1 to 6) postoperatively compared to those knees treated for FTCL[53]. The results of the current study have demonstrated that knees with PTCL, in addition to higher variability in functional outcomes have overall worse functional outcomes that persist to beyond five-years. This finding is contrary to Maier *et al*. who, reporting the outcomes of 32 knees with PTCL at a mean follow-up of 3.5 years (range 0.8 to 6.9) found no difference in functional outcomes, compared to knees managed with OUKA for FTCL. However, Maier *et al*. did find a higher reoperation rate in knees with PTCL, with forty percent of reoperations for unexplained pain, which is consistent with the results of this study [68].

Why patients with PTCL have worse functional outcomes is unclear but may be related to patient or disease factors. One possibility is that patients with PTCL are presenting earlier in their disease process and as such may have different tolerance levels to pain and as such their postoperative recovery may be different[53]. Alternatively, it may be that pain is mediated differently in PTCL, as compared to FTCL. As cartilage does not have a nerve supply, in early osteoarthritis it may be that the pain is predominantly driven by inflammatory mediators as opposed to mechanoreceptors, and as such the response to treatment may be different as the disease progresses[206,207]. Finally, it is known that at post-mortem PTCL is a common finding in the asymptomatic knee and as such it must be acknowledged that despite a complete assessment in some cases of PTCL the pain may be referred other sites and the medial compartment may not be the cause of symptoms.

The strengths of this study are that it is the largest, consecutive, series of patients treated with OUKA for PTCL in the medial compartment with a comprehensive clinical follow-up. The main limitation is that it represents the mid-term follow-up of a highly selected cohort of patients and probably does not represent outcomes of OUKA in the population of patients with PTCL, which may well do worse. Additionally, due to not all patients having MRI this aspect of the study was underpowered and there may be selection bias for this imaging modality. As such a further, appropriately powered, study in a consecutive series of patients with PTCL undergoing OUKA, in which different MRI features and their association with outcomes, is required. In particular the relationship between the presence of a suprapatellar effusion and outcomes may be of particular interest, as in this study a trend towards improved outcomes was observed.

The clinical relevance of this study is that it supports the indication for medial OUKA as proposed by Goodfellow *et al.* which states that there should be FTCL on both the femur and tibia in the medial compartment to achieve optimal results, as in the setting of PTCL worse results are seen[52]. Whilst some knees with PTCL do achieve good and excellent outcomes at present we cannot identify which knees these will be and further work is required to identify biomarkers that may be predictive of outcomes following OUKA in the early arthritis population, however at present based on the results of this study patients with PTCL do not represent optimal candidates for OUKA.

Additionally, as MRI has not been validated for the selection of patients for OUKA, and we and others have identified that it may be misleading on account of false positive assessment of partial-thickness cartilage loss, which this study has identified as having worse results, this study would caution against its use in the assessment of the medial compartment in the workup for OUKA as it may suggest there is full-thickness cartilage loss when there is not.

4.4.2 Anterior cruciate ligament

This study found that the macroscopic status of the intact ACL does not affect long-term functional outcomes or implant survival of the OUKA. In around a third of patients undergoing OUKA the ACL was found to be intact but not macroscopically normal and progressive macroscopic ACL damage was found to be is associated with increasing age, male gender, and a more extensive anteromedial tibial defect. In this cohort there was some evidence that macroscopic ACL damage was associated with lower pre-operative functional scores, with a significantly lower pre-operative AKSS-O score recorded in those knees with longitudinal splits compared to those with those knees with a normal ACL. Following OUKA at ten-years no difference in functional outcome assessed by the OKS and AKSS-O and AKSS-F scores, or in activity level assessed by the TAS was found between groups with those knees with macroscopic ACL damage at the time of operation having a significantly greater improvements in functional status from preoperative, assessed by OKS score, compared to those knees with a normal ACL. At fifteen-years no difference in implant survival, or failure mechanism, was detected between groups.

In the native knee the intact ACL plays a pivotal role in knee kinematics and is important for femoral rollback, the screw-home mechanism and normal gait[208]. In addition the mechanoreceptors within the ACL play a key role in proprioception, loss of which is associated with poor knee function[209]. ACL degeneration is strongly associated with osteoarthritis and a correlation exists between radiological grade of osteoarthritis and degree of degeneration to the ACL[210]. In the native knee ACL injury is associated with instability and a decline in activity[211,212]. Furthermore there is emerging evidence that in patients undergoing TKA, where the ACL is routinely excised, those patients with an intact ACL at the time of surgery have significantly worse functional outcomes post-operatively compared to those with those with pre-existing ACL deficiency[213]. This evidence, together with studies

reporting improved functional outcomes in ACL preserving procedures such as UKA, compared to TKA, would support that, if intact, the ACL should be preserved[214,215].

This study has found that provided the ACL is not friable and fragmented or absent, as assessed at the time of surgery, the macroscopic status of the ACL should not be considered a contraindication to OUKA. Furthermore the evidence suggests that those patients with marked macroscopic damage may benefit more than those patients with a macroscopically normal ACL by virtue of their significantly lower pre-operative functional scores and greater improvement from baseline score at ten-years.

The strengths of this study are that it represents a large, consecutive series of patients undergoing OUKA, with standardised patient selection and surgical management, and comprehensive, independent, long-term follow-up. One of the limitations of this study is that the results are based on macroscopic ACL status which is a crude measurement of ACL integrity. Nonetheless we feel the results are valid as pre-operative imaging of the ACL has poor sensitivity and specificity at assessing the status of the ACL and histological data would not be practical to obtain. Furthermore macroscopic status is clinically relevant and practical to obtain ensuring that the results of this study can be applied directly to clinical practice. Other limitations are that the size of the reciprocal femoral defect was not measured, which is in part due the operative technique leaving the femoral samples sub-optimal for analysis, and that the follow-up protocol did not include any objective assessment to assess for ACL rupture. Whilst this remains a limitation, if ACL rupture did occur it would either have been symptomatic, leading to complications which would have affected the clinical assessment, or alternatively it would have been asymptomatic in which case it would have been of no consequence.

This study has demonstrated that macroscopic damage to the intact ACL is associated with a larger anteromedial tibial defect and may be associated with worse pre-operative function. However

excellent long-term functional outcomes and survival can be seen following OUKA provided that the ACL is demonstrated to be intact at the time of surgery by direct assessment with a ligament hook regardless of its macroscopic status.

4.4.3 Lateral osteophytes

This study demonstrated that the presence of lateral osteophytes does not affect long-term functional outcomes or implant survival following OUKA. In around two-thirds of knees undergoing OUKA, lateral osteophytes were observed and 18% of these were large Grade 3 osteophytes. Increasing incidence and size of lateral osteophytes was associated with younger age at joint arthroplasty and increased BMI, with those knees that had Grade 3 osteophytes also having a higher grade of macroscopic ACL damage at the time of operation, compared to those without osteophytes.

At ten-years no difference in functional outcome assessed by the OKS and AKSS-O and AKSS-F scores, or in activity level assessed by the TAS was found between knees without lateral osteophytes and knees with lateral osteophytes (Grade 1 – 3) or on subgroup analysis of those knees with large (Grade 3) osteophytes. At fifteen-years no difference in implant survival, or failure mechanism, was detected between groups. In knees with Grade 3 lateral osteophytes there was only one failure with the fifteen-year survival calculated as 98% (95%CI 83 to 100). Whilst, due to the small number of knees (50) in this group, caution must be taken with interpretation of this results, this finding provides further support that lateral osteophytes should not be seen as a contraindication to medial OUKA in the setting of full-thickness lateral cartilage at baseline.

Assessing whether location of osteophytes influenced outcomes at ten-years no difference in OKS, AKSS-F or TAS was seen between groups. Whilst the AKSS-O was found to be lower in knees with lateral femoral osteophytes compared to other groups the small number of knees in this subgroup

with ten-year functional results limits the strength of this finding. As no difference in improvement from baseline to ten-years was seen between this, and other groups and no difference in implant survival was observed at fifteen-years, this group does not appear to have worse outcomes and as such, whilst further studies are warranted, the current evidence does not support restricting OUKA in these cases.

The results of this study are supported by the results of a previous case-control study investigating the aetiology of lateral compartment disease progression following OUKA which identified lateral osteophytes in 42% of controls which did not have lateral progression (lateral compartment Kellgren Lawrence Grade 1) demonstrating that lateral osteophytes are common and are not synonymous with lateral compartment disease[75]. Whilst in this study increasing Kellgren Lawrence grade in the lateral compartment was associated with lateral compartment disease progression it must be noted that in this study it is not reported whether knees were scored Kellgren Lawrence grade 2 and above on account of the presence of lateral osteophytes or joint space narrowing as either or both of these features may present to achieve such a score.

The results of this study suggest that the presence of lateral osteophytes represents a general manifestation of disease, rather than a compartment specific indicator of damage. In this series it was interesting to note that younger age at joint arthroplasty and increased BMI were both associated with an increasing size and incidence of lateral osteophytes. The reasons for this association are unclear, however metabolic syndrome (body mass index (BMI) ≥ 30 kg/m^2 with two out of three of: hypertension, insulin resistance or dyslipidemia) has been reported to be associated with increased osteophyte formation secondary to increased pro-inflammatory cytokine activity [81]. Cytokines interlukin-6 (IL-6) and tumour necrosis factor–alpha (TNF-α), which are associated with osteophyte formation, have previously been correlated with pain scores and as such it may be an increased pro-inflammatory cytokine burden, as opposed to the presence of lateral osteophytes, which we have demonstrated to be asymptomatic following OUKA, that leads patients to seek

surgery sooner rather than later[216-218]. In addition to lateral osteophytes intraarticular pro-inflammatory cytokines may result in notch osteophyte formation which may explain the increasing macroscopic ACL damage seen to be associated with the presence of large Grade 3 lateral osteophytes in this study.

In this study all patients satisfied the indications for medial OUKA and had AMOA with full-thickness lateral cartilage at baseline. In this situation lateral osteophytes do not compromise the outcome and therefore they should not be considered to be a contraindication and can be ignored. The clinical relevance of this study is that it highlights the importance of ensuring that when performing OUKA an appropriate assessment of the lateral compartment is performed to ensure there is full-thickness lateral cartilage which will be discussed further in **Chapter 5**.

The strengths of this study are that it represents a large series of patients undergoing OUKA, with standardised patient selection and surgical management, and comprehensive, independent, long-term follow-up. Limitations of the study are that the results represent those of the developer surgeons and further correlation of these results is required. Additionally, whilst the lateral compartment was inspected visually at the time of operation no formal pre-operative assessment of the status of this compartment was undertaken. Finally, due the relatively small number of knee with Grade 3 lateral osteophytes (50 knees) it must be acknowledged that the study is underpowered to detect small, but potentially clinically relevant, differences in this subpopulation of knees with large osteophytes.

The clinical relevance of this study is that it highlights the importance of an appropriate assessment of the lateral compartment as in the setting of full-thickness cartilage at operation lateral osteophytes do not compromise long-term functional outcome or implant survival.

4.4.4 Patellofemoral joint disease

This study has demonstrated that neither the presence of anterior knee pain, radiographic medial PFJ disease or intra-operative exposed bone at the medial patella facet influence the long-term functional outcome or implant survival following medial OUKA and as such these factors should not be regarded as contraindications for this procedure. In the presence of radiographic lateral PFJ and intra-operative exposed bone at the lateral patella facet this study found that whilst the improvement from baseline function was less, for OKS and Q12 OKS (In the last four weeks could you walk down a flight of stairs) respectively, compared to those knees with no lateral PFJ disease, no difference in absolute functional outcomes scores was seen. As such these findings, coupled with evidence of no difference in implant survival suggests that lateral PFJ disease may not represent an absolute contraindication to OUKA.

This study builds on short term functional outcome data which has previously provided evidence that, unlike fixed-bearing UKA, for OUKA anterior knee pain, radiographic medial facet PFJ disease and intra-operative exposed bone at the medial patella facet are not contraindications[50,18686]. The data presented here conflicts with the early results from this case series which found that knees with lateral radiographic PFJ disease had significantly worse improvements from baseline function as well as absolute functional outcome at two-years post-operatively, as this study, at a mean follow-up of ten-years, found no difference in absolute scores based on clinical, radiographic or intra-operative assessment.

The results of this study are reassuring, as not only were revision rates found to be low in the setting of anterior knee pain or medial or lateral facet PFJ disease but also no failures were reported to be due to PFJ disease. In one revised patient who reported anterior knee pain pre-operatively partial-thickness cartilage loss in the medial facet and superficial damage in the lateral facet was noted at the time of index operation. Following their index procedure the anterior knee pain resolved and

achieved a significant improvement in knee function prior to developing lateral progression for which they were revised to primary TKA at 6.9 years. At the time of revision surgery, whilst Outerbridge Grade III changes were noted at the patellofemoral joint, a decision was not made to resurface the PFJ and this patient has made a good post-operative recovery highlighting the lack of correlation between PFJ degenerative change and knee function.

Why PFJ disease does not affect functional outcomes or survival following OUKA is unclear and may relate to disease and implant factors[86]. Whilst cross-sectional studies of patients with knee pain have demonstrated an incidence of radiographic PFJ disease in 30% of those aged 34 to 55 post-mortem studies have demonstrated that significant PFJ disease can occur in individuals who had not previously reported knee pain[206,219]. As such it is likely that many cases of PFJ disease are likely asymptomatic. This argument is supported by findings that the location of pre-operative pain does not correlate with the pattern and severity of intraarticular PFJ disease and that this study has found that PFJ disease does not influence post-operative outcomes following OUKA[87,88].

Implant design may be another reason why the OUKA appears to be PFJ friendly with, as identified in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**), revision for PFJ symptoms being rare. Due to the inlay spherical design of the femoral component the anterior part of the component does not impinge on the patella, which contrasts with onlay fixed-bearing designs where this can happen, and revision for PFJ problems is common, particularly in the second decade[132,220]. Additionally, the OUKA has been reported to maintain normal knee kinematics and as such avoids overloading of the PFJ which is seen in other implant designs[22].

In addition to disease and implant design factors, other factors in assuring good outcomes in the setting of PFJ disease may include operative factors, such as the removal of patella, trochlear or tibial anvil osteophytes which are undertaken as part of the OUKA procedure may be responsible for the resolution in symptoms. Additionally, restoration of pre-disease limb alignment, as is

achieved with OUKA, would be expected to restore pre-disease patella tracking which may serve to mitigate any future complications and permit normal function of the PFJ[88].

Limitations in the present study are that whilst the study was powered to address the primary outcome of the impact of different patterns and grades of PFJ arthritis as assessed intra-operatively the relatively small numbers of patients with lateral patella facet full-thickness cartilage loss (51 knees) gives an increased risk of a Type 1 error decreasing the certainty with which we are able to exclude a small, but potentially clinically relevant, difference in outcomes in this sub population. Additionally, this study was not adequately powered to assess the impact of structural change, as assessed radiologically by the Ahlback Score, on outcomes. Whilst analysis based on Altman scores and the presence of anterior knee pain assessed clinically, were adequately powered again the sample size was small giving an increased risk of a Type 1 error. Other limitations are that no specific assessment for the presence of anterior knee pain was performed at last follow-up and also repeat radiographic analysis of the PFJ was not performed to assess for radiographic progression of PFJ disease. This was not performed as skyline views do not form part of radiographic follow-up and, whilst the presence, or absence of radiographic PFJ progression is of interest it is the clinical outcomes that are the most clinically relevant.

Overall this study found that neither the presence of anterior knee pain, radiographic medial PFJ disease nor intra-operative exposed bone at the medial patella facet influence the long-term functional outcome or implant survival following medial OUKA. Whilst radiographic lateral PFJ disease and intra-operative exposed bone at the lateral patella facet, were associated with smaller improvements from baseline function for OKS, compared to those knees with no lateral PFJ disease, no difference in absolute functional outcomes scores or implant survival was seen. These findings provide evidence that the status of the PFJ should not be regarded as a contraindication for OUKA.

4.5 Summary

This chapter has explored whether various disease factors, including PTCL, macroscopic ACL disease, lateral osteophytes and PFJ disease influence the outcomes of OUKA.

The most significant findings of this chapter is that knees with PTCL in the medial compartment at operation had significantly worse functional outcomes at one, two and five-years post-operatively with a quarter of knees with PTCL reporting fair or poor results and a fifth failing to achieve a clinically significant functional improvements from baseline status, double that seen in knees with FTCL bone on bone arthritis. This finding, coupled with the finding that knees with PTCL had almost three times the reoperation rate, predominantly for unexplained pain, supports the view that medial OUKA should be reserved for patients with FTCL in the medial compartment. Whilst some patients with PTCL do achieve good results, at present, based on patient demographics, and MRI, we cannot identify which these will be and as such OUKA cannot be advised in this situation. Further work is required to confirm these findings and to try to identify biomarkers that may be predictive of outcomes following OUKA in the early arthritis population.

This chapter also identified that, provided the ACL was functionally intact, and not friable and fragmented or absent, then the macroscopic status of the intact ACL does not influence functional outcome at ten-years or implant survival at fifteen-years and as such should not be seen as a contraindication to OUKA.

Additionally this chapter identified that whilst in the setting of AMOA lateral osteophytes are common, and associated with younger age at joint arthroplasty, in the setting of full-thickness lateral cartilage their presence does not influence ten-year functional outcomes or fifteen-year implant survival of OUKA and as such do not represent a contraindication to medial OUKA.

Finally this chapter identified that found that neither the presence of anterior knee pain, radiographic medial PFJ disease nor intra-operative exposed bone at the medial patella facet influence the ten-year functional outcome or fifteen-year implant survival following medial OUKA. Whilst radiographic lateral PFJ disease and intra-operative exposed bone at the lateral patella facet, were associated with smaller improvements from baseline function for OKS, compared to those knees with no lateral PFJ disease, no difference in absolute functional outcomes scores or implant survival was seen. As such these findings provide evidence that the status of the PFJ should not be regarded as a contraindication for medial OUKA.

Chapter 5 Optimum radiographic assessment of the knee

5.1 Introduction

In **Chapter 3** it was identified that the previously published patient factor contraindications based on the patient age (<60 years), weight (≥82kg) and activity level (high activity) do not influence outcomes, provided disease factors are standardised. Moreover if these thresholds had been applied to the developer surgeons' series there would have been a decrease in caseload and usage which, as outlined in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**), would likely be associated with worse outcomes.

Based on the long-term data presented in **Chapters 2** and **Chapter 4** the evidence suggests that to achieve optimum outcomes the decision to proceed with OUKA should be based on the pathoanatomy of disease. Specifically the patient should have bone on bone arthritis in the medial compartment, a functionally intact, but not necessarily macroscopically normal ACL, preserved full-thickness lateral cartilage, a functionally intact MCL, and the absence of bone loss with grooving to the lateral patella facet.

Radiographic methods of assessment of the ACL, MCL and patellofemoral joint were reviewed in **Chapter 1** (**1.2.4 Imaging in unicompartmental knee arthroplasty**) and have been confirmed in recent analysis[13,110,117]. As such this chapter focuses on the optimum assessment of the medial and lateral tibiofemoral compartments. To do this the role of standing full extension view (SEV) radiographs, standing fixed flexion 20° view (FFV20) radiographs, standing fixed flexion 45° view (FFV45) radiographs, as well as varus and valgus stress radiographs in the assessment of the medial and lateral tibiofemoral compartments of the knee was examined by performing a fluoroscopic study, as well as assessing their performance in clinical practice.

5.2 Fluoroscopic Study

5.2.1 Patients and methods

To define the optimum radiographic assessment of the medial and lateral tibiofemoral compartments within the arthritic knee a fluoroscopic study was undertaken (Ethics Reference: South Central – Oxford B REC 15/SC/0476; **Appendix 4**). The aim of the study was to assess the accuracy of different radiographic views at demonstrating cartilage loss and joint space narrowing assessed by measurement of joint space width (JSW) within the medial and lateral compartments of the knee.

Participants aged 50 years and older with radiographic evidence of knee arthritis were considered eligible for the study. Participants with a history of high tibial osteotomy or previous intra-articular fracture were excluded as it was felt that these may present difficulty in image interpretation due to changes in the tibial slope.

Under fluoroscopic guidance standing SEV, FFV20, FFV45 and supine varus and valgus stress radiographs at 20° flexion were obtained with the fluoroscope beam aligned parallel to the tibial plateau. A 25 mm calibration ball was used in all images sited at the level of the fibula head.

Images were measured using custom measuring software (Matlab, Massachusetts, USA). To reduce bias, analysis was performed in a random order with the assessor blinded to the acquisition method.

As not all patients underwent arthroscopy or arthrotomy direct assessment of the joint, which represents the gold standard, was not possible and as such for this study manual, clinician performed, stress views were defined as the standard for comparison.

5.2.2 Statistical methods

A previous study evaluating the reliability of different radiology techniques at detecting changes in JSW in knees, using a distribution based approach, proposed a minimum clinically important difference in the medial compartment JSW between two radiographs in patients with osteoarthritis to be 0.64 mm with a population standard deviation of 0.32 mm[221]. Using a power analysis for a sample paired means test at a power of 0.9 and significance level of 0.01 the required sample size was calculated as eight knees.

To assess for differences in JSW seen on SEV, FFV20, FFV45 and varus and valgus stress radiographs paired Student t-tests were performed. To assess for linear correlation between JSW seen with the different views the Pearson's correlation coefficient was calculated. As linear correlation assesses the strength of a relationship between two variables, and not the agreement between them, to compare the accuracy and agreement of the different views statistical methods for assessing agreement between two methods of clinical measurement as described by Bland and Altman were used with manual, clinician performed, stress views defined as the gold standard for comparison[222,223].

A p-value of < 0.05 was deemed statistically significant with no adjustment being made for multiple testing due to *a priori* hypothesised associations between increased force and decreased JSW[224].

5.2.3 Results

Fluoroscopic evaluation was undertaken on eight knees, all female. The mean age was 68 years (range 63 to 75).

5.2.3.1 Assessment of the medial compartment

The mean medial compartment JSW on manual, clinician performed, varus stress radiographs was 2.9 mm (SD 2.5). In the standing position, in full extension (SEV), the mean medial compartment JSW was significantly greater at 4.8 mm (SD 2.9; $p = 0.005$). Upon flexing to 20° (FFV20), compared to full extension, a significant reduction of medial JSW was seen (mean difference 2.0 mm (95%CI 0.9 to 3.1 mm); $p = 0.004$). Upon flexing to 45° (FFV45), compared to 20° flexion, the medial JSW increased by a mean 1.2 mm (95%CI -0.5 to 2.9 mm) however this was not statistically significant ($p = 0.14$). No difference was observed between medial JSW measured between the SEV and FFV45 (mean difference 0.78 mm (95%CI -1.1 to 2.6 mm); $p = 0.36$) (**Figure 5.1**).

Compared to the medial JSW observed on manual, clinician performed, varus stress the JSW on SEV was significantly greater (mean difference 1.8 mm (95%CI 0.8 to 2.9 mm); $p = 0.005$). No difference was observed in medial JSW between manual, clinician performed, varus stress and FFV20 radiographs (mean difference -0.2 mm (95%CI -0.8 to 0.3 mm); $p = 0.40$) or FFV45 radiographs (mean difference 1.1 mm (95%CI -0.5 to 2.7 mm); $p = 0.16$) (**Figure 5.1**).

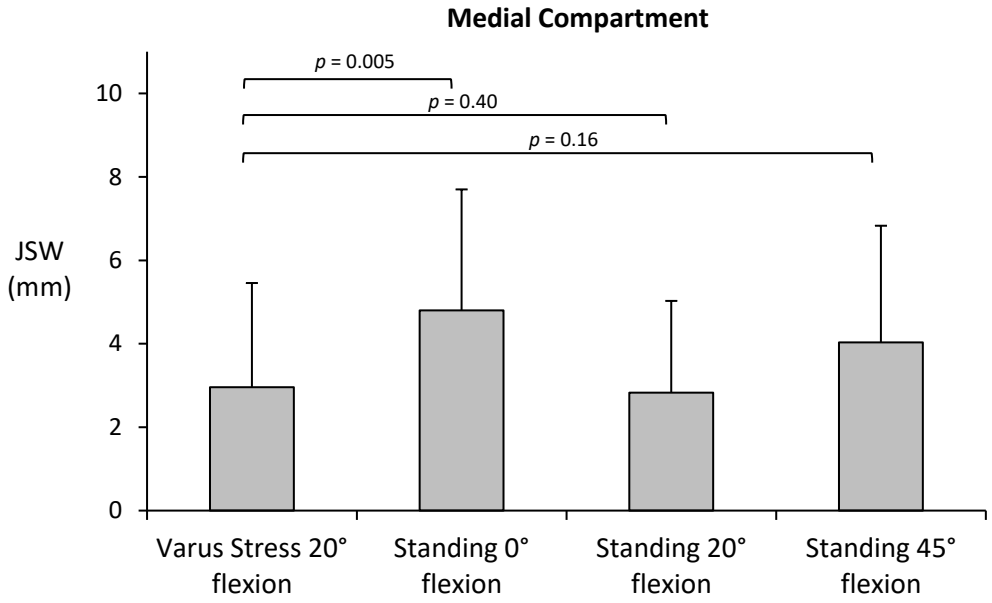


Figure 5.1: Medial compartment joint space width assessed using different radiographic techniques.

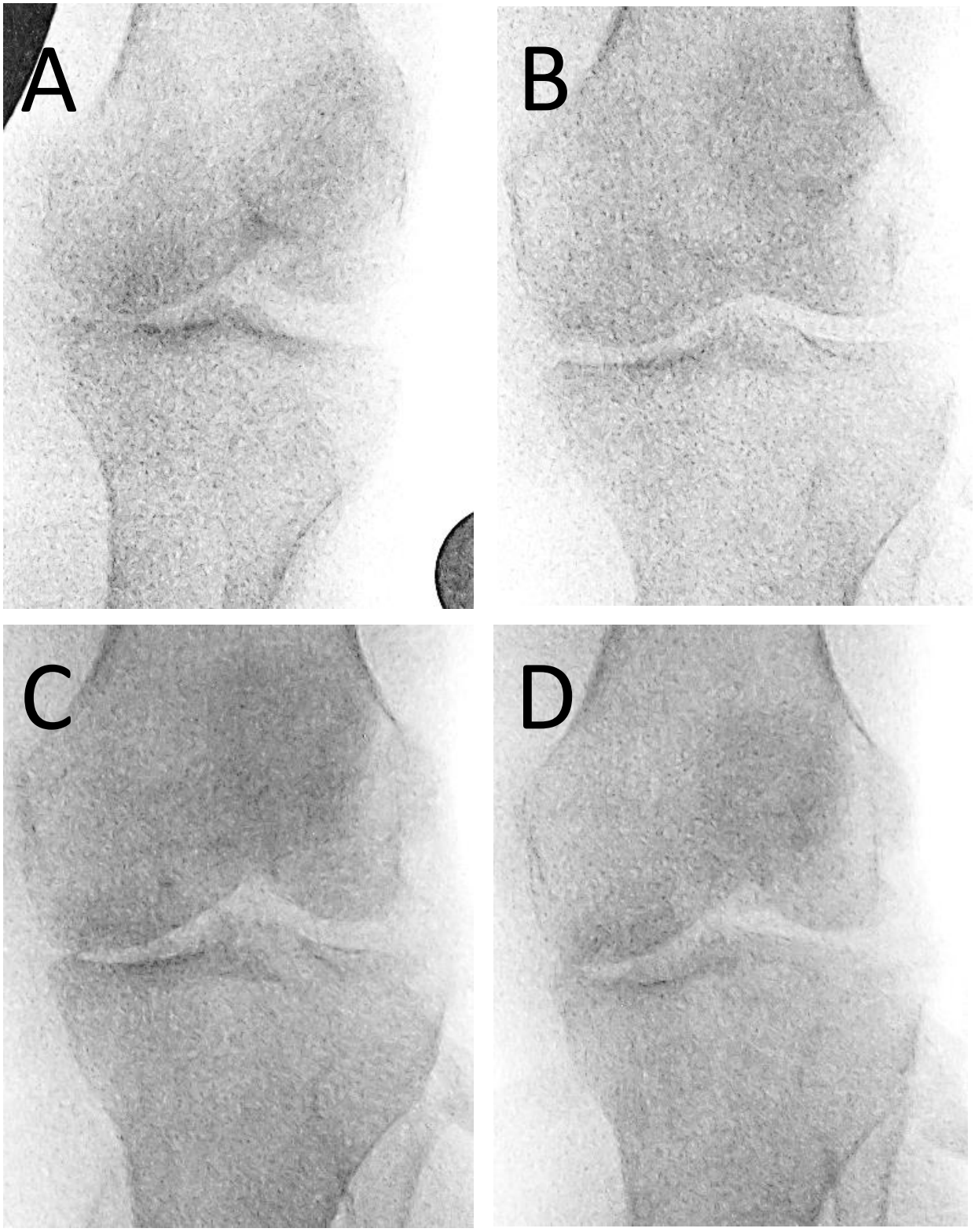


Figure 5.2: Left knee medial compartment joint space width assessed using different radiographic techniques. A: Varus Stress. B: Standing 0° flexion. C: Standing 20° flexion. D: Standing 45° flexion. Medial compartment joint space width obliterated on all but standing 0° flexion view (B).

Medial compartment JSW measured on manual, clinician performed, varus stress radiographs correlated strongly with medial JSW measured on SEV (ρ = 0.90; p = 0.002), FFV20 (ρ = 0.96; p < 0.001) and FFV 45 (ρ = 0.74; p = 0.04) (**Figure 5.3**).

Bland-Altman analysis demonstrated that SEV radiographs underestimated the medial JSW by -1.84 mm (95%CI -2.91 to -0.78 mm) compared to manual, clinician performed, varus stress, whereas no difference in medial JSW was seen between FFV20 (mean difference -0.22 mm (95%CI -0.35 to 0.79 mm) and FFV45 (mean difference -1.07 mm (95%CI -2.68 to 0.53 mm) and varus stress radiographs with FFV20 having the best performance compared to the gold standard of clinician performed varus stress radiograph (**Figure 5.4** and **Table 5.1**).

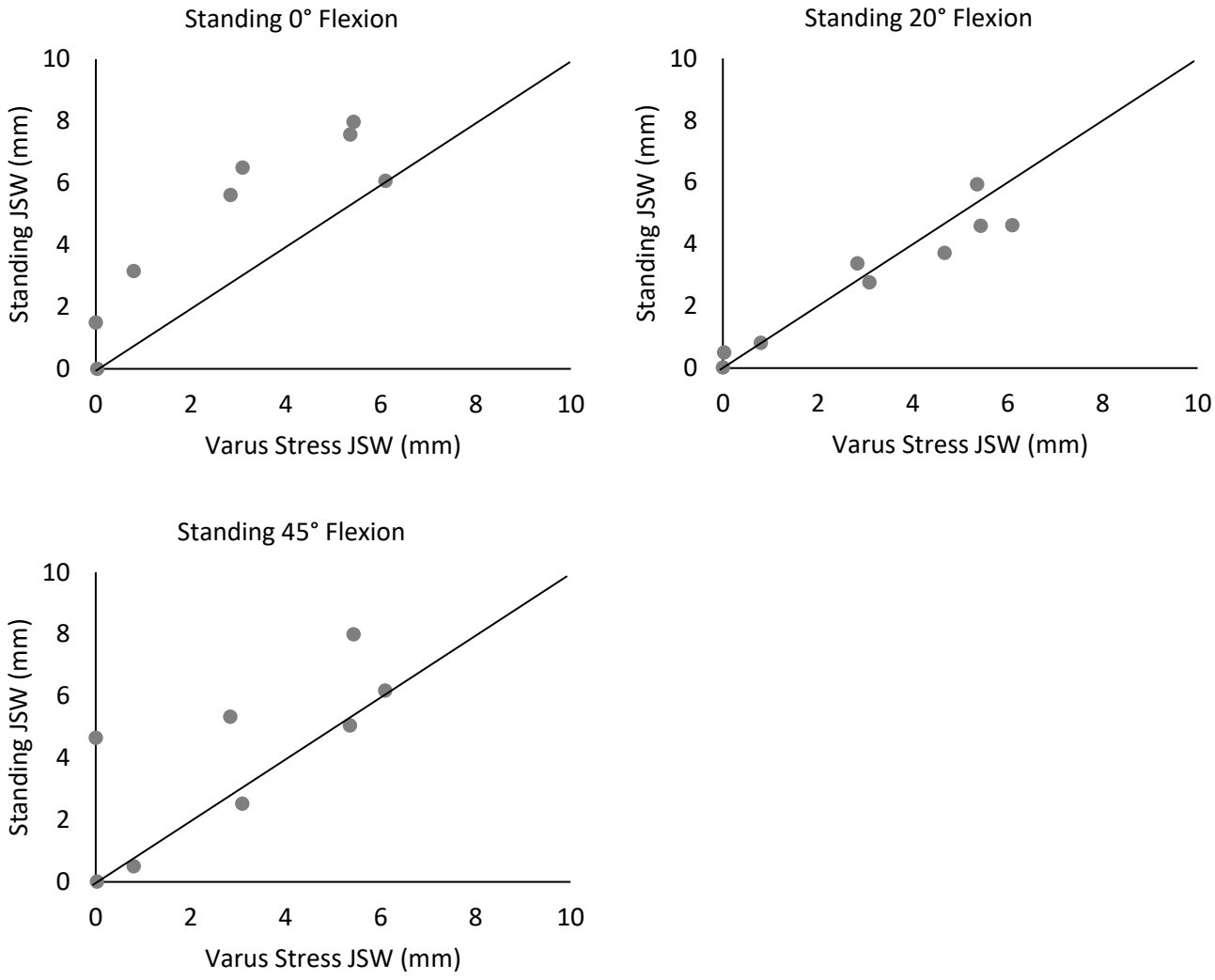


Figure 5.3: Scatter plot comparing medial joint space width measured on varus stress compared with medial JSW at varying degrees of knee flexion. A strong positive correlation between medial compartment joint space width measured on varus stress radiographs and standing extension view ($p = 0.002$), fixed-flexion 20° view ($p < 0.001$) and fixed-flexion 45° view ($p = 0.04$) radiographs was observed. Line x=y.

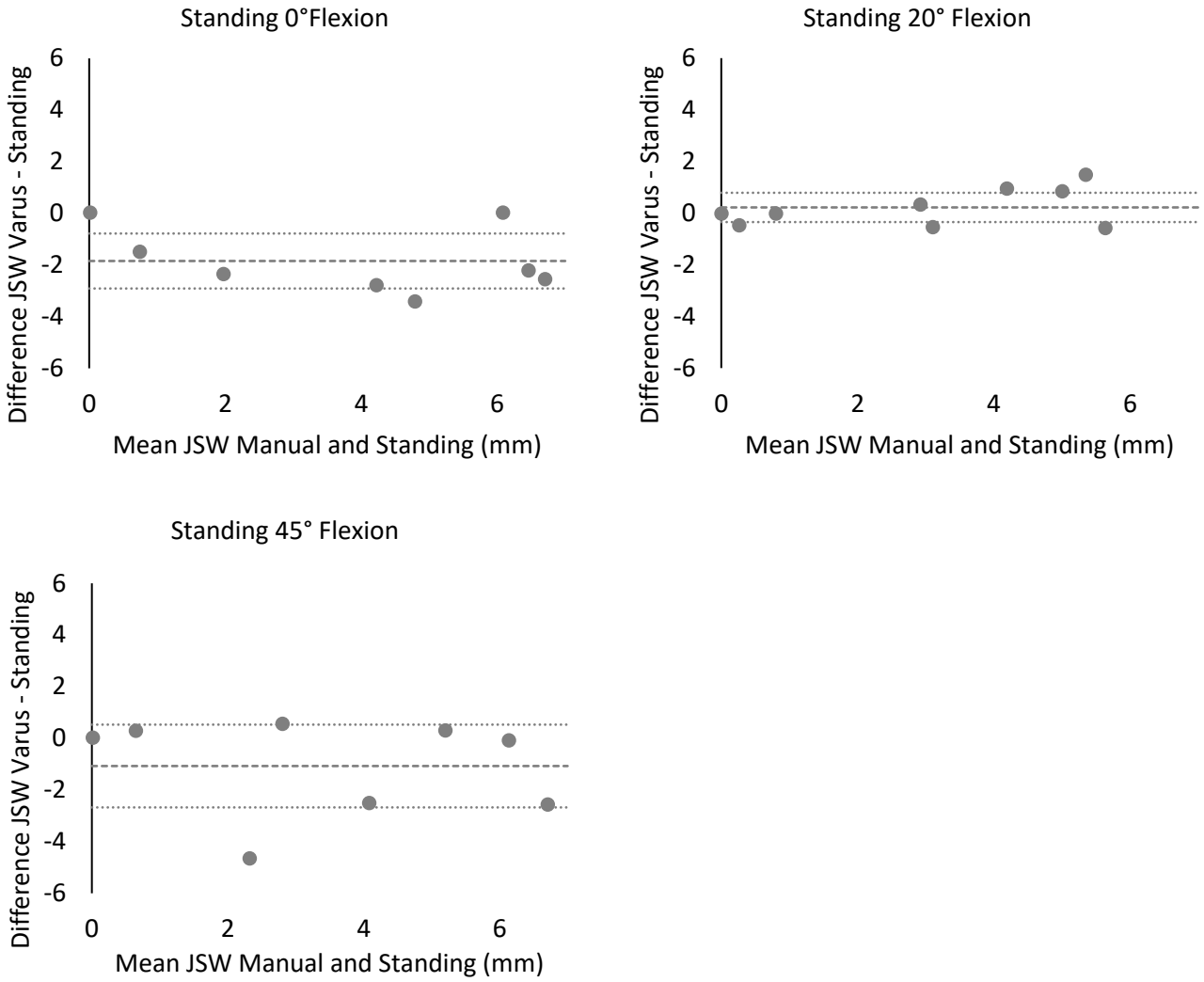


Figure 5.4: Bland-Altman plot comparing medial joint space width measured on varus stress compared with medial JSW at varying degrees of knee flexion. Mean estimates of agreement with 95% confidence intervals displayed.

Table 5.1: Bland-Altman estimates of agreement for the difference between medial JSW measured on varus stress of the knee compared with medial JSW at varying degrees of knee flexion.

	Mean Difference (mm)	95% CI
Standing 0° Flexion	-1.84	-2.91 to -0.78
Standing 20° Flexion	-0.22	-0.35 to 0.79
Standing 45° Flexion	-1.07	-2.68 to 0.53

5.2.3.2 Assessment of the lateral compartment

The mean lateral compartment JSW on manual, clinician performed, valgus stress was 7.2 mm (1.3SD). In the standing position, in full extension (SEV), the mean lateral compartment JSW was significantly greater at 8.8 mm (1.9SD; p = 0.02). Upon flexing to 20° (FFV20), compared to full extension, a significant reduction of lateral JSW was seen (mean difference -1.9 mm (95%CI -0.2 to -0.7 mm); p = 0..4). Upon flexing to 45° (FFV45), compared to FFV20, no difference in lateral JSW was seen (mean difference 0.3 mm (95%CI -0.5 to 1.5 mm); p = 0.54). No difference was observed between lateral JSW measured with SEV and FFV45 views (mean difference -1.6 mm (95%CI -4.1 to 1.0 mm); p = 0.19) (**Figure 5.5**).

Compared to the lateral JSW observed on manual, clinician performed, valgus stress the JSW with SEV was significantly greater (mean difference 1.7 mm (95%CI 0.4 to 3.1 mm); p = 0.2). No difference was observed in lateral JSW between manual, clinician performed, valgus stress and FFV20 (mean difference 0.1 mm (95%CI -0.7 to 1.0 mm); p = 0.74) or FFV45 (mean difference -0.1 mm (95%CI -1.4 to 1.3 mm); p = 0.90) (**Figure 5.5**).

Lateral compartment JSW measured on valgus stress radiographs was not found to be correlated with JSW on SEV (ρ = 0.47; p = 0.20) radiographs. A strong positive correlation between lateral compartment JSW measured on valgus stress radiographs and FFV20 ((ρ = 0.81; p = 0.008) and FFV45 ((ρ = 0.77, p = 0.03) radiographs was observed (**Figure 5.6**).

Bland-Altman analysis demonstrated that SEV radiographs underestimated lateral JSW by -1.7 mm (95%CI -0.38 to -3.08 mm) compared to manual, clinician performed, valgus stress, whereas with FFV20 (mean difference -0.13 mm (95%CI -0.72 to 0.97 mm) and FFV45 radiographs (mean difference -0.08 mm (95%CI -1.44 to 1.29 mm) no difference was seen (**Figure 5.7** and **Table 5.2**).

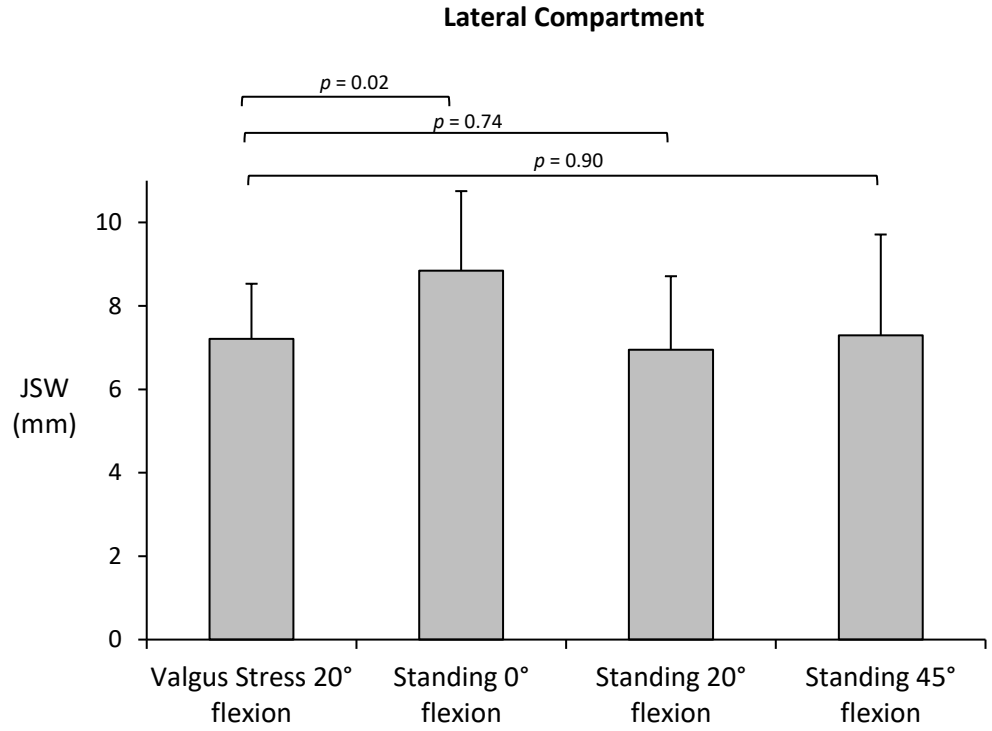


Figure 5.5: Lateral compartment joint space width assessed using different radiographic techniques.

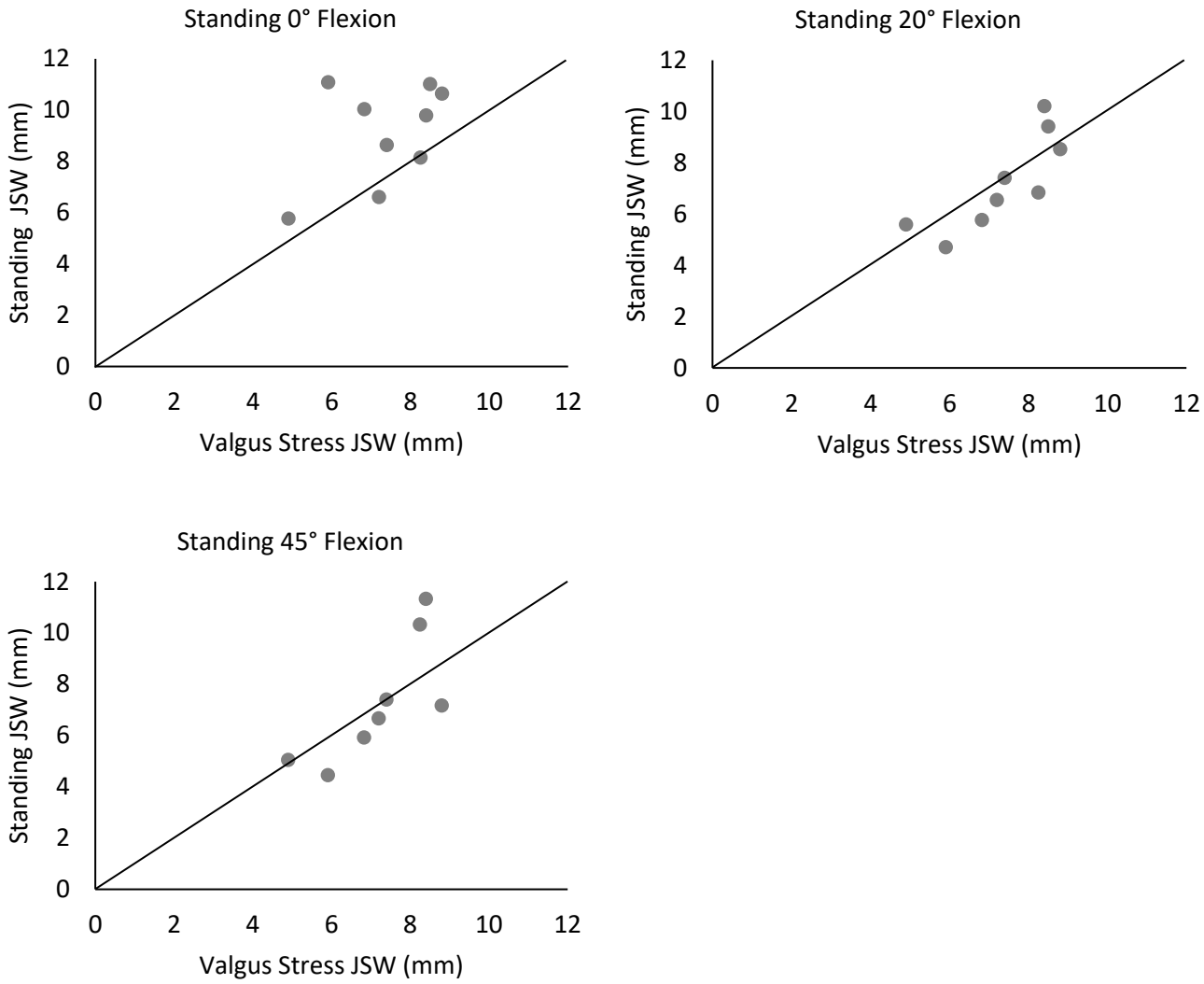


Figure 5.6: Scatter plot comparing lateral joint space width measured on valgus stress compared with lateral joint space width at varying degrees of knee flexion. Lateral compartment joint space width measured on valgus stress radiographs was not found to be correlated with standing extension view (p = 0.20) radiographs. A strong positive correlation between lateral compartment joint space width measured on valgus stress radiographs and fixed-flexion 20° view (p = 0.008) and fixed-flexion 45° view (p = 0.03) radiographs was observed. Line x=y.

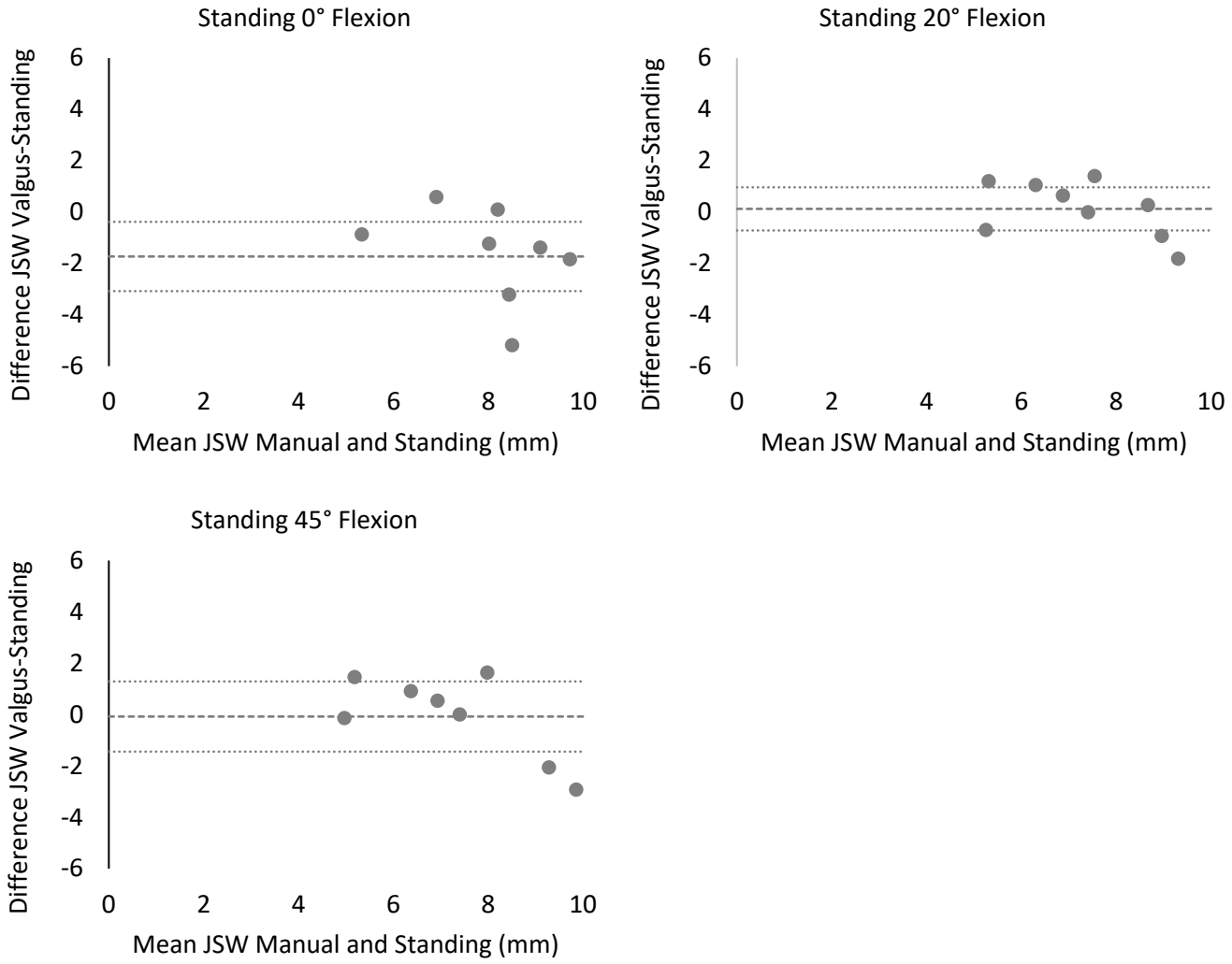


Figure 5.7: Bland-Altman plot comparing lateral JSW measured on valgus stress compared with lateral JSW at varying degrees of knee flexion. Mean estimates of agreement with 95% confidence intervals displayed.

Table 5.2: Bland-Altman estimates of agreement for the difference between lateral JSW measured on valgus stress of the knee compared with lateral JSW at varying degrees of knee flexion.

	Mean Difference (mm)	95% CI
Standing 0° Flexion	-1.73	-3.08 to -0.38
Standing 20° Flexion	0.13	-0.72 to 0.97
Standing 45° Flexion	-0.08	-1.44 to 1.29

5.2.4 Discussion

This study has demonstrated that standing extension view radiographs, which are the most commonly performed in clinical practice, do not provide an appropriate representation of JSW as they underestimate the medial tibiofemoral compartment JSW and overestimate the lateral tibiofemoral compartment JSW, both by around 1.8 mm compared to stress radiographs. The relevance of this with regards to patient selection for OUKA is that in the medial compartment standing extension views are less likely to demonstrate full-thickness cartilage loss, bone on bone arthritis, which in **Chapter 4** (**4.4.1 Partial-thickness cartilage loss in the medial compartment**) was identified as critical to achieve optimum outcomes. In this scenario, when bone on bone is not identified radiographically, often MRI is performed, however, as identified in **Chapter 4** (**4.3.1.5 MRI sub-study of patients with partial-thickness medial compartment disease**) the results of MRI may be misleading in this scenario with MRI findings of FTCL on both the tibia and femur seen in one in three of knees in the partial-thickness cartilage loss cohort.

In this study it was found that for the medial compartment varus stress radiographs at 20° flexion and standing fixed-flexion 20° radiographs (FFV20) had the best performance with no difference in performance seen between the two different acquisition methods. Where full-thickness cartilage loss in the medial compartment is not demonstrated on varus stress radiographs or FFV20, and AMOA is suspected, the results from **Chapter 4** (**4.3.1.5 MRI sub-study of patients with partial-thickness medial compartment disease**) would caution against using MRI to confirm this finding due to its poor performance in this scenario, and arthroscopy with a view to proceeding directly to OUKA where criteria are met should be considered[105].

At 45° flexion (FFV45) there was an increase in medial compartment JSW and whilst this did not reach statistical significance the greater variance in medial JSW measurements seen at this degree of flexion limits the clinical application of this technique. The increase in medial JSW and increase

in variance seen at 45° flexion likely relate to the pathoanatomy of disease. It has previously been reported that in AMOA the centre of the medial lesion is typically seen at 10.9° flexion (SD 3.5°), expanding posteriorly as the size of the lesion increases with, on average, the posterior edge of the anteromedial lesion being at 24.1° flexion[12]. As such at 45° flexion those patients with small to medium anteromedial lesions will see an increase in medial JSW at this flexion angle as the femur will be articulating with preserved posterior tibial cartilage, with only those with an extensive anteromedial lesions articulating within, or on, the margins of the chondral defect.

A further consideration as to why a reduced JSW may be seen on flexion may be in part due to increased force across the joint secondary to engagement of the quadriceps mechanism, however as maximal force occurs at 45° flexion, with this study finding an increased JSW at this degree of flexion, the influence of quadriceps contraction is viewed to be minimal.

These results of this study remain consistent with cross sectional studies in moderate to severe osteoarthritis which have reported a 1.3 mm difference in 1102 Japanese knees and 0.7 mm difference in 545 Finnish knees between SEV and FFV[225,226]. In both the Japanese and Finnish studies the flexion angle was not set and as such further refinements in the flexion angle may yield greater differences in JSW. These differences in JSW between standing radiographs taken in full extension and varus stress radiographs or standing radiographs at 20° flexion may also explain why it has been observed that some knees with Kellgren Lawrence 2 and 3 on standing full extension radiographs do well following OUKA as it has been reported that between 19 and 33% of those knees with moderate osteoarthritis (Kellgren Lawrence 2 to 3) on SEV demonstrate medial full-thickness loss of cartilage with obliteration of JSW on FFV radiographs[225-227].

In the lateral compartment the overestimation of JSW means that few cases of lateral compartment disease will be identified, and as the lateral compartment is difficult to assess at operation it may result in inappropriate cases undergoing OUKA. For the lateral compartment it was found that

valgus stress radiographs at 20° flexion and standing radiographs at 20° flexion and 45° flexion had similar performances, although again greater variance in lateral JSW measurements with flexion radiographs in the lateral compartment, as compared to the medial compartment, were noted. The variability may represent variability in the outcomes of the technique or may represent variability in the disease. In the lateral compartment previous work has established the location of the lateral lesion to be a lot more variable with the centre of the lateral tibial cartilage lesion reported to occur at 40.5° flexion with a range from 7.8° to 72.9° flexion[12].

As seen in the medial side, the reductions in lateral JSW between SEV and FFV of the knee have been reported previously, albeit with smaller differences seen in the lateral compartment compared to the medial compartment[226]. Additionally it has been reported that in the lateral compartment fewer knees, 5.6%, demonstrate lateral full-thickness cartilage loss on FFV that has not been evident on SEV[226]. The reasons for this are unclear as to whether the differences are due to differences in the performance of FFV with regards to their sensitivity and specificity at detecting disease, as there was no intra-operative correlation of findings, or whether these differences reflect the lower incidence of lateral compartment disease.

The limitations of this study are that it was performed in a small number of patients, all female, who all had predominantly mild to moderate radiographic medial sided disease with no intra-operative correlation of the radiographic findings performed. The limitations with respect to the medial compartment are that whilst mean JSW was presented, and demonstrated to vary depending on the radiographic technique used, the evidence from **Chapter 4 (4.4.1 Partial-thickness cartilage loss in the medial compartment)** would suggested that the decision to proceed with OUKA is dependent on whether, or not, bone on bone arthritis is demonstrated in the medial compartment as opposed to the degree of cartilage loss as represented by JSW. To investigate the performance of different radiographic techniques based on the presence or absence of radiographic bone on bone arthritis a larger cross sectional study is required, and this will be

presented later in this chapter. The limitations of the study population with respect to the lateral compartment is that none of the study participants had severe medial OA with associated marked varus alignment. The relevance of this is that, as this study has established, on SEV as medial JSW decreases, lateral JSW increases and as such it is in this subgroup that SEV might grossly over estimate lateral JSW compared to valgus stress. Additional limitations are that the performance of valgus stress views at 45° was not assessed on account of the fluoroscopic images performed at this flexion angle not being appropriate for inclusion due to malalignment of the tibial plateau and/or poor image quality secondary to position of the knee relative to the fluoroscopic beam. Nonetheless the results are supported by previous literature and build on this by demonstrating equivalence of varus stress radiographs at 20° flexion and fixed-flexion 20° radiographs for assessment of the medial compartment.

Based on this study it has been established that SEV do not represent the optimum method of assessing either lateral or medial JSW. For the medial compartment this study supports the use of either varus stress radiographs at 20° or FFV20 radiographs with both investigations having equivalent results. For the lateral compartment the findings are less clear as valgus stress radiographs at 20° flexion and FFV20 and FFV45 radiographs all had similar performances, although flexion views had greater variance in lateral JSW measurements with the clinical significance of this being unclear.

5.3 Clinical Study

5.3.1 Patients and methods

To establish the performance of SEV, stress and flexion radiographs in clinical practice a cross sectional study was performed. All patients aged over 40 years who underwent stress radiographs or flexion radiographs and were listed for arthroscopy or arthroplasty by Professor HG Pandit, Mr CAF Dodd or Professor DW Murray between 1 January 2014 and 16 April 2017 were considered eligible for inclusion in the study.

SEV represented the standard of care during the recruitment period. Stress radiographs and standing flexion radiographs were performed on a clinical need basis for the workup of patients with osteoarthritis of the knee. Stress radiographs were performed with the patient supine, knee flexed to approximately 20°, with the radiographic beam alignment parallel to the tibial plateau. Standing flexion radiographs were performed posteroanterior with the patient's patella resting on the detector and the radiographic beam aligned parallel to the tibial plateau. The degree of flexion of the knees was determined by the radiographer. In line with clinical experience, and supported by data presented in this chapter, where bone on bone arthritis was demonstrated in the medial compartment on standing radiographs in full extension varus stress radiographs and standing flexion radiographs were not performed as the knees already met criteria for performing OUKA and these additional views would be expected to also demonstrate bone on bone arthritis.

Pre-operative radiographs were assessed with the assessor blinded to the treatment received. For each radiograph the medial and lateral tibiofemoral compartments were scored independently. Each compartment was scored as either: bone on bone arthritis, partial-thickness cartilage loss (PTCL) or preserved full-thickness cartilage. Bone on bone arthritis was equivalent to OARSI grade

3 tibiofemoral narrowing, PTCL equivalent to OARSI grade 1 and 2 tibiofemoral narrowing and preserved full-thickness cartilage equivalent to OARSI grade 0 tibiofemoral narrowing.

The gold standard to which radiographs were compared was direct visualisation of the medial and lateral tibiofemoral compartments at the time of arthroscopy or arthrotomy which were obtained from our institutional database and review of operation notes.

The key questions this study set out to determine, with respect to patient selection for medial OUKA, were:

- What is the performance of SEV, varus stress and flexion radiographs at identifying bone on bone arthritis in the medial compartment?
- What is the performance of SEV, valgus stress and flexion radiographs at identifying preserved full-thickness cartilage in the lateral compartment?
- What is the optimum radiograph or combination of radiographs to perform and what is its performance at identifying suitability for medial OUKA as determined by bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment?

5.3.2 Statistical analysis

The performance of SEV, stress (varus and valgus) and standing flexion radiographs at predicting bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment was determined using standard, binary classification, methods to assess performance (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy).

5.3.3 Results

Between 1 January 2014 and 16 April 2017, 306 patients were included in the study. The mean age of patients was 67.4 years (range 41.8 to 97.3). Medial OUKA was performed in 217 (70.9%), lateral UKA in 48 (15.7%), TKA in 35 (11.4%) and 6 (1.9%) underwent arthroscopy. SEV radiographs were available in 297 knees (97.1%), stress radiographs in 143 knees (46.7%; varus 101 knees, 33.0%; valgus 136 knees, 44.4%) and standing flexion radiographs in 61 knees (19.9%).

The performance of the different radiographs at identifying bone on bone arthritis in the medial compartment and full-thickness preserved cartilage in the lateral compartment is outlined in **Table 5.3** and **Table 5.4**.

In this cohort the prevalence of medial compartment bone on bone arthritis was 79%. For the medial compartment the sensitivity at identifying bone on bone arthritis of SEV was 62%, indicating that SEV identified 62 of 100 knees with bone on bone arthritis. The sensitivity of varus stress radiographs and standing flexion radiographs was 95%, indicating that they identified 95 of 100 knees with bone on bone arthritis.

In this cohort the prevalence of lateral compartment disease, PTCL or bone on bone arthritis was 26%. For the lateral compartment the specificity at identifying full-thickness preserved cartilage was 62% for SEV, 79% for valgus stress radiographs and 53% for standing flexion radiographs. These results indicate that out of 100 knees without full-thickness preserved cartilage, *i.e.* inappropriate for medial OUKA, SEV would identify 62 of them, valgus stress radiographs 79 of them and standing flexion radiographs 53 of them.

Based on this analysis the optimum views to establish bone on bone arthritis in the medial compartment would be either varus stress radiograph or standing flexion radiographs and the optimum view to identify preserved full-thickness cartilage in the lateral compartment would be the valgus stress radiograph. The performance of a combination of these views at identifying

suitability for medial OUKA as determined by bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment is outlined in **Table 5.5**.

Table 5.3: Performance of standing full extension, varus stress and standing flexion radiographs at identifying bone on bone arthritis in the medial compartment.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Standing full extension	62	100	100	40	70
Varus stress	95	95	99	64	95
Standing flexion	95	100	100	52	95

Table 5.4: Performance of standing full extension, valgus stress radiographs and standing flexion radiographs at identifying preserved full-thickness cartilage in the lateral compartment.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Standing full extension	99	62	88	96	89
Valgus stress	100	79	96	100	97
Standing flexion	98	53	86	89	86

Table 5.5: The performance of a different techniques at identifying suitability for medial OUKA as determined by bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Standing extension radiographs	64	89	94	50	71
Fixed-flexion radiographs	82	85	95	58	83
Varus/valgus stress radiographs	92	89	96	79	91

5.3.4 Discussion

This study has built on the fluoroscopic study and demonstrated that, in clinical practice, standing radiographs have a poor sensitivity, 62%, at identifying bone on bone arthritis in the medial compartment and that the optimum assessment of this compartment is either a varus stress radiograph or standing flexion radiographs whose sensitivity was found to be 95%. With regards to the lateral compartment the optimum views to identify preserved full-thickness cartilage was found to be the valgus stress radiograph. Whilst standing flexion radiographs were found to have a high sensitivity, 98%, their specificity was found to be low, 53%, indicating that standing flexion radiographs have a high false positive rate, 47%. This data builds on the fluoroscopic study which found high variance in the measurement of lateral joint space width with standing flexion radiographs, particularly at 45° flexion.

To explain why a high false positive rate for preserved full-thickness cartilage is seen with standing flexion radiographs it is worth considering how flexion radiographs work. First we must consider Ahlback's original observation that when a patient with medial osteoarthritis moves from supine to standing, in addition to narrowing of the medial JSW a reciprocal widening of the lateral compartment is seen[100]. Then, pairing this with the observation that in many patients with advanced AMOA an ulcer is seen on the medial aspect of the lateral femoral condyle, this would suggest that as arthritis progresses in one compartment, typically the medial compartment, the femur impinges of the tibial spine resulting in relative unloading of the lateral compartment. Thus single flexion angle flexion radiographs may be unable to demonstrate bi-compartmental disease.

To support this argument the performance of standing flexion radiographs in different disease patterns can be assessed. In knees with purely lateral compartment disease (all grades) and a preserved medial compartment the specificity of standing flexion views at identifying full-thickness preserved cartilage was 89% indicating that out of 100 knees without full-thickness preserved

cartilage, *i.e.* inappropriate for medial OUKA, standing flexion views would identify 89 out of 100. This contrasts with knees with bi-compartmental disease where the specificity was 0%, indicating that in this scenario flexion views are unable to identify lateral compartment disease (**Figure 5.8**).

In general bi-compartmental disease will be visible on plain standing extension radiographs in a high proportion of knees and flexion or stress views would not be indicated in these cases. However, in some knees, 7% in this study, bi-compartmental disease was not be visible on SEV and in this scenario the results of standing flexion radiographs may be misleading. This study indicates that valgus stress radiographs represent the optimum assessment method for the lateral compartment in this population, as without these views it is not possible to identify, in the presence of medial compartment disease whether there is lateral compartment disease or not.

There are limitations to this study. Firstly, the population chosen in which to perform this study was all patients who based on their initial standing full extension radiographs may have be considered candidates for OUKA. This population was selected as it represents the clinical population in which the decision around appropriateness for OUKA is made. Whilst inclusion criteria could have included all patients with symptoms of OA, this would not have reflected the clinical question being asked in the study. Secondly, as clinical correlation was required, there was a requirement for all patients to have undergone operative intervention, arthroscopy or arthrotomy. As radiographic findings, particularly those of PTCL, may affect a surgeon's decision to operate it must be acknowledged that this may affect the results seen. Thirdly, in this study all radiographic views were not conducted in all knees due to time restrictions in the radiology department and as such a direct comparison of techniques has not been possible. Finally, the SEV and flexion radiographs were not standardised with regards to degree of flexion of the knee as due to fixed flexion deformity being common in osteoarthritis not all patients may have been able to achieve full extension, which like the degree of flexion for flexion radiographs, which as reviewed in the first part of this chapter, may influence the measurement of JSW.

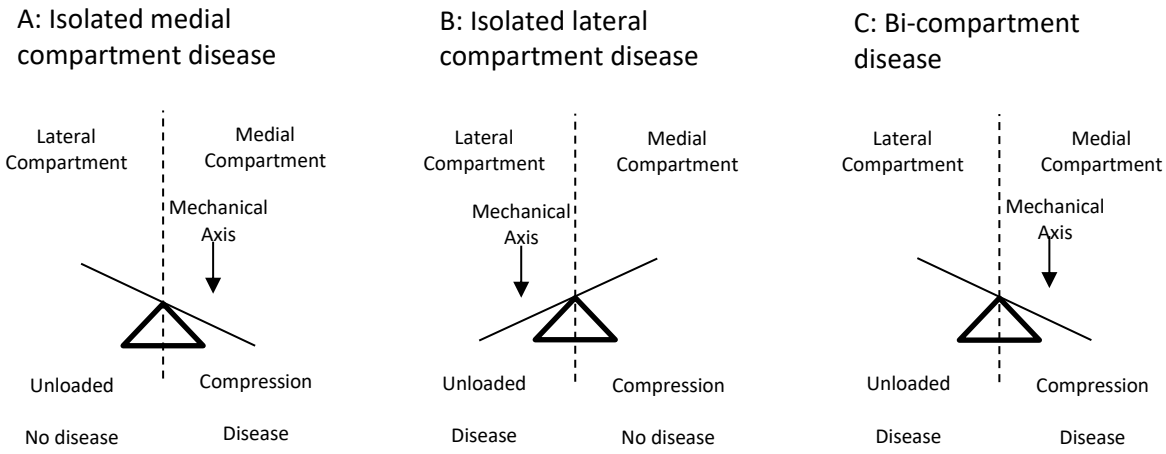


Figure 5.8: Schematic diagram of forces within the knee in medial (A), lateral (B) and bi-compartmental disease (C) during flexion radiographs. It is hypothesised that in true unicompartmental disease the diseased compartment is under compression secondary to a shift in the mechanical axis of the limb whereas in bi-compartmental disease the mechanical axis remains in the medial compartment resulting In the lateral compartment being unloaded resulting in poor performance of flexion views in this scenario.

Whilst a detailed fluoroscopic study of the role of flexion views at both 20° and 45° flexion in patients with bi-compartmental disease, not visible on standing full extension radiographs, would help confirm the findings reported in this study, as this scenario is relatively rare, it would be anticipated that recruitment would be difficult.

Overall, this study has found that the optimum radiograph to identify bone on bone arthritis in the medial compartment is either a varus stress radiograph or standing flexion radiographs, with both radiographic techniques considered to be equivalent. For the lateral compartment, to identify preserved full-thickness cartilage, the optimum view was found to be the valgus stress radiograph. When a combination of these views is performed, and suitability for medial OUKA defined as the presence of bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment, the overall accuracy was found to be 91%.

5.4 Summary

This chapter has identified that standing radiographs in full extension do not represent the optimum radiographic assessment of either the medial or lateral tibiofemoral compartments as they under estimate JSW by around 1.8 mm and have a low accuracy at detecting bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment.

For the medial compartment to identify bone on bone arthritis either varus stress radiograph or standing flexion radiographs, both at 20° flexion, should be used. For the lateral compartment to identify preserved full-thickness cartilage valgus stress radiographs should be used, with a combination of these views being 91% accurate at determining bone on bone arthritis in the medial compartment and preserved full-thickness cartilage in the lateral compartment, and as such suitability for OUKA.

Chapter 6 Development and validation of a novel stress device for applying valgus and varus stress to the knee

6.1 Introduction

As has been highlighted in **Chapter 5** varus and valgus stress radiographs can assist in assessing the pattern and severity of arthritis within the knee. Despite stress radiographs being recommended for the workup for UKA, in the UK only 17% of surgeons report using them in clinical practice[95,228].

One of the limiting factors associated with the use of stress radiographs is that they are resource and training dependent. Typically they require a surgeon trained in the technique to attend the radiology department which may divert their attention away from other clinical duties, adding to the cost and time to acquire these images. Additionally, there is a risk of harmful cumulative radiation exposure to medical staff if stress radiographs are performed regularly.

This chapter will discuss alternatives to manual, clinician applied, varus and valgus stress and discuss the development and validation of a novel stress device for the knee.

6.2 Review of existing stress devices

To establish what alternative methods to clinician applied varus and valgus stress existed a comprehensive search was performed to identify commercially available methods of applying varus and valgus stress to the knee. Searches identified three current methods:

- Patient Directed Valgus Stress Radiographs (2016)[229]
- Telos Stress Device (1977)[230]
- Varus Valgus Stress Device (2010)[231]

6.2.1 Patient directed valgus stress radiographs

Inventors: Cook KD & Mauerhan DR

Year: 2016

Country: USA

Description: With the patient supine, knees flexed over a 163 mm high triangular foam bolster, a 279 mm diameter ball coated in a nonslip surface is placed between the patient's legs, just proximal to the ankles, with their heels resting on the examination table. The radiographic tube is angled cephalad 7° to 10°, centered on the inferior pole of the patella. The knee is rotated such that the patella is anterior.

The patient is asked to adduct their legs, to squeeze the ball, while maintaining contact of heels with the table. The radiograph is taken whilst the patient is applying maximal force.

Validation: In 75 of 78 examinations (96%) the findings of the patient directed valgus stress radiographs matched the findings of a manually performed valgus stress (lateral compartment: full-thickness loss, partial-thickness loss or preserved). In 3 of 78 examinations (4%) the patient-directed stress did not adequately correct the varus deformity, which was correctable on manually performed valgus stress.

Using manually performed valgus stress as the gold standard in this series 72 examinations demonstrated preserved lateral cartilage, 3 lateral compartment disease and 2 shortening of the MCL with incomplete correction of the deformity.

Reference: Mauerhan DR, Cook KD, Botts TD, Williams ST. Patient-Directed Valgus Stress Radiograph of the Knee: A New and Novel Technique. American Journal of Orthopedics (2016) 45:44-6[229]

6.2.2 TELOS Device

Inventor: Tulaszewski O

Year: 1977

Country: Germany

Description: The TELOS (TEchnicaL solutions for OSteosynthesis) device was originally designed to quantitatively assess the ACL and PCL and later modified to assess the LCL and MCL by performing varus and valgus stress. With the patient in a supine position, knee in full extension, posts are used to apply three point fixation. For varus stress two posts are placed on the lateral side of the knee, one proximal to the joint and one distal, and one post is located at the level of the joint on the medial side. The three posts are linked by way of a rigid bar running parallel to the leg permitting a varus stress to be applied by advancing the central post laterally against the knee. A force of 150 Newton is delivered by way of a digital system. A valgus stress is applied by reversing the configuration of the bars.

Validation: No direct comparison with manual stress radiographs performed.

A significant decrease in joint space width with varus and valgus stress radiographs was noted compared to standard weight bearing views

Reference: Tallroth K & Lindholm TS. Stress radiographs in the evaluation of degenerative femorotibial joint disease. Skeletal Radiology (1987) 16:617-620[230]

6.2.3 Varus valgus stress device

Inventor: Osti L

Year: 2010

Country: Australia

Description: With the patient in a supine position, knee flexed to 30° (method not described), a post is clamped to the radiology table at the level of the knee joint to act as a fulcrum. A circumferential strap is applied to the calf distal to the knee joint. The circumferential strap is attached to the edge of the radiology table by way of a further strap running perpendicular to the leg and consisting of a force gauge and tensioner. The tensioner can apply a force up to a maximum of 100 Newton to deliver varus or valgus stress depending on the orientation of the fulcrum and direction of force.

Validation: No direct comparison with manual stress radiographs performed.

A significant decrease in joint space width with varus and valgus stress radiographs was noted compared to standard weight bearing views

Reference: Eriksson K, Sadr-Azodi O, Singh C, Osti L & Bartlett L. Stress radiography for osteoarthritis of the knee: a new technique. KSSTA (2010) 18:1356–1359[231]

6.2.4 Limitations of current devices

Whilst these devices have benefits over manual clinical performed varus and valgus stress they also have some limitations. The patient directed valgus stress radiographs, whilst simple to perform, do not control the amount of force applied and in the validation study for this device in 4% of cases the patient was unable to apply adequate force. In this validation study the incidence of lateral compartment disease was low (4%), meaning that in this population the risk of a patient directed valgus stress radiographs indicating the lateral compartment was full-thickness preserved cartilage when it was not (false positive) was low. If, however, the incidence of lateral compartment disease within the population was higher then this risk would increase substantially.

Whilst the TELOS and Varus Valgus stress devices did provide a reliable mechanism of applying force they were not user friendly due to their bulky designs. Additionally, the forces used were between 100 to 150 Newton's which is quite a lot of load and likely to cause harm as it has previously been reported that patients can report discomfort when and abduction or adduction forces of greater than 40 Newton are applied[232].

As none of the existing methods of performing varus and valgus stress radiographs appeared ideal a decision was made to develop a novel stress device for the knee.

6.3 Medical devices

Any device used in humans for the purpose of diagnosis is considered a medical device with, within the EU, medical devices governed by a series of three directives which came into effect on 1 January 1993. These directives are:

- Active Implantable Medical Devices Directive (AIMDD) 90/385/EEC – covering all powered implants or partially powered implants.
- In-vitro Diagnostic Medical Devices Directive (IVDD) 98/79/EEC – covering devices related to the examination of human specimens, including blood and tissue.
- Medical Devices Directive (MDD) 93/42/EEC – covering all devices related to the diagnosis, prevention, monitoring, treatment or alleviation of disease.

Any medical device destined for the UK market must comply with these regulations, where appropriate, with all trials and applications for regulatory approval conducted in line with guidance from the Medicines and Healthcare products Regulatory Agency (MHRA), the UK body responsible for regulation of medicines and medical devices and enforcement of the medical device directives.

6.4 IDEAL-D Framework

Historically, unlike regulatory approval of pharmaceuticals, approval for medical devices was based on preclinical evidence alone. More recently total product life cycle evaluations have been used in some sectors, including joint arthroplasty where through the 'Beyond Compliance Initiative' preclinical data and post market evaluations by National Joint Registries provide long-term real world data to improve safety and assess efficacy of various interventions. The IDEAL (Idea, Development, Exploration, Assessment, Long-term study) framework is a model, developed by expert consensus, for assessing and reporting new surgical procedures from first use through to adoption into practice[233-236]. Its use has been adapted for medical devices through the IDEAL-D ('D' for device) framework and the development and validation of a novel device for performing varus

and valgus stress radiographs of the knee has been conducted in line with its recommendations[237,238].

The IDEAL-D framework has five stages:

- Stage 0 – Pre-clinical development
- Stage 1 – Idea
- Stage 2 – Development
- Stage 3 – Assessment
- Stage 4 – Long-term studies

6.4.1 Stage 0 – Preclinical development

Prior to commencing device development a patient and public involvement (PPI) session was conducted to identify any patient barriers. PPI identified that when patients attended clinic they had no prior pre-conceptions about what imaging to expect and had faith that their surgeon would obtain imaging that would provide all the necessary information to optimally treat their condition.

Whilst PPI revealed that patients understood that the ultimate decision to proceed with any operation, i.e. UKA as opposed to TKA, was typically made at the time of operation, and that often clinical tests are not 100% sensitive and specific, the group still felt it was important to identify pre-operatively what the likely course of treatment was as this was important for them in order to manage their post-operative expectations as well as plan their rehabilitation.

PPI revealed a preference for imaging modalities that could be performed during the same clinic appointment and ones where the pathology could be indicated to them visually such that they could ‘see what was going on’. Provided it aided diagnosis and treatment, the PPI group did not

have any concerns about additional radiation exposure or additional cost to the health care service though were aware of cost in the broader terms of health care provision.

In addition to PPI, development sessions were also spent with radiographers to discuss their current experience of stress radiographs of the knee and their views on medical device development. All radiographers (*n* = 12) had been involved with varus and valgus stress views of the knee. For the majority their involvement had been conducting the imaging whilst a surgeon applied the stress. A minority (n = 2), one from overseas, and one senior radiographer, had been trained to apply stress to the knee though neither had used this technique recently and it was not part of their present role. A minority (n = 2) of radiographers had used a medical device to perform varus and valgus stress radiographs.

For those radiographers involved in stress views where the surgeon applied the stress, the major concern was the delay in attendance by the surgeon, typically due to them being in clinic. They also reported variability in technique by surgeons, with some approaches appearing more painful than others. For those radiographers who had previously performed stress radiographs, their concern was the cumulative radiation exposure if stress radiographs became a routine part of their role. For those radiographers who had previously used medical devices to perform stress radiographs their concern was that typically these devices were large, locked to the radiology tables, used high forces and were likened by patients and staff to 'torture devices'. It was strongly felt that any device developed should be patient and radiographer friendly to encourage its use.

Finally, surgeons who had experience of performing and interpreting stress radiographs were consulted and they identified that any such device should hold the knee in a degree of flexion and control knee rotation together with having a method of applying controlled varus and valgus force.

Based on these consultations the key attributes to a successful design were identified:

- Ease of use
- Maintenance of knee flexion
- Control of knee rotation
- Controlled application of varus and valgus force
- Comfort

6.4.1.1 Design Considerations

6.4.1.1.1 Preclinical development: Ease of use

One of the major issues identified by radiographers with existing stress devices was that, in general, they are bulky, difficult to store and time consuming to setup. Current devices on the market either apply stress by using a fulcrum secured to the radiology table (Varus Valgus Stress Device), which unlike operating tables are not designed to accommodate clamps, or apply stress by using the principles of three point fixation and linking the three points with a rigid bar (TELOS). By removing need to clamp the device to the table and/or have components linked by a rigid bar significant savings both in terms of the size and complexity of device could be achieved.

To design around this issue two methods were evaluated. The first method involved developing a condensed version of the three point fixation method and the second involved using the contralateral leg. For the first method a jig was developed that consisted of a circumferential strap for the distal femur and circumferential strap for the proximal tibia linked by rigid bars with a 20° bend in their mid-portion at which point was located a method of applying a controlled force. The jig was designed to be securely fastened to the knee with femur and tibia strap equidistant from

the knee joint such that the joint was held in 20° flexion with alternating force form the medial side applying a varus force and from the lateral side applying a valgus force. (**Figure 6.1**).

Preliminary preclinical testing of this device revealed that when a force was applied, external rotation, rather than varus stress, and internal rotation, rather than valgus stress resulted. The reason for this is because, unlike when the leg is held in full extension, once the knee is flexed to 20° any force applied at the knee joint flexion results in a moment around the axis between the proximal and distal fixed points as opposed to a true varus or valgus force (**Figure 6.2**).

Due to the limitations of using the three point fixation method to apply force instead, focus was turned to using the contralateral leg. To apply a varus force the initial design revolved around placing a wedge proximal to the knee joint between the thighs and bringing both legs together and thus using the contralateral limb as a fixed point, whilst for valgus stress rather than fixing the knee and abducting the distal tibia, as is typically done with manual stress to permit using the contralateral leg as a relatively fixed point, a decision was made to fix the distal tibia and adduct the knee, thus resulting in a valgus stress (**Figure 6.3**). Using a prototype device the concept of using the contralateral leg to apply force underwent preclinical testing.

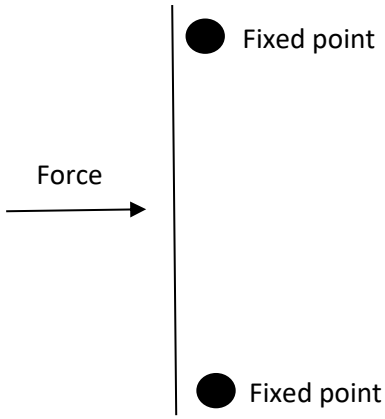


Figure 6.1: Method of applying varus and valgus force using three point fixation.

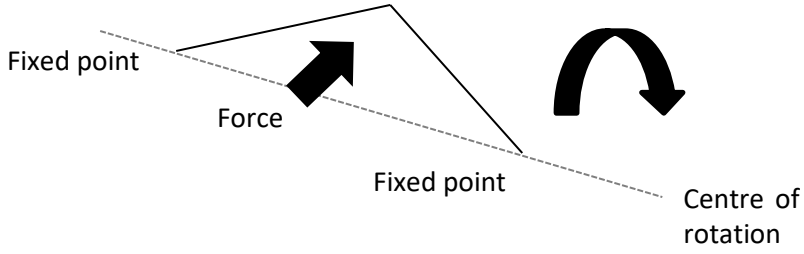


Figure 6.2: Limitations of applying valgus and varus force using three point fixation to the flexed knee. In flexion varus force to the knee results in internal rotation around the axis of rotation which runs between the proximal distal and distal fixed points and valgus results in external rotation.

6.4.1.1.2 Preclinical development: Varus stress

For the varus stress, as seen with the three point fixation method, when the distal tibia were adducted together using a simple strap, there was a tendency for the force to result in external rotation as opposed to varus force. By keeping the ankle dorsiflexed and maintaining the foot in 5° to 10° degree of internal rotation the risk of external rotation during the application of varus force was decreased, however to increase reliability of this technique it was felt that an engineered solution to control rotation of the limb during varus stress was required.

Initial consideration was paid to the use of a strap proximal to the knee, however this did not adequately control rotation, and so attention was switched to more distal constraints. Whilst the use of a boot-like application was considered it was felt that this would compromise the overall design aim of developing a simplistic device and therefore alternative ideas were explored. Initial designs developed to apply an adduction force to the midfoot held some promise but were only effective when the foot was held rigidly in dorsiflexion, due the mobility of the midfoot, requiring a cooperative participant. Ultimately a strap was developed that can be applied whilst the patient is supine, holds the ankle in dorsiflexion and applies adduction with internal rotation when tightened (**Figure 6.4**).

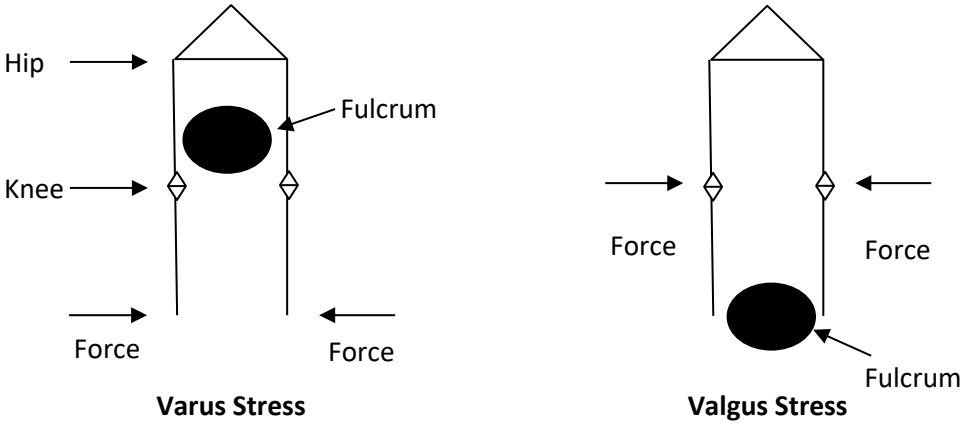


Figure 6.3: Concept of varus and valgus stress using the contralateral leg.

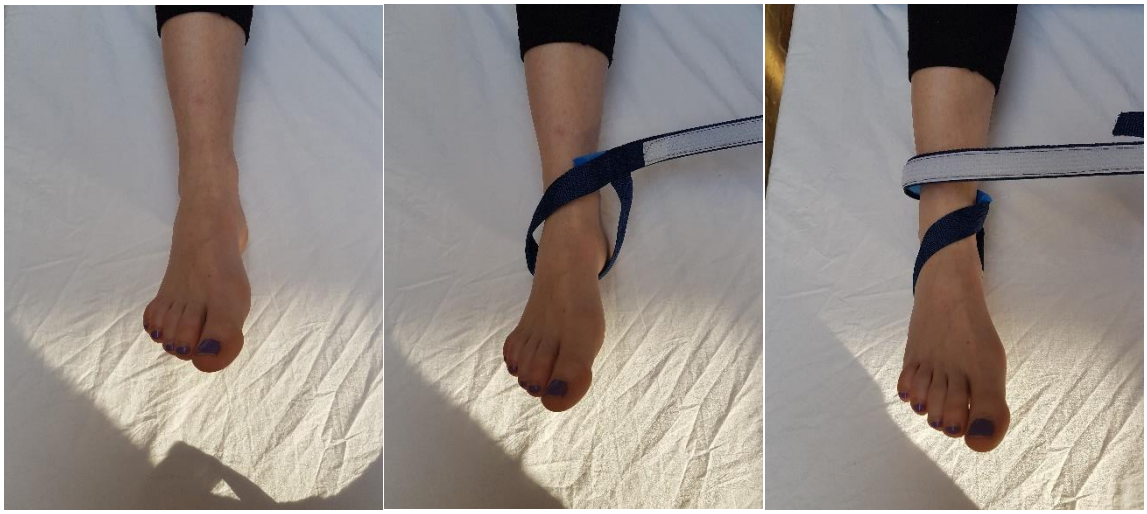


Figure 6.4: Ankle Strap. The loop is placed over the foot with a strap that passes circumferentially behind the ankle from the medial side before running anterior to the ankle and connecting centrally to a reciprocal strap on the contralateral side.

6.4.1.1.3 Preclinical development: Valgus stress

For the valgus stress, as seen with the three point fixation method, when the knees are adducted together using a simple strap, there is a tendency for the leg to internally rotate resulting in loss of valgus stress. As with the application of varus stress it was felt that this was best dealt with by controlling the limb distally and so cutouts in the foot block were made to hold the ankle dorsiflexed and the feet externally rotated. In preclinical testing rotating the feet controlled the internal rotation when a stress was applied in the majority of participants. However, in younger females with perceived greater ligamentous laxity and/or hip anteversion, internal rotation persisted and it was clear that further interventions were required to control the rotation of the limb. Therefore, attention was paid to the method of applying force, which at that time was a simple circumferential strap proximal to the knee joint fastened and tightened anteriorly. As the strap was tightened it would not only apply an adduction force to the knee, but also an internal rotation force to one limb, which was increased at higher forces where there was increased friction between the skin and the strap (**Figure 6.5**). By fastening and tightening the strap at the posterior aspect of the knees the force was converted to an external rotation force on one limb but in practical terms this position of the strap was impractical as well as resulting in an asymmetrical force being applied (**Figure 6.6**).

As such a strap that fastened at the front, but tightened symmetrically at the rear was developed such that, in addition to adduction, an external rotation moment was applied. The combination of this strap and external rotation of the feet in the foot blocks resulted in no issues with internal rotation during preclinical testing (**Figure 6.7**).

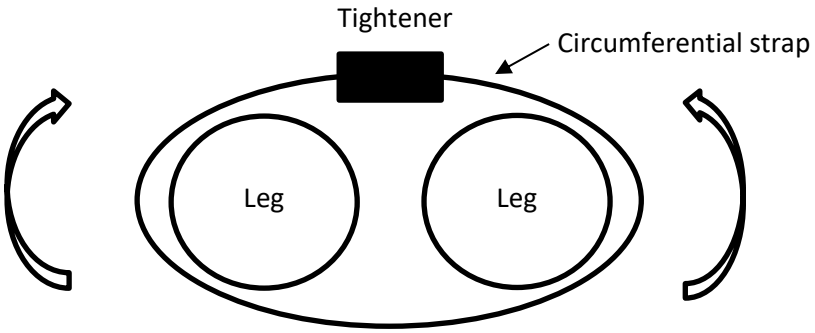


Figure 6.5: Circumferential strap tightening anteriorly. When a circumferential strap is applied around the legs and tightened anteriorly it results in internal rotation of the legs.

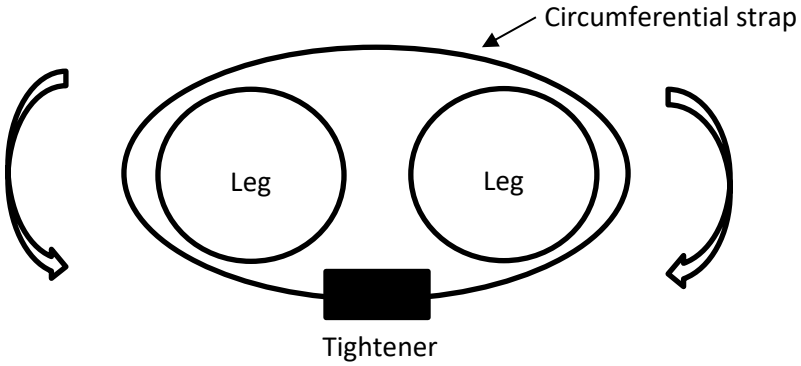


Figure 6.6: Circumferential strap tightening posteriorly. When a circumferential strap is applied around the legs and tightened posteriorly it results in external rotation of the legs however tightening posteriorly is impractical.

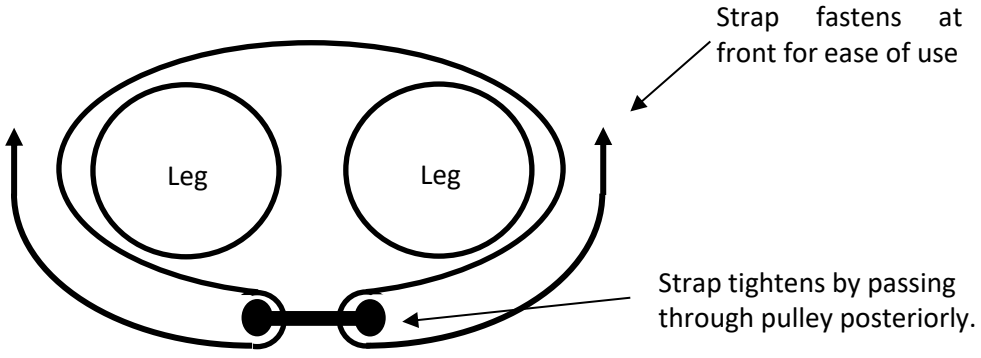


Figure 6.7: Novel strap to overcome the impracticality of tightening posteriorly. A strap was developed that tightens posteriorly and fastens anteriorly resulting in external rotation during tightening when applying a valgus force to resist the risk of internal rotation when applying a valgus force to a flexed knee.

6.4.1.1.4 Preclinical development: Controlled application of force

Various methods of force application were considered, including preloaded straps, however for simplicity and to comply the requirements of the Medical Devices Directive (MDD) 93/42/EEC that any medical device should fail safely and in a manner that does not result in harm, a decision to use a spring balance that would indicate when the correct force had been applied was chosen with the correct force to be defined during Stage 2 testing.

6.4.1.2 Approvals for use in the clinical environment

Once a prototype device had been developed and met all preclinical testing requirements it was reviewed by infection control, manual handling and radiology who all indicated that they had no concerns about its use. The MHRA were contacted to confirm that as the device had been developed and would be used in-house that the Medical Devices Regulations would not apply and MHRA authorisation would not be required for proof of concept clinical testing. Finally Directorate Approval for proof of concept clinical testing was sought and granted.

6.4.2 Stage 1 – Idea: Proof of concept

With consent the stress device was evaluated between 01 October 2014 and 01 October 2015 in a 50 of patients as part of their workup for knee arthroplasty. Based on this experience several modifications to the design were made.

6.4.2.1 Materials

To comply with infection control regulations the initial prototype, which was made of foam, had been coated in adhesive poly vinyl chloride (PVC) which is inert and resistant to cleaning materials. Whilst this material provided good protection to the device it was found during proof of concept testing that its application to the knee bolster did not permit the knees to move during the application of valgus stress as the back of the knees would become stuck to the plastic due to perspiration. As a result higher forces, than anticipated during preclinical testing, were required to stress the knee.

The ideal material for the bolster needed to be radiolucent, safe for contact against skin, non-absorbable, compatible with abrasive cleaners used in patient areas, and permit movement of the knees during the application of stress to the knee. Closed cell ethylene vinyl acetate foam (Evazote) has a long history of use in medical devices and positioning aids as well as for shin pads, knee pads and mouth guards. Ethylene vinyl acetate foams are latex-free, non-toxic and hypoallergenic and we are not aware of any reported complications arising from skin contact. Furthermore ethylene vinyl acetate foams are radiolucent (and MRI lucent) and as such will not result in interference with currently used imaging protocols or require an increased dosage for imaging. Ethylene vinyl acetate foams are also lightweight, soft to touch as well as compatible with existing infection control policies as they are closed cell in nature are non-absorbable and do not react with current cleaning products.

6.4.2.2 Density of bolster

In addition to the types of material used attention was paid to the density of materials. Closed cell ethylene vinyl acetate foam is available from densities from 25kg/m^3 to 80 kg/m^3. Whilst during

preclinical testing, with in general slim legs, the lower density foams provided adequate support to hold the knee in 20° flexion but in clinical testing it was found that in patients with an increased BMI the low density foams did not provide adequate support. In addition to resulting in de-standardisation of the technique, the lack of support provided by the low density foam led to difficulties in aligning the X-ray beam with the tibial plateau, with the alignment of the beam 10° rostral found to be consistent where adequate support to the back of the knee was provided. After evaluation a 50kg/m^3 density foam was selected as this was found to provide adequate support, yet remained comfortable for patients.

6.4.2.3 Positioning of straps for valgus stress

During preclinical development and initial proof of concept testing when performing a valgus stress the circumferential straps were applied and tightened proximal to the knee joint as, due to the distal tibia being fixed, it was felt that the more proximal the application of the strap the greater the lever arm and as such this would permit a greater valgus force to be applied to the knee. During proof of concept testing it became clear in some participants that, in addition to a valgus force being applied, the device was also resulting in lateral subluxation of their tibia on their femur (**Figure 6.8**). To manage this the straps were applied distal to the knee and this effect was removed (**Figure 6.9**).

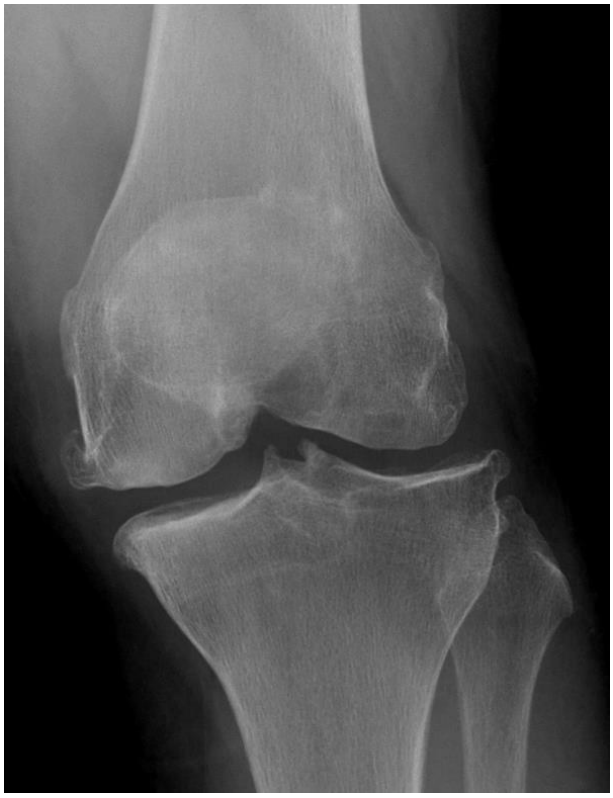


Figure 6.8: Subluxation of femur on tibia on application of stress when circumferential strap passes proximal to the knee.

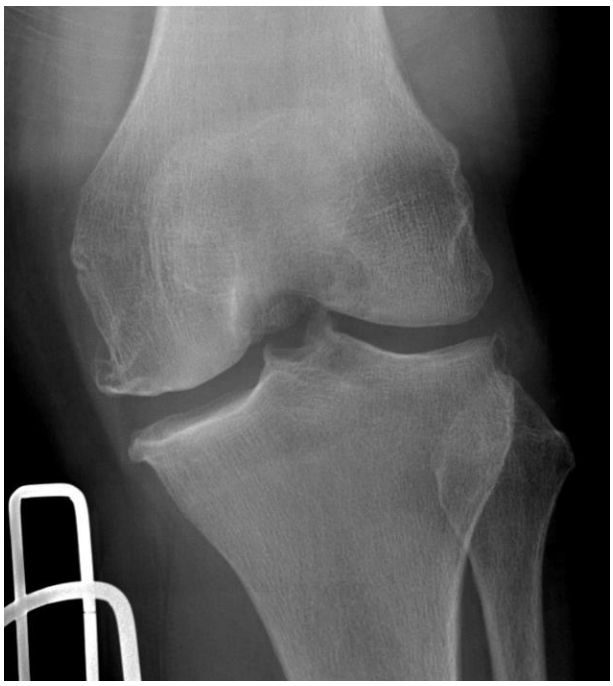


Figure 6.9: No subluxation of femur on tibia on application of stress when circumferential strap passes distal to the knee.

6.4.2.4 Modularity of the system

A final development point taken from proof of concept testing was that, unlike preclinical testing, significantly more variations in anatomy and body habitus were encountered. This ranged from patients with marked constitutional varus, requiring a further block between their knees when performing a varus stress test, to high BMI patients that required the foot block to be wider between their legs to give space between their knees to permit a valgus stress to be applied by the device. This variation in anatomy and body habitus led to the design being moved towards a modular system with additional blocks available, where required, for particular clinical scenarios. In addition, the separate shaped blocks for valgus and varus stress were joined together to permit them being used for one role in one position and another role when turned 90°.

6.4.2.5 Novel stress device for the application of varus and valgus stress to the knee

At the end of preclinical testing a further device was made incorporating the necessary modifications identified in proof of concept testing. The device taken forward for clinical evaluation consisted of five components:

- Component 1: Triangular Bolster
- Component 2: Shaped blocks
- Component 3: Square blocks
- Component 4: Foot strap
- Component 5: Knee strap

Figure 6.10: Stress Device: Component 1 (Triangular Bolster). This bolster rests behind the knees to passively position them in 20° flexion.

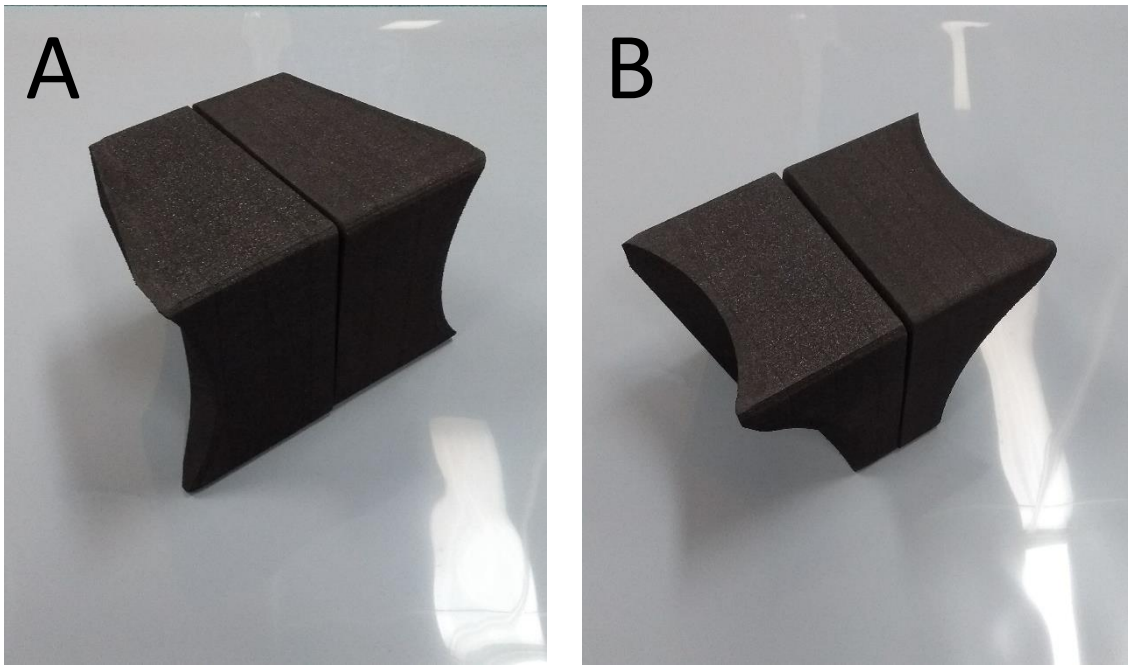


Figure 6.11: Stress Device: Component 2 (Shaped Blocks). These rectangular shaped blocks are mirror images of one another with imprints on either side designed to engage with the inside of the thigh just proximal to the knee for the application of varus stress (A), and with the feet and ankles for the application of valgus stress (B).

Figure 6.12: Stress Device: Component 3 (Square Block). These square blocks are designed to fit between the shaped blocks as required to accommodate variations in anatomy and body habitus.

Figure 6.13: Stress Device: Component 4 (Foot Strap). This is a strap configured in a 'figure-of-eight' shape with a central mechanism to permit tensioning. The loops at the end of the strap are passed over the feet with the straps pointing medially. The straps are passed circumferentially around the posterior of the ankle before moving anterior and then medially to engage with the tensioning component in the midline. The tensioning component, which has been designed to permit simultaneous tensioning of both sides, consists of a spring balance which will indicate when an appropriate force (to be determined in Stage 2 development) has been applied.

Figure 6.14: Stress Device: Component 5 (Knee strap). This strap has been designed to fasten anteriorly and tension posteriorly. The tensioning component, which has been designed to permit simultaneous tensioning of both sides, consists of a spring balance which will indicate when an appropriate force (to be determined in Stage 2 development) has been applied.

6.4.2.6 Instructions for use

Once a prototype device had been developed, instructions for its use in performing varus and valgus stress were standardised as follows:

6.4.2.6.1 Varus stress

1. With the patient supine and the knees resting on the apex of the triangular bolster the shaped blocks are placed between the knees.
2. The loop of the right foot strap is placed over the right foot with the tail of the strap directed medially. The strap is then passed circumferentially around the ankle starting posteriorly and running from medial to lateral before emerging anteriorly and passing towards the midline. The left foot strap is applied in a similar manner.
3. The ankle should be dorsiflexed and internally rotated to 5° and resting on the radiology table.
4. The straps are passed into the tensioner, tightened and secured to apply a varus force.
5. Rotational alignment of the leg is confirmed by the user to ensure the tibial tubercles are facing anteriorly.
6. The X-ray beam is directed 10 degrees cephalic in the coronal plane, centered on the knee.
7. The X-ray is taken.
8. The X-ray is assessed prior to the strap and knee block being removed to ensure it is aligned parallel to the tibial plateau and in neutral rotation. If the X-ray is mal-aligned the image should be repeated.

6.4.2.6.2 Valgus stress

1. With the patient supine, and the knees resting on the apex of the triangular bolster, the shaped blocks together with one modular block are placed between the feet.
2. The ankles should be dorsiflexed and externally rotated 15° and resting on the radiology table.
3. The knee strap is applied circumferentially around both legs, 100 mm distal to the distal pole of the patella.
4. The straps are tightened and secured to apply a valgus force.
5. Alignment of the leg is confirmed by the user to ensure the tibial tubercles are facing anteriorly.
6. The X-ray beam is directed 10 degrees cephalic in the coronal plane, centered on the knee.
7. The X-ray is taken.
8. The X-ray is assessed prior to the strap and knee block being removed to ensure it is aligned parallel to the tibial plateau and in neutral rotation prior to removing the strap around the knee and foot block. If the X-ray is mal-aligned the image should be repeated.

6.4.3 Stage 2 – Development: Fluoroscopic Validation

To validate the device a fluoroscopic validation study was undertaken (Ethics Reference: South Central – Oxford B REC 15/SC/0468 (**Appendix 4**)). The aim of the study was to validate the device against the gold standard of clinician performed stress views. In addition the study aimed to define the forces required for varus and valgus stress and confirm the optimum alignment of the X-ray beam when using the new device.

6.4.3.1 Patients and methods

Participants aged over 50 years and older with radiographic evidence of knee arthritis were considered eligible for the study. Participants with a history of high tibial osteotomy or previous intra-articular fracture were excluded as it was felt that these may present difficulty in image interpretation due to changes in the tibial slope.

Under fluoroscopic guidance manual, clinician performed, varus and valgus stress was applied sequentially to the knee with the patient supine and the knee flexed using the triangular bolster and the fluoroscope beam aligned parallel to the tibial plateau.

Using the device, outlined above, and in accordance with standardised methods for use, varus and valgus stress of 0 Newton, 10 Newton, 20 Newton and 30 Newton force were sequentially applied of the knee. Fluoroscopic images aligned parallel to the tibial plateau were taken at each force with removal of the force between each image. A 25 mm calibration ball was used in all images sited at the level of the fibula head.

Images were measured using custom measuring software (Matlab, Massachusetts, USA). To reduce bias, analysis was performed in a random order with the assessor blinded to the acquisition technique.

During stress radiographs, both manual, clinician performed, and device performed at different forces the patient was asked to score any pain they had from 0, no pain, to 10, worst pain imaginable.

6.4.3.2 Statistical methods

Statistical evaluation was conducted as outlined previously (**Chapter 5: 5.3 Statistical methods**).

6.4.3.3 Results

Fluoroscopic evaluation was undertaken on nine knees, all female. The mean age was 70 years (range 63 to 77).

6.4.3.3.1 Varus stress

The mean medial compartment JSW on manual, clinician performed, varus stress was 3.9 mm (SD 2.1). In the supine position, with no force applied, the mean medial compartment JSW was 8.7 mm (SD 1.4). On the application of 10 N force a significant reduction of medial JSW was seen (mean difference 5.3 mm (95%CI 2.5 to 8.1 mm); p = 0.003). No further significant reductions in medial JSW, compared to 10 N force, were observed at 20 N (p = 0.05) and 30 N (p = 0.08) (**Figure 6.15**).

Compared to the medial JSW observed on manual, clinician performed, varus stress the JSW with a device performed varus stress using 10 N force was significantly larger (mean difference 0.6 mm (95%CI 0.1 to 1.1 mm); p = 0.04). No difference was observed in medial JSW between manual, clinician performed, varus stress and device performed varus stress using 20 N (p = 0.88) or 30 N force (p = 0.68) (**Figure 6.15**).

Assessing the lateral compartment on the application of varus stress a reciprocal widening was seen of between of 0.3 mm to 1.0 mm for every 10 N of force applied providing further evidence that the medial compartment was acting as the pivot and was, therefore, under compression.

No correlation was observed between the medial compartment JSW on manual, clinician performed varus stress and medial JSW with the patient supine and no force applied (ρ = 0.12; p < 0.77). A significant positive correlation was observed between the medial compartment JSW on manual, clinician performed, varus stress and device performed varus stress at 10 N (ρ = 0.97; p < 0.001), 20 N (ρ = 0.95; p < 0.001) and 30 N (ρ = 0.97; p < 0.001) (**Figure 6.16**).

Bland-Altman analysis demonstrated that at 10 N varus force the device underestimated medial JSW by -0.59 mm (95%CI -1.12 mm to -0.06) compared to manual, clinician performed varus stress, whereas at 20 N (mean difference 0.04 mm (95%CI -0.61 to 0.70 mm) and 30 N (mean difference 0.09 mm (95%CI -0.41 to 0.59 mm) force good accuracy was seen between then device and gold standard of clinician performed views (**Figure 6.17** and **Table 6.1**).

The mean VAS pain score on manual, clinician performed, varus stress was 4.0 (range 2 to 6). The mean VAS pain score at 10 N force was 0.9 (range 0 to 4), 20 N force was 1.3 (range 0 to 5) and at 30 N force was 4.9 (range 3 to 7). The mean VAS pain scores at 10 N (p = 0.01) and 20 N (p = 0.01) force were significantly lower than manual, clinician performed, varus stress. No difference in mean VAS pain score was seen at 30 N compared with manual, clinician performed, varus stress (p = 0.58).

All knees were found to be well aligned at 10° cephalic beam angulation.

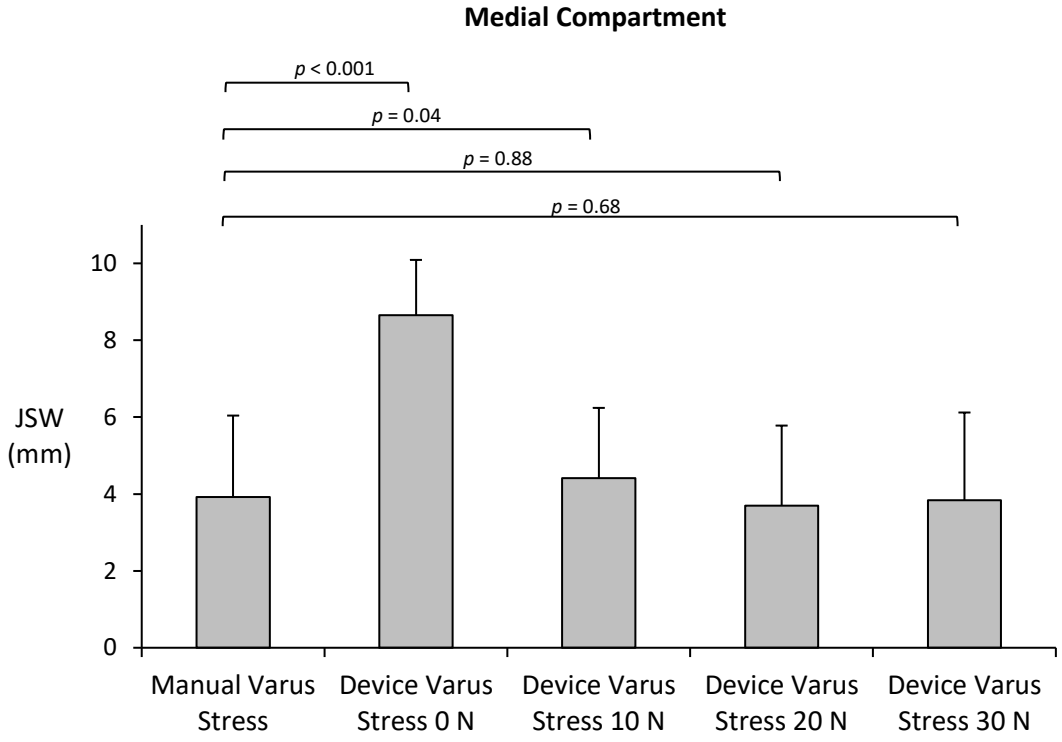


Figure 6.15: Medial compartment joint space width upon manual varus stress and with different forces applied.

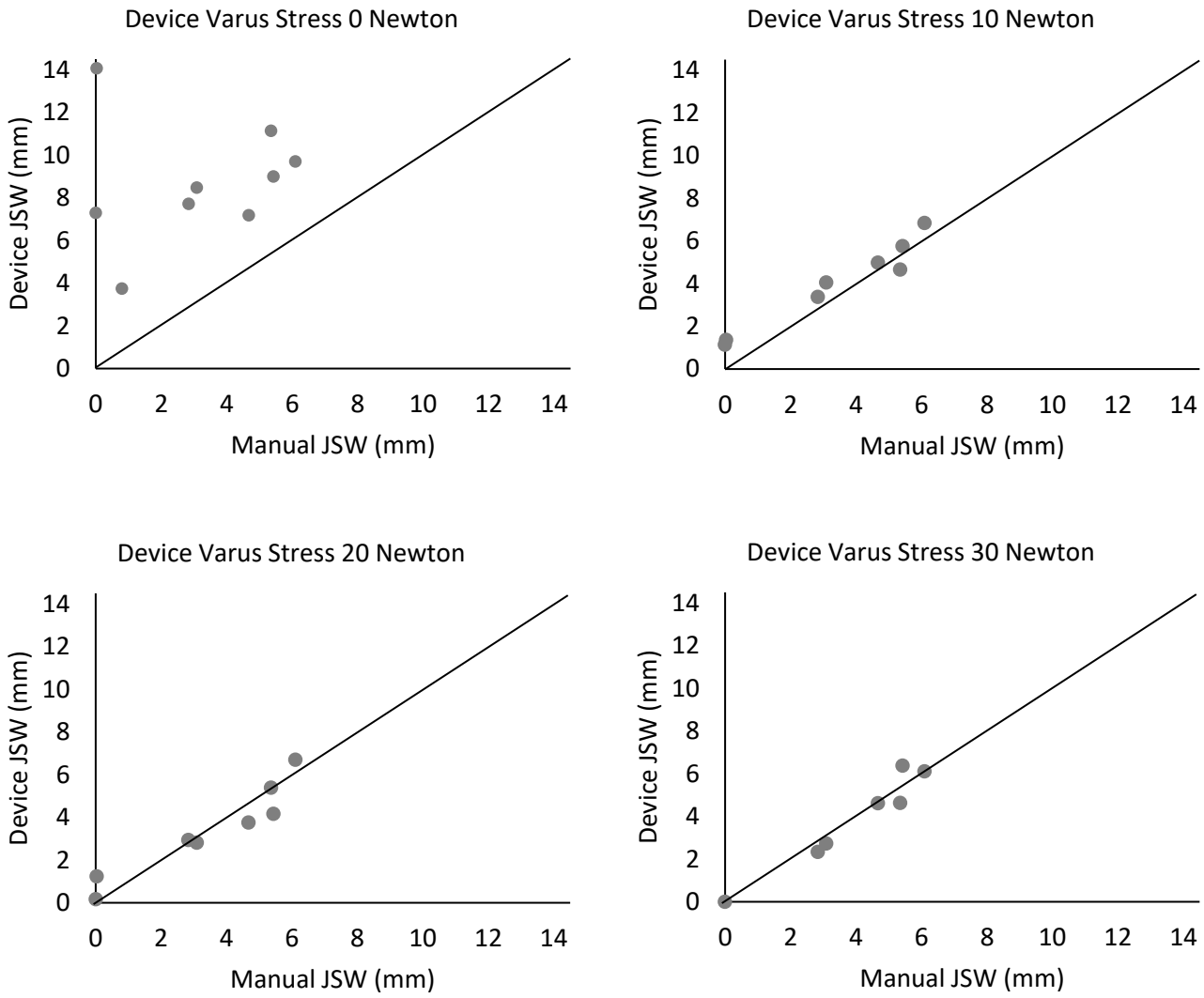


Figure 6.16: Correlation of medial compartment joint space width from manual varus stress radiographs and varus stress using the device at different forces. Line x=y.

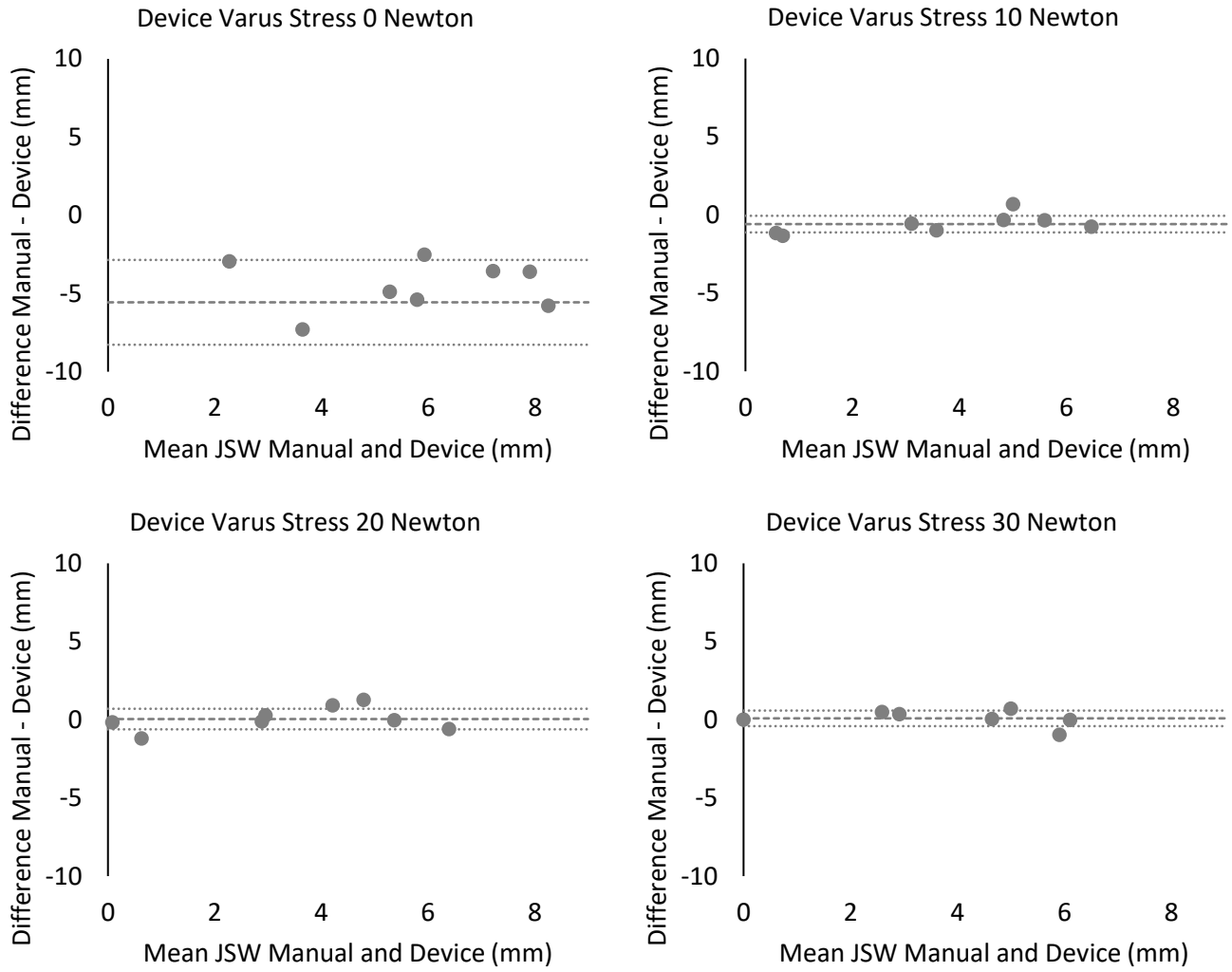


Figure 6.17: Bland-Altman plot comparing medial joint space width measured on varus stress performed manually compared with varus stress performed with the use of a device at different levels of force. Mean estimates of agreement with 95% confidence intervals displayed.

Table 6.1: Bland-Altman estimates of agreement for the difference between medial JSW measured on varus stress of the knee using the device compared with manual stressing.

	Mean Difference (mm)	95% CI
Device 0 Newton	-5.56	-8.27 to -2.85
Device 10 Newton	-0.59	-1.12 to -0.06
Device 20 Newton	0.04	-0.61 to 0.70
Device 30 Newton	0.09	-0.41 to 0.59

6.4.3.3.2 Valgus stress

The mean lateral compartment JSW on manual, clinician performed valgus stress was 7.4 mm (SD 1.38). In the supine position, with no force applied, the mean lateral compartment JSW was 8.22 mm (SD 1.30). On the application of 10 N force no reduction in lateral JSW was seen (mean difference 0.84 mm (95%CI -0.18 to 1.85 mm); $p = 0.09$). With 20 N force a significant reduction of 1.1 mm (95%CI 0.3 to 1.8 mm); $p = 0.01$) was seen with no further significant reduction in lateral JSW, compared to 20 N force observed at 30 N ($p = 1.00$) (**Figure 6.18**).

No difference was observed in lateral JSW between manual, clinician performed, valgus stress and device performed valgus stress using 10 N ($p = 0.98$), 20 N ($p = 0.28$) or 30 N force ($p = 0.79$) (**Figure 6.18**).

Assessing the medial compartment on the application of valgus stress a reciprocal widening was seen of between of 0.5 mm to 0.8 mm for every 10 N of force applied providing further evidence that the lateral compartment was under compression.

A significant positive correlation was observed between the lateral compartment JSW on manual, clinician performed, valgus stress and device performed valgus stress at 10 N ($\rho = 0.81$; $p = 0.008$), 20 N ($\rho = 0.96$; $p < 0.001$) and 30 N ($\rho = 0.84$; $p = 0.01$) (**Figure 6.19**).

Bland-Altman analysis demonstrated that at 10 N (mean difference -0.01 mm (95%CI -0.68 mm to 0.66), 20 N (mean difference 0.23 mm (95%CI -0.22 to 0.67 mm) and 30 N (mean difference 0.28 mm (95%CI -0.17 to 0.74 mm) force good accuracy was seen between the device and gold standard of clinician performed views (**Figure 6.10** and **Table 6.2**).

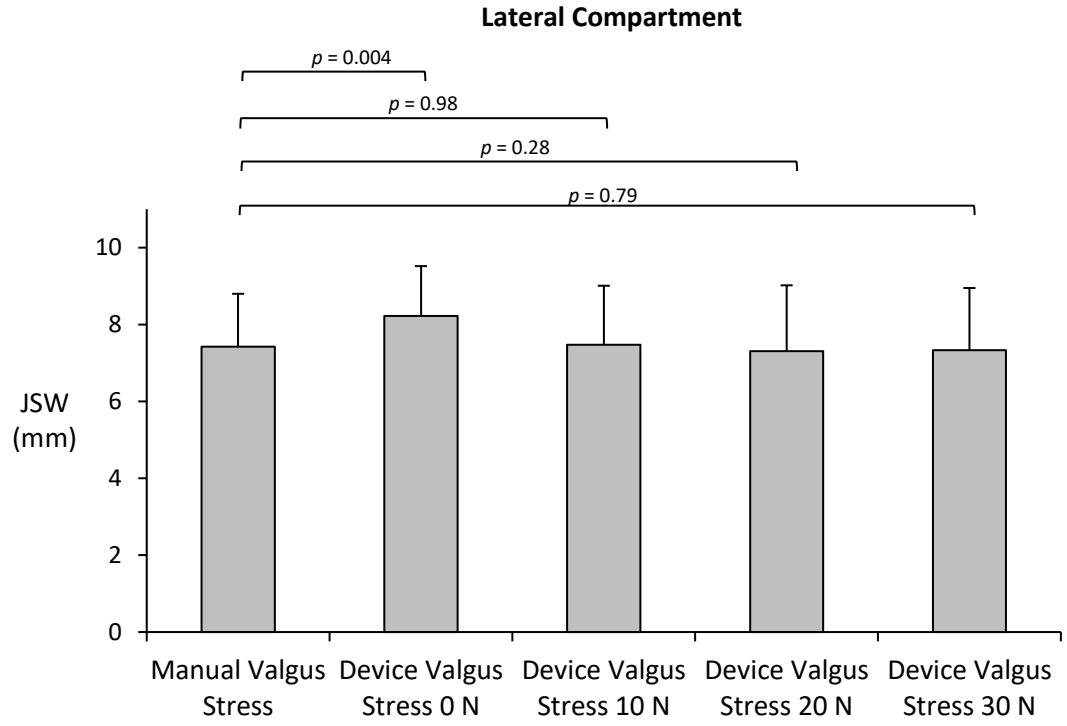


Figure 6.18: Lateral compartment joint space width on manual valgus stress and with different forces applied.

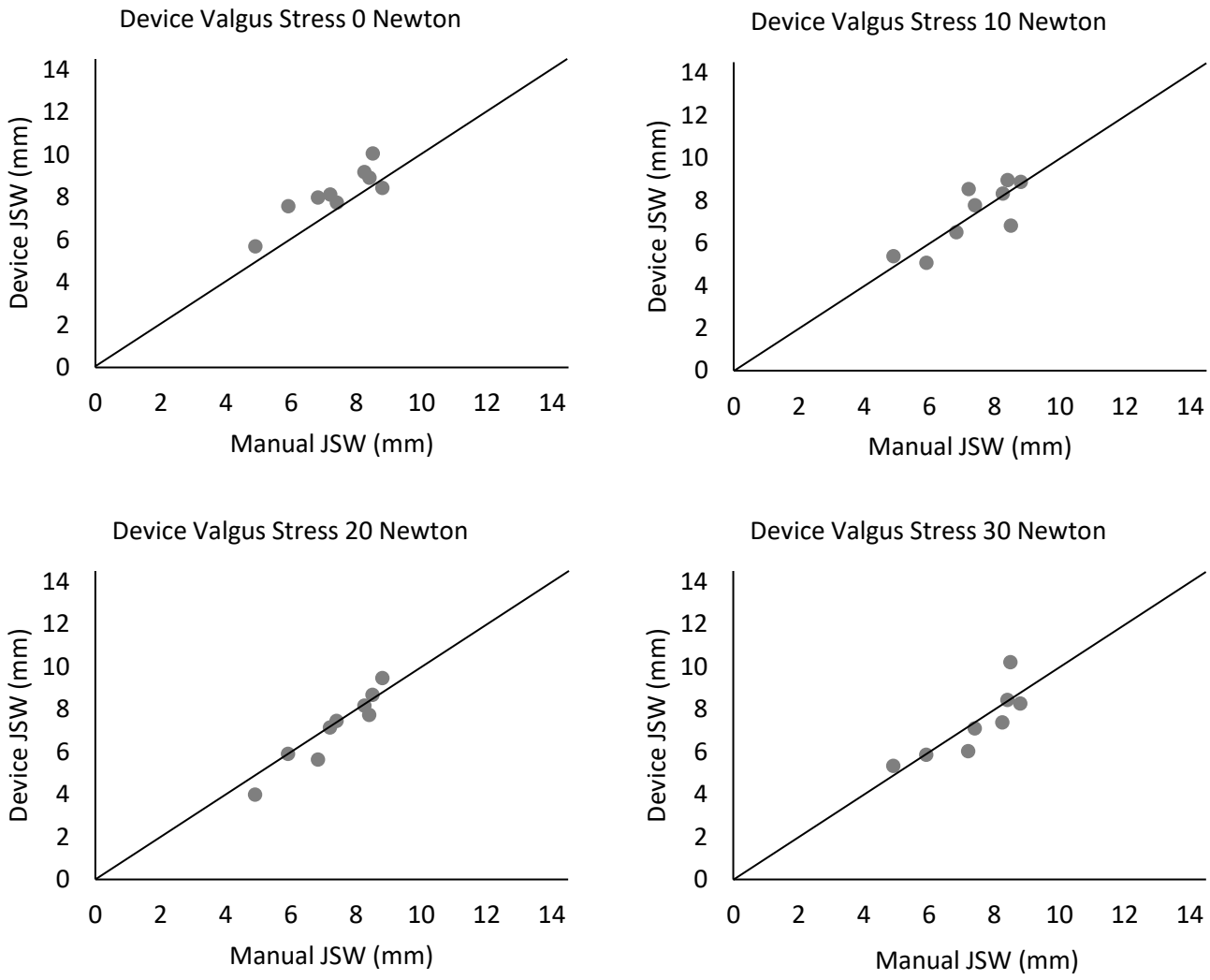


Figure 6.19: Correlation of lateral compartment joint space width from manual valgus stress radiographs and valgus stress using the device at different forces. Line x=y.

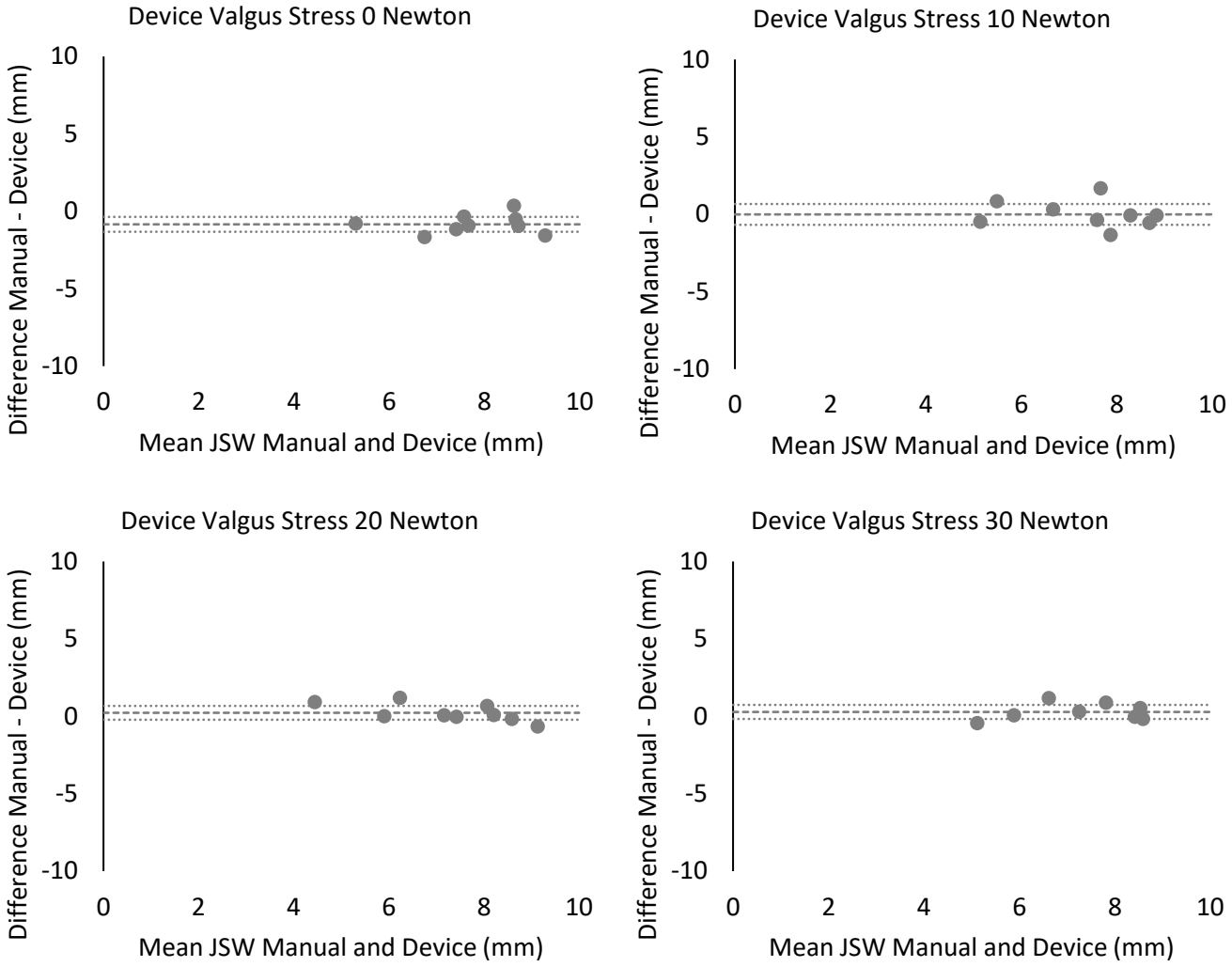


Figure 6.20: Bland-Altman plot comparing lateral joint space width measured on valgus stress performed manually compared with valgus stress performed with the use of a device at different levels of force. Mean estimates of agreement with 95% confidence intervals displayed.

Table 6.2: Bland-Altman estimates of agreement for the difference between lateral JSW measured on valgus stress of the knee using the device compared with manual stressing.

	Mean Difference (mm)	**95% CI**
Device 0 Newton	-0.84	-1.32 to 0.36
Device 10 Newton	-0.01	-0.68 to 0.66
Device 20 Newton	0.23	-0.22 to 0.67
Device 30 Newton	0.28	-0.17 to 0.74

The mean VAS pain score on manual, clinician performed, valgus stress was 3.7 (range 2 to 6). The mean VAS pain score at 10 N force was 0.4 (range 0 to 2), 20 N force was 1.6 (range 0 to 5) and at 30 N force was 5.4 (range 3 to 9). The mean VAS pain scores at 10 N (p = 0.03) and 20 N (p = 0.02) force were significantly lower than manual, clinician performed, valgus stress. No difference in mean VAS pain score was seen at 30 N compared with manual, clinician performed, valgus stress (p = 0.55).

All knees were found to be well aligned at 10° cephalic beam angulation.

6.4.3.4 Discussion

This validation study demonstrated that the medical device could accurately perform varus and valgus stress in the clinical scenario. In all knees acceptable alignment with the tibial plateau was seen at 10° cephalic beam angulation, and the use of the stress device at 10 N and 20 N resulted in lower patient reported pain scores than manual, clinician performed, views.

For varus stress 20 N force was required. At this level of force the device had good accuracy compared to manual, clinician performed varus stress and was well tolerated by patients with a mean pain VAS of 1.3, compared to a mean pain VAS of 4.0 with clinician performed stress. At 30 N no increase in accuracy was seen, however this level of force was associated with an increase in mean pain VAS (4.9).

For valgus stress 10 N force was required. At this level of force the device had good accuracy compared to manual, clinician performed valgus stress and was well tolerated by patients with a mean pain VAS of 0.4, compared to a mean pain VAS of 3.7 with clinician performed stress. At both 20 N and 30 N no increase in accuracy was seen, however 30 N was associated with an increase in mean pain VAS (5.4).

There are some limitations to this study. Firstly the study population was small, all female, and had a mean age of 70 years and as such may not be representative of the wider patient group with knee osteoarthritis. The relevance of this with regards to stress radiographs is that it is known that the biomechanical properties of the ligaments within the knee are different between men and women, as well as subject to age related changes, which may have an impact of the performance of stress radiographs. Secondly, due study selection criteria, including exclusion of patients with prior tibial plateau fracture, as well as local population demographics, such as a low incidence of tibia vara, the performance of stress radiographs in these situations, where the incidence of osteoarthritis may be higher, is unknown and requires further validation. Thirdly, as this was a fluoroscopic study, performed in a controlled environment, it must be acknowledged that the quality of image acquisition may not be achievable in widespread clinical practice. Finally, in this study clinician performed stress radiographs, as opposed to intra-operative findings, assessed at arthroscopy or at arthrotomy, were considered the gold standard presenting limitations in terms of variability of the application of stress as well as lack of clinical outcomes, limiting interpretation of the clinical relevance of these results.

Overall, the strengths of this study are that it reports the preliminary findings of a novel technique to perform varus and valgus stress radiographs of the knee demonstrating that the device is accurate compared to manual, clinician performed stress views, consistent in terms of knee position with respect to radiographic alignment, can deliver controlled varus and valgus force and is comfortable for patients.

6.4.4 Stage 3 – Independent Assessment

Using a prototype device that used 20 N force for both varus and valgus stress the clinical effectiveness of stress radiographs was assessed independently by radiographers in the workup of patients with osteoarthritis of the knee. A 20 N force was chosen, predominantly to aid manufacturing, but also to simplify device use. The device was used in line with the instructions for use (**Chapter 6: 6.4.4.1 Instructions for Use**) on a clinical need basis.

Between 11 January 2016 and 28 February 2017, 49 stress radiographs, 20 varus and 29 valgus, were performed on 32 knees. The mean age of patients was 65 (range 48 to 91) with 59% (19 knees) being male. Of the 32 knees six cases have been managed non-operatively, three cases are awaiting surgery and 23 cases have been managed with arthroplasty (14 medial OUKA, 5 lateral UKA, 4 TKA). Of those 23 knees that have undergone surgery in all but two cases the operative findings matched those indicated by pre-operative stress radiographs. In both of the cases where the findings of stress radiographs did not match the intra-operative findings, the stress radiographs indicated preserved full-thickness medial cartilage and bone on bone arthritis in the lateral compartment, and a decision to proceed with lateral UKA was made. However, following arthrotomy, medial compartment osteoarthritis was noted and ultimately TKA was implanted. The results of this series are outlined in **Table 6.3**. Overall in four of the 32 cases (13%) stress radiographs demonstrated bone on bone arthritis (two medial compartment on varus stress, two lateral compartment on valgus stress) which had not been demonstrated on the AP standing images (**Figure 6.21**).

Table 6.3: Outcomes of independent assessment of a novel stress device.

Case	Standing AP Medial	Standing AP Lateral	Varus Medial	Valgus Lateral	Comments
001	PTCL	Preserved	PTCL	Preserved	Non operative management
002	PTCL	Preserved	PTCL	Preserved	Non operative management
003	Preserved	Preserved	Preserved	BoB	TKA[1]
004	BoB	Preserved	-	Preserved	Medial UKA
005	PTCL	Preserved	PTCL	Preserved	Arthroscopy +/- medial UKA (listed)
006	PTCL	Preserved	PTCL	Preserved	Arthroscopy +/- medial UKA (listed)
007	BoB	Preserved	-	Preserved	Medial UKA (listed)
008	PTCL	Preserved	PTCL	Preserved	Non operative management
009	Preserved	BoB	Preserved	-	Lateral UKA
010	Preserved	PTCL	Preserved	BoB	Lateral UKA
011	Preserved	BoB	Preserved	BoB	Lateral UKA
012	Preserved	BoB	Preserved	-	Lateral UKA
013	PTCL	Preserved	BoB	Preserved	TKA[2]
014	Preserved	BoB	Preserved	BoB	Lateral UKA
015	BoB	Preserved	-	Preserved	Medial UKA
016	BoB	Preserved	BoB	Preserved	Medial UKA
017	PTCL	Preserved	PTCL	Preserved	Non operative management
018	PTCL	Preserved	PTCL	Preserved	Non operative management
019	BoB	Preserved	-	PTCL	Non operative management
020	Preserved	BoB	Preserved	-	TKA[1]
021	PTCL	Preserved	-	Preserved	TKA[3]
022	BoB	Preserved	-	Preserved	Medial UKA
023	PTCL	Preserved	PTCL	Preserved	Medial UKA. Medial PTCL at operation.
024	BoB	Preserved	BoB	Preserved	Medial UKA
025	BoB	Preserved	-	Preserved	Medial UKA
026	BoB	Preserved	BoB	Preserved	Medial UKA
027	PTCL	Preserved	BoB	Preserved	Medial UKA
028	PTCL	Preserved	-	Preserved	Medial UKA
029	BoB	Preserved	-	Preserved	Medial UKA
030	PTCL	Preserved	-	Preserved	Medial UKA for medial femoral AVN.
031	BoB	Preserved	-	Preserved	Medial UKA
032	BoB	Preserved	-	Preserved	Medial UKA

BoB: Bone on bone arthritis, PTCL: Partial-thickness cartilage loss, Preserved: Preserved full-thickness cartilage

[1] Listed for lateral UKA. Medial osteoarthritis noted following arthrotomy and TKA performed.
[2] History of PCL rupture.
[3] Patient choice to receive TKA. Appropriate for UKA at operation.

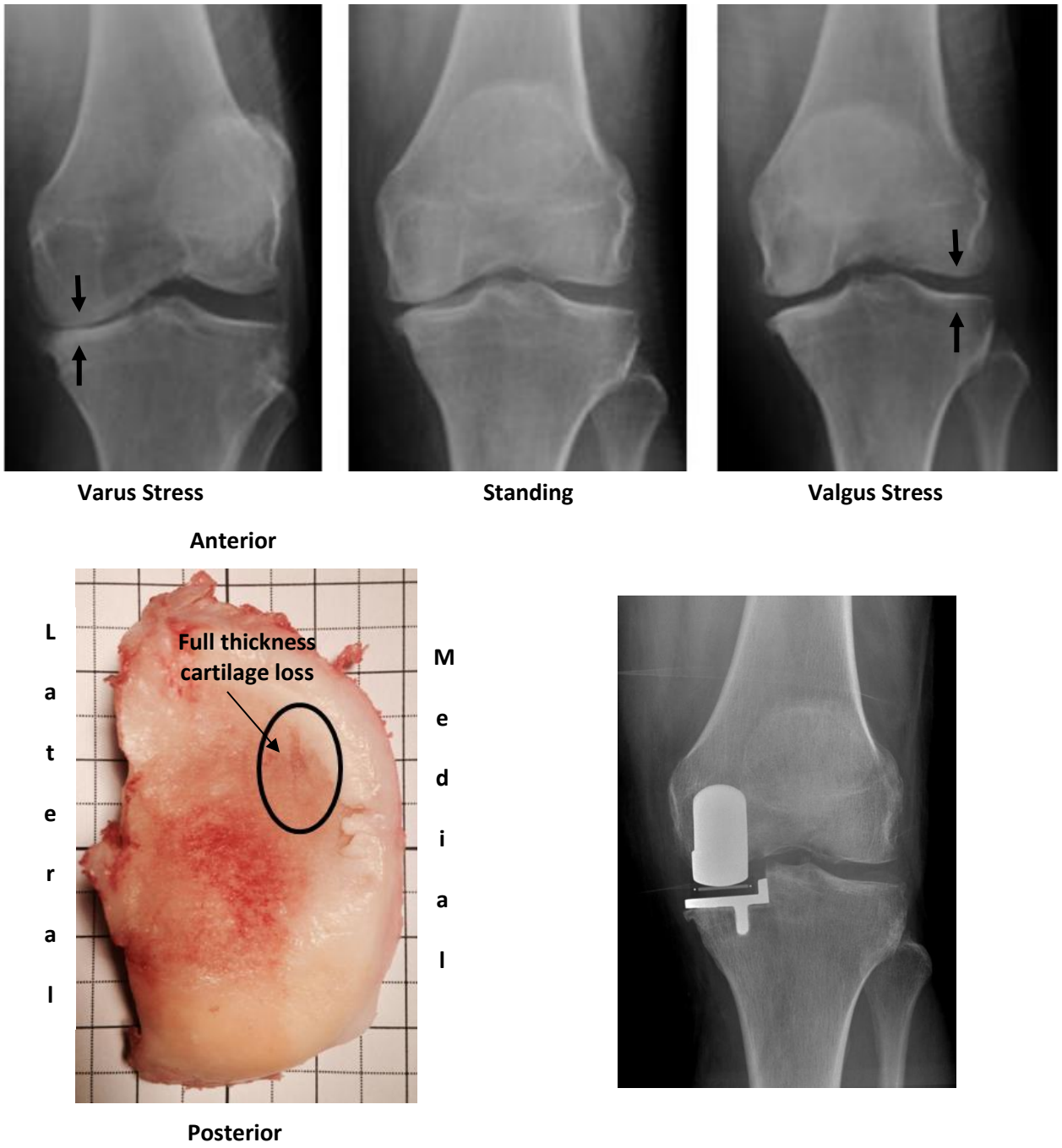


Figure 6.21: Exemplar stress radiographs from independent assessment of the novel stress device. Varus and valgus stress radiographs of the left knee using the stress device demonstrating bone on bone arthritis in the medial compartment (black arrows) with full-thickness cartilage in the lateral compartment (white arrows). Intra-operative correlation was obtained and the patient underwent successful OUKA.

6.5 Summary

Whilst further, larger, long-term studies are needed with ongoing assessment of the performance (Stage 4) of the device this chapter has outlined an alternative to manually applied varus and valgus stress that could be employed in hospitals to assist in the workup of patients with knee arthritis.

This chapter has identified that relatively low forces are required to perform varus and valgus stress radiographs, and that the magnitude of these forces does not cause discomfort for patients. It has been shown that with the use of the device acceptable alignment can be achieved using a consistent radiographic beam position. Additionally, it has been demonstrated that the device can be used independently by radiographers and that the findings of the stress radiographs accurately represent the findings at the time of operation.

The limitations of the device is that it performs stress radiographs at 20° flexion. Whilst, as discussed in **Chapter 5** (**5.1 Introduction**), this may be appropriate for the medial compartment in the lateral compartment the tibial cartilage lesion typically is more posterior, at around 45° of flexion. Whilst attempts were made to develop a stress device for use at this degree of flexion the lack of control over rotation of the knee when applying a valgus force led was the major factor limiting its development. Whilst stress radiographs at 45° flexion may theoretically have a better performance, in **Chapter 5** (**5.3 Clinical Study**) the overall accuracy of valgus stress radiographs, performed at 20° flexion, at identifying preserved full-thickness cartilage in the lateral compartment was 97%. Thus this validation study, combined with the evidence presented in **Chapter 5** (**5.2 Fluoroscopic Study** and **5.3 Clinical Study**), supports the use of this novel device for the application of varus and valgus stress to the knee in the workup for patients with knee arthritis.

Chapter 7 Development and validation of a radiological decision aid to determine suitability for medial OUKA

7.1 Introduction

As identified in **Chapter 3** and **Chapter 4** the key factors in patient selection for OUKA for AMOA are the identification of: bone on bone osteoarthritis in the medial compartment, a functionally normal ACL, retained full-thickness cartilage in the lateral compartment, a functionally normal MCL, and absence of severe damage laterally to the PFJ[51,52,88]. When these disease factors are standardised, as identified in **Chapter 3,** patient factors such as age, weight and activity level do not appear to influence outcomes following OUKA.

In **Chapter 5** it was identified that either a fixed-flexion radiograph, or varus stress radiograph, both at 20° flexion, and aligned to the tibial plateau are best at identifying bone on bone osteoarthritis in the medial compartment (**5.2.3.1 Assessment of the medial compartment**) and that valgus stress radiographs are best at confirming retained full-thickness cartilage in the lateral compartment (as well as a functionally normal MCL) (**5.2.3.2 Assessment of the lateral compartment**). In **Chapter 1** (**1.2.4 Imaging in unicompartmental knee arthroplasty**) it was reported that the presence of preserved posterior bone in the medial compartment on a true lateral radiographs have a performance similar to MRI at identifying a functionally intact ACL and that skyline radiographs are able to exclude severe damage to the lateral patella facet.

Building on the findings of earlier chapters this chapter will cover the development and validation of a radiological decision aid to determine suitability for medial OUKA and test the hypothesis that

[*] This chapter has been published as "Radiological Decision Aid to determine suitability for medial unicompartmental knee arthroplasty: development and preliminary validation" Bone and Joint Journal (2016). **Appendix 1**.

the pattern and severity of arthritis, and therefore patient suitability for medial OUKA, can be reliably determined using a structured radiological assessment in combination with an atlas-based decision aid.

This chapter covers the development of the Decision Aid and investigates its performance in predicting suitability for OUKA in a consecutive cohort of patients undergoing knee arthroplasty (OUKA or TKA) under the care of an independent surgeon who was not involved in its development. The mid-term functional outcomes and implant survival in those knees where the Decision Aid advised OUKA, and who underwent OUKA have also been investigated.

7.2 X-ray Knee Instability and Degenerative Score (X-KIDS)

The concept of a radiographic, atlas-based, patient selection tool for UKA was first proposed by Oosthuizen *et al.*[239]. The X-ray Knee Instability and Degenerative Score (X-KIDS) is a scoring tool designed to identify whether, for an individual knee, UKA or TKA should be the treatment of choice. Based on six radiographic views (standing AP, lateral, standing PA 15° flexion, standing PA 45° flexion and varus and valgus stress views in 20° flexion) knees are scored for narrowing, osteophytes and subluxation in both the coronal and sagittal plane. For narrowing the medial and lateral compartments are assessed with a compartment considered narrowed if there is bone on bone arthritis identified on either the: standing AP, standing PA 15° flexion, standing PA 45° flexion or varus and valgus stress views in 20° flexion. Where bone on bone is identified a compartment is awarded 3 points, provided the other compartment of the knee had a joint space width of 5 mm or greater on all views. If the other compartment has a joint space width of under 5 mm then the knee is scored as 6 points. For osteophytes one point was awarded if there was a medial and/or lateral osteophyte. Subluxation was assessed on the standing AP view and lateral view. Subluxation on the

AP view was awarded one point if present, however this was removed if the subluxation corrected on either varus or valgus stress view at 20° flexion. Subluxation seen on the lateral view was awarded two points with a maximum of three points overall if subluxation, not correctable of stress views, was observed on both the AP and lateral views.

Overall knees could receive a maximum of 10 points with a score of 3 or 4 indicating UKA to be the treatment of choice, 5 indicating that UKA may be appropriate pending clinical findings and surgical correlation and a score of greater than 5 indicating that TKA is indicated. In an internal validation study Oosthuizen *et al.* reported X-KIDS to be 92.3% accurate at determining the optimum treatment option in 336 knees[239].

While X-KIDS takes a structured approach to assessment of the knee its use in patient selection for OUKA is not supported by the data presented in **Chapter 4** and **Chapter 5**. Firstly, looking at the recommended radiographic views in X-KIDS, it would appear that all radiographic views should be performed, independent of their findings. In clinical practice a large proportion of patients demonstrate bone on bone arthritis on their standing radiograph, predominantly in the medial compartment (**5.3 Clinical Study**), and in these cases there seems little benefit to performing standing PA 15° flexion and varus stress views in 20° flexion to further assess the medial compartment as it will not change the scoring of the knee. Additionally, the data in **Chapter 5** (**5.2.3.1 Assessment of the medial compartment**) does not demonstrate that there is any superiority between standing PA 20° flexion and varus stress views in 20° flexion for assessment of the medial compartment and, as such, in those cases that do not demonstrate bone on bone arthritis on their standing radiograph there does not seem a need to perform both views and one view should be performed depending on local preference.

Another concern with the X-KIDS score is the inclusion of osteophytes as a predictor of outcomes as in **Chapter 4** (**4.4.3 Lateral Osteophytes**) it was reported that these do not effect functional

outcomes or risk of failure. Furthermore, X-KIDS does not assess the PFJ, and whilst it was demonstrated in **Chapter 4** (**4.4.4 Patellofemoral Joint Disease**) that medial PFJ disease, however bad, and lateral PFJ disease that does not have evidence of bone loss with grooving do not affect outcomes, lateral facet bone loss with grooving, which is estimated to occur in around 1% of cases, is known to be associated with adverse outcomes.

Finally, there are issues with the way that scores are calculated using X-KIDS. The data presented in **Chapter 4** has identified that many of the factors associated with optimum outcomes following OUKA (bone on bone osteoarthritis in the medial compartment, a functionally normal ACL, retained full-thickness cartilage in the lateral compartment, a functionally normal MCL, and absence of severe damage laterally to the PFF with bone loss and grooving) are binary in nature, with all required to be met, whereas the X-KIDS Score is a points-based system that has the potential to be interpreted incorrectly. For example, a knee with no joint space narrowing, but subluxation in sagittal plane and a medial osteophyte, as maybe seen in early osteoarthritis secondary to ACL insufficiency, would score 3 points and UKA would be advised, which would mean, as established in **Chapter 4**, that a poor outcome would be expected.

7.3 Development of a radiological decision aid for OUKA

As for OUKA the X-KIDS scoring system is not supported by evidence presented in this thesis the decision was made to produce a radiological decision aid specific for OUKA. Based on these disease factors identified in **Chapter 4** and radiographic views identified in **Chapter 1** and **Chapter 5** an atlas-based radiographic Decision Aid for medial OUKA in the setting of AMOA was developed. The Decision Aid consists of five sections, each assessing one of the five criteria, with radiographic view and exemplar radiographs provided to demonstrate when the criteria are met, as well as exemplar radiographs that demonstrate when the criteria are not met (**Figure 7.1**). Example radiographs of

knees meeting the criteria to perform OUKA were taken from the first 1000 consecutive OUKA reported in **Chapter 2** (**2.1 Oxford Experience: Results of a consecutive series of 1000 knees**). Examples of knees not meeting criteria are taken from a series of patients undergoing TKA during the same time period. Illustrative radiographs for each criterion were selected by consensus by the Decision Aid development team. Each criteria is assessed by way of a binary, yes-no, polar question with all criteria required to be met to perform OUKA for an indication of AMOA.

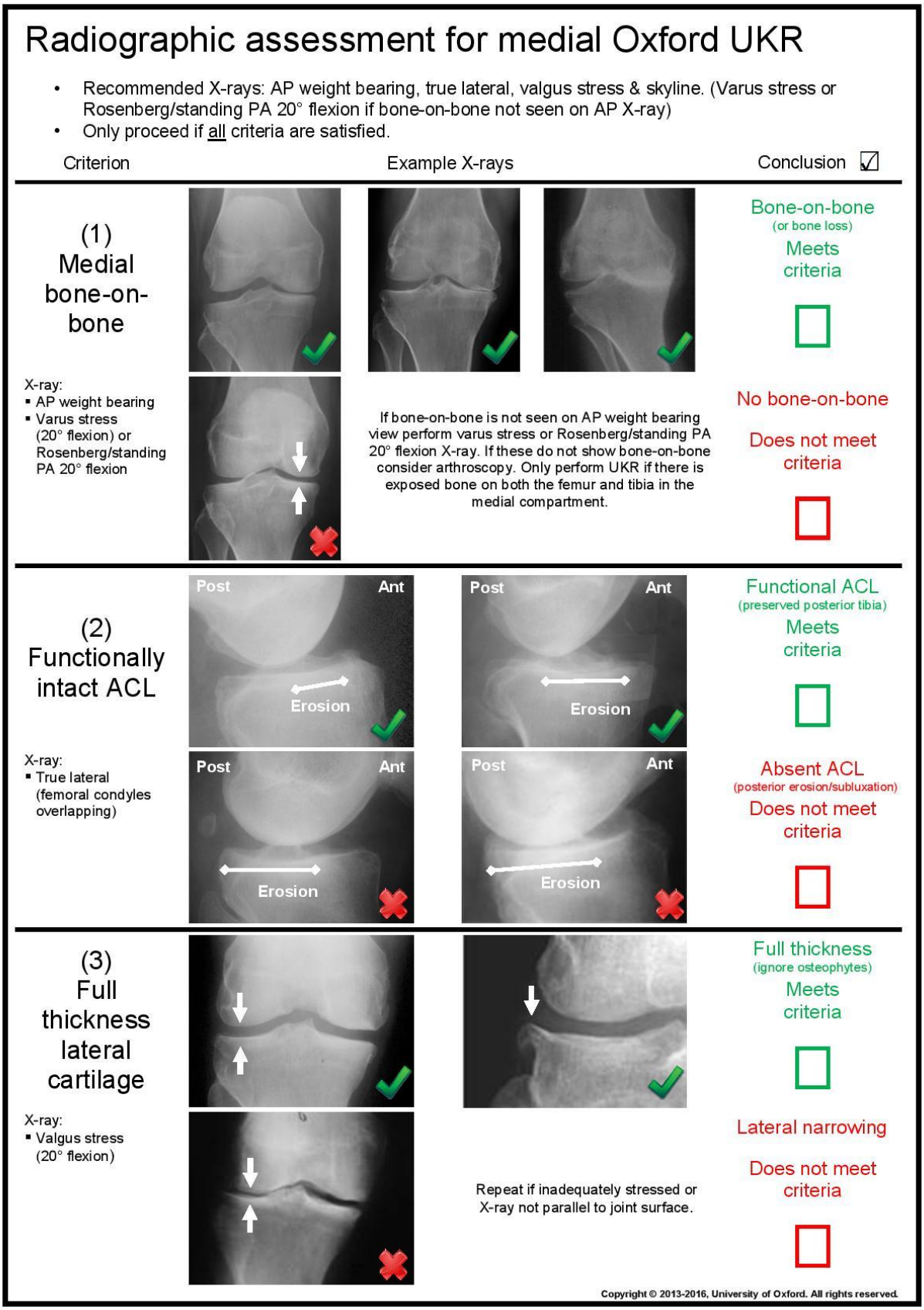
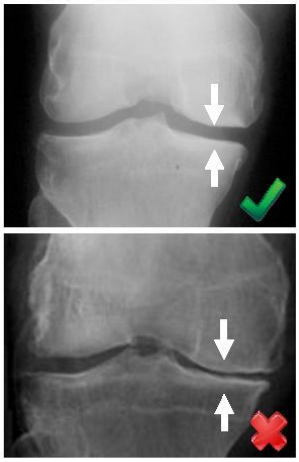
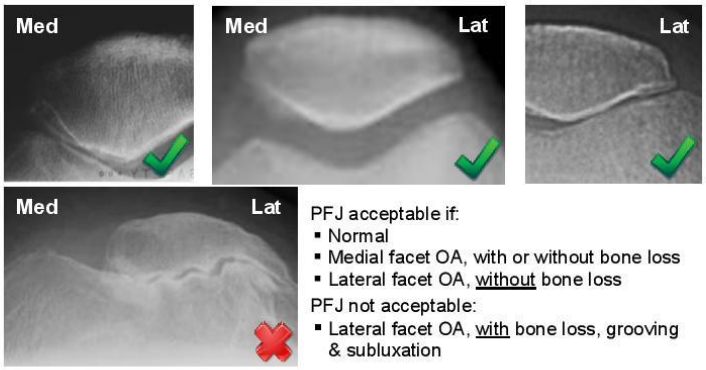


Figure 7.1: Radiographic decision aid for OUKA (page 1).

Radiographic assessment for medial Oxford UKR

Criterion	Example X-rays	Conclusion ☑
(4) Functionally normal MCL (correctable intra-articular deformity) X-ray: ▪ Valgus stress (20° flexion)		Correctable deformity (Normal medial opening) Meets criteria ☐ Not correctable (Incomplete medial opening) Does not meet criteria ☐
	Repeat if inadequately stressed or X-ray not parallel to joint surface	
(5) Acceptable patello-femoral joint X-ray: ▪ Skyline	 PFJ acceptable if: ▪ Normal ▪ Medial facet OA, with or without bone loss ▪ Lateral facet OA, without bone loss PFJ not acceptable: ▪ Lateral facet OA, with bone loss, grooving & subluxation	Meets criteria ☐ Does not meet criteria ☐

The primary indication for the Oxford UKR is antero-medial OA. The diagnosis of antero-medial OA is based on the radiographic criteria shown above [1]. Medial avascular necrosis is also an indication.

The following factors do not preclude Oxford UKR if all other criteria are met:

- Isolated medial pain is not a requirement. Pre-operative anterior knee pain has been reported to not compromise the outcome [2,3].
- Patient's age, weight and activity level [4-6].
- Chondrocalcinosis (cartilage calcification on X-ray), lateral marginal osteophytes or medial tibial subluxation (which should correct when the UKR is implanted if the ACL is intact) [6-8].

The final decision on whether to perform UKR is made when the knee has been opened and directly inspected. The following factors do not preclude Oxford UKR if all other criteria are met:

- Full thickness cartilage loss on the non-weight bearing medial side of the lateral femoral [9].
- Full thickness cartilage loss in the patellofemoral joint

[1] Hamilton TW et al. Validation of a Radiological Decision Aid to Determine Suitability for Medial Mobile-bearing Unicompartmental Knee Replacement. NIHR Doctoral Research Training Camp Poster. July 2015.
[2] Berend K et al. Does Preoperative Patellofemoral Joint State Affect Medial Unicompartmental Knee Arthroplasty Survival? AAOS Poster No. P204. February 2011.
[3] Liddle AD et al. Preoperative pain location is a poor predictor of outcome after Oxford unicompartmental knee arthroplasty at 1 and 5 years. KSSTA 21:2421-6, 2013.
[4] Berend K. et al. Obesity, Young Age, Patellofemoral Disease and Anterior Knee Pain: Identifying the Unicondylar Arthroplasty Patient in the United States. Orthopedics. 30:19–23, 2007.
[5] Kang, S. et al. Pre-operative Patellofemoral Degenerative Changes Do Not Affect the Outcome After Medial Oxford Unicompartmental Knee Replacement. JBJS Br. 93-B:476–8, 2010.
[6] Pandit H. et al. Unnecessary Contraindications for Mobile-bearing Unicompartmental Knee Replacement. JBJS Br. 93-B:622–8, 2011.
[7] Goodfellow JW, O'Connor J, Pandit H, Dodd C, Murray D. Unicompartmental Arthroplasty with the Oxford Knee (2nd Edition), Goodfellow Publishers, Oxford, UK, 2015. [8] Kumar V et al. Comparison of Outcomes after UKA in Patients With and Without Chondrocalcinosis: A Matched Cohort Study. KSSTA 2015 *online* 19 March 2015.
[9] Kendrick BJ et al. The implications of damage to the lateral femoral condyle on medial unicompartmental knee replacement. JBJS Br 92(3)374-9, 2010.

Figure 7.1: Radiographic decision aid for OUKA (page 2).

7.4 Validation of a radiological decision aid for OUKA

7.4.1 Patients and methods

Between 1st January 2008 and 31st December 2008, 550 consecutive primary TKA or primary medial OUKA were performed by an experienced OUKA surgeon (Dr KR Berend) at an independent centre (Joint Implant Surgeons, New Albany, USA) not involved with the development of the Decision Aid. All patients signed an institutional review board approved general research consent allowing for retrospective review. The gold standard with which the Decision Aid was compared was actual treatment received, which was determined by an experienced OUKA surgeon based on history, examination, radiographic assessment including stress radiographs, and intra-operative assessment in line with the recommended indications as described by Goodfellow *et al.*[52].

Suitability for OUKA was determined by assessing pre-operative radiographs using the radiographic Decision Aid (**Figure 7.1**) with the assessor blinded to the treatment received. Twelve percent of radiographs (*n* = 227 of 1962 radiographs) were re-assessed at three-months by myself and also by Mr A Clave, Consultant in Orthopaedics and Trauma, Nice, France.

Patients were followed up independently using a standard protocol. Functional outcomes were assessed using the: AKSS-O, AKSS-F, Lower Extremity Activity Scale (LEAS) and the University of California, Los Angeles (UCLA) Activity Score[119,240,241]. Where patients had died, information about the status of their knee, and the presence of further operation was obtained via primary and secondary care records as well as via patient's relatives where appropriate.

Performance of the Decision Aid was assessed by calculating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy at identifying suitability for OUKA. Performance was calculated based on radiographic assessment alone, and radiographic assessment combined with results of pre-operative findings from patient: history, examination,

prior clinical investigations and surgeon assessment. Patient history factors assessed included: patient preference for implant type (i.e. successful contra-lateral arthroplasty) and history of inflammatory arthritis (OUKA contra-indicated). Patient examination factors included expected flexion of under 110° which is required to prepare the femur at the time of operation. Prior clinical investigations included the results of a direct assessment of the joint at arthroscopy as well as MRI demonstrating SONK. Other findings from MRI, including the status of the tibiofemoral joint and ACL, were not taken into account as these have not been demonstrated to affect patient outcomes and should not be used for patient selection[116]. Surgeon assessment included cases where the patient may have been suitable for OUKA however a pre-operative decision was made by the surgeon to proceed with TKA.

7.4.2 Statistical methods

To assess for differences in functional outcome between subgroups, non-parametric tests (Mann–Whitney U) were performed. Life-table analysis was performed to assess survival using implant-related re-operations, which included any re-operations in which components were changed, in which the bearing was replaced for dislocation, and any re-operations in which new components were inserted as the endpoint. Confidence intervals were calculated using the method described by Peto *et al*.[126].

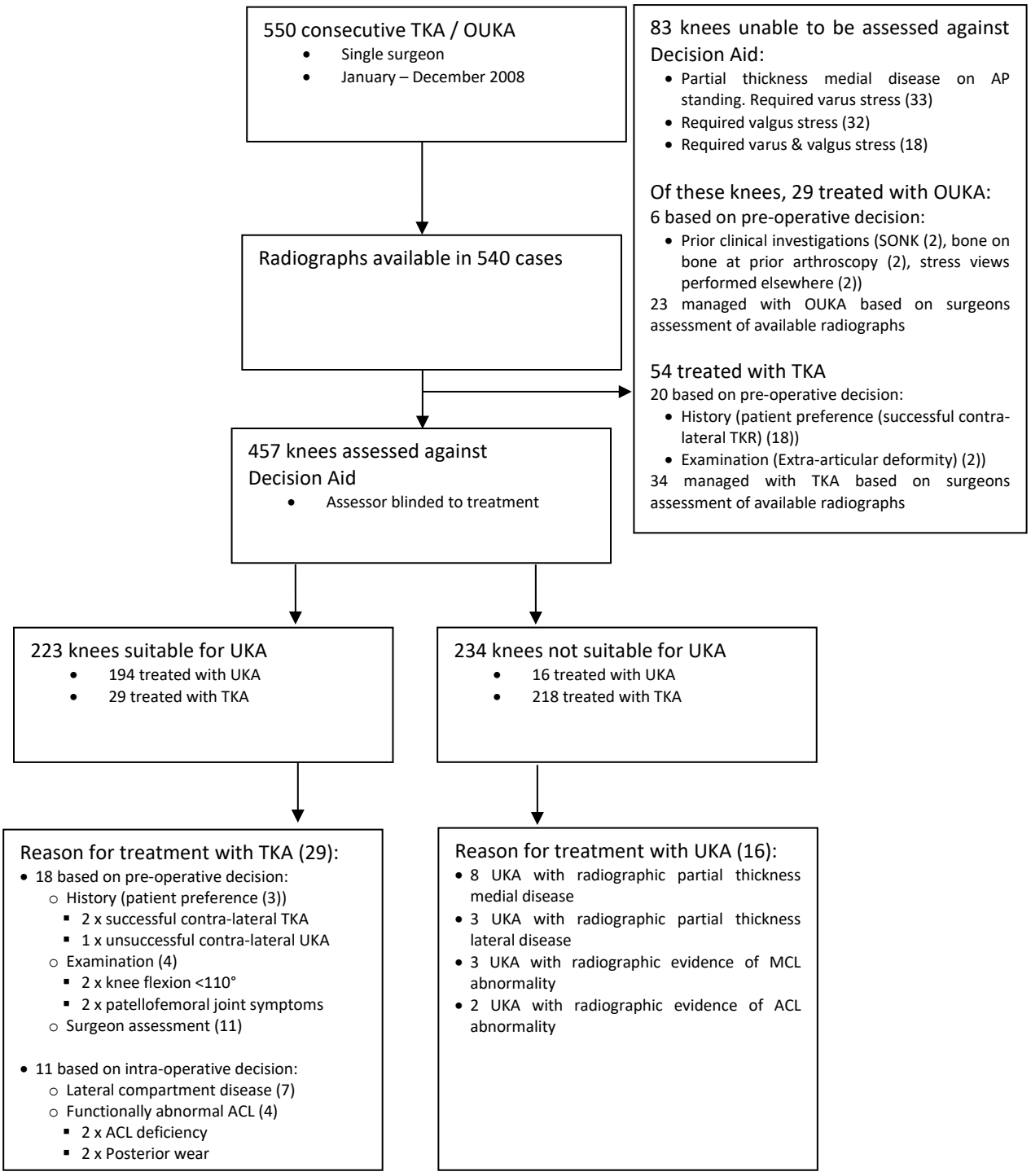


Figure 7.2: Flow of study patients in the validation of decision aid study.

7.4.3 Results

Of the 540 knees (356 patients) in which radiographs were available, 239 (44%) underwent medial OUKA and 301 (56%) underwent TKA. Complete sets of radiographs were not available in 83 knees (29 OUKA, 54 TKR) which included two cases of SONK, leaving 457 knees for assessment against Decision Aid criteria (**Figure 7.2**, **Table 1**).

Based on the radiographic Decision Aid 49% (223) of knees were deemed suitable for OUKA and 51% (234) were not suitable. There was excellent intra (Cohen's kappa 0.90) and inter-observer (Cohen's kappa 0.85) agreement.

Of those 234 knees identified as not suitable for OUKA, 40% (93 knees) did not meet one radiographic criteria, 38% (88 knees) did not meet two criteria, 22% (52 knees) did not meet three criteria and <1% (1 knee) did not meet four criteria. Of those knees that did not meet radiographic criteria, 46% (108 knees) had partial-thickness cartilage loss (PTCL) in the medial compartment, 45% (105 knees) had posterior bone loss on their true lateral radiographs indicating ACL insufficiency, 67% (157 knees) had evidence of lateral compartment disease, 11% (25 knees) had evidence of MCL shortening and 16% (37 knees) evidence of bone loss with grooving to the lateral PFJ.

The functional outcomes of knees treated with OUKA are outlined in **Table 7.2**. In the 194 knees meeting Decision Aid criteria for OUKA, who received OUKA, there were four implant related reoperations at a mean of 3.8 years (range 0.9 to 6.4). There was one case of instability (0.9 years), one case of lateral compartment progression of arthritis (6.1 years), one case of femoral loosening associated with ACL deficiency (6.4 years) and one case due to an unknown cause with the operation performed elsewhere (2.0 years). The five-year survival in this cohort was 98.9% (95%CI 96.6 to 100) (**Table 7.3**).

Table 7.1: Pre-operative patient demographics of patients managed with OUKA and TKA.

	OUKA Mean (SD) (*n* = 239)	TKA Mean (SD) (*n* = 301)	*p*
Time from surgery in years	6.7 (0.4)	6.7 (0.5)	0.23
Follow-up in years	3.9 (1.8)	2.8 (2.4)	**<0.001**
Age in years	63.2 (10.3)	65.8 (10.2)	**0.01**
% male	41.0	40.2	0.85
BMI	31.9 (7.3)	33.3 (7.6)	**0.02**

Table 7.2: Functional outcomes in those undergoing OUKA.

	Decision Aid appropriate for OUKA Mean (SD)	Decision Aid not appropriate for OUKA Mean (SD)	*p*
Flexion			
Preoperative	115.8 (8.8)	109.2 (11.9)	**<0.001**
Postoperative	117.8 (7.8)	112.0 (11.4)	**<0.001**
Improvement from baseline	2.1 (10.6)	2.7 (12.7)	0.65
Knee Society Objective Score			
Preoperative	38.6 (13.9)	40.4 (18.9)	0.69
Postoperative (most recent)	87.7 (16.2)	90.2 (13.6)	0.63
Improvement from baseline	49.1 (21.4)	49.1 (22.7)	0.98
Knee Society Functional Score			
Preoperative	57.5 (15.5)	51.7 (18.9)	**0.001**
Postoperative (most recent)	72.9 (22.7)	64.2 (25.1)	**<0.001**
Improvement from baseline	15.3 (22.9)	12.2 (24.9)	0.12
Lower Extremity Activity Score			
Preoperative	9.5 (2.8)	9.1 (2.9)	0.09
Postoperative (most recent)	9.9 (2.9)	9.7 (3.0)	0.44
Improvement from baseline	-8.1 (3.8)	-7.7 (3.7)	0.32
UCLA Score			
Postoperative (most recent)	6.2 (2.5)	5.3 (1.9)	**0.04**

Table 7.3: Implant survival in Decision Aid appropriate for OUKA knees that underwent OUKA.

FU (Y)	Number at start	Revised	Withdrawn	At Risk	Annual Failure	Survival	95% CI	95% CI
0 to 1	194	0	7	190.5	0.000	100	100	100
1 to 2	187	1	7	183.5	0.005	99.5	98.4	100
2 to 3	179	1	25	166.5	0.006	98.9	97.2	100
3 to 4	153	0	57	124.5	0.000	98.9	97.0	100
4 to 5	96	0	19	86.5	0.000	98.9	96.6	100

In 29 knees the Decision Aid indicated suitability for OUKA however TKA was performed (18 pre-operative decision, 11 intra-operative decision). Knees that were identified by the Decision Aid as suitable for OUKA but underwent TKA had significantly worse postoperative flexion (110° (SD11) v 118° (SD 8), p<0.001) and Knee Society Functional Scores (63.2 (SD20) v 72.9 (SD23), p=0.04) compared to knees managed with OUKA who were identified as suitable. No other differences in functional scores were seen between these groups and no difference in functional outcome was detected between those knees identified as suitable for OUKA that underwent TKA and those identified as not suitable for OUKA who were treated with TKA. There were no cases of failure in this group at a mean follow-up of 3.2 years (range 0 to 7) or in those knees (218 knees) not meeting Decision Aid criteria for OUKA who were treated with TKA at a mean follow-up was 2.9 years (range 0 to 7).

In 16 knees that did not meet Decision Aid criteria for OUKA, OUKA was performed (**Figure 7.2**). Of these 16 knees: eight had radiographic partial thickness medial disease, three radiographic partial thickness lateral disease, three radiographic evidence of MCL abnormality and two radiographic evidence of ACL abnormality. At a mean follow-up of 4.3 years (range 1 to 6) knees that were identified as not suitable for OUKA but underwent OUKA had significantly lower flexion, AKSS-Functional Score and UCLA score compared to those knees identified as suitable for OUKA and were treated with OUKA (**Table 7.2**) however they also had lower pre-operative functional scores, and no difference in improvement from baseline was observed. In this group there was one case of failure, due to progression of arthritis in the lateral compartment at 2.3 years. The five-year survival (93.1% (95%CI 77.6 to 100)) in knees not suitable for OUKA that underwent OUKA was lower than those identified as suitable for OUKA treated with OUKA, however due to small numbers it was not possible to assess the significance of this difference.

The performance of the Decision Aid is outlined in **Table 7.4**. A sensitivity analysis, performed to assess the role of skyline and stress radiographs in the workup for medial OUKA, demonstrated a decrease in accuracy of 1% and 5% respectively if these X-rays were not performed (**Table 7.5**).

Table 7.4: Performance of the Decision Aid in predicting suitability for OUKA.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Radiology alone	92	88	87	93	90
Radiology plus history	92	90	88	94	91
Radiology plus examination	92	90	89	93	91
Radiology plus surgeon assessment	92	93	92	94	93
Radiology plus results of prior investigations	93	88	87	93	90
Radiology plus all of above	93	96	95	94	94

History: Patient preference for implant type (i.e. successful contra-lateral arthroplasty).
Examination: Clinical finding influencing implant selection (i.e. predicted flexion <110° under anaesthetic, required to perform OUKA)).
Surgeon assessment: Pre-operative decision made by the surgeon to proceed with TKA based on patient assessment.
Prior investigations: Prior arthroscopy demonstrating indication or MRI demonstrating SONK.

Table 7.5: Sensitivity analysis: Skyline and stress-X-ray.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All radiographic and clinical findings	93	96	95	94	94
Radiographic and clinical findings - No skyline X-ray	93	94	93	94	93
Radiographic and clinical findings - No Stress X-ray	88	90	90	89	89

7.4.4 Discussion

This study, which was undertaken in a cohort of patients operated on by an experienced OUKA surgeon who was not involved with the development of the Decision Aid, found the sensitivity and specificity of the radiographic Decision Aid at predicting suitability for OUKA to be 92% and 88% respectively. When the radiographic findings were combined with pre-operative factors that influence implant selection (i.e. patient request for TKA or flexion so limited that is was impossible to implant an OUKA) the sensitivity and specificity increased to 93% and 96% respectively. In those patients who met Decision Aid criteria for OUKA and in whom OUKA was performed excellent survival, 99% at five-years (95%CI 97 to 100), and functional outcomes were achieved. Taken together this suggests that the Decision Aid is a useful tool for identifying appropriate patients for OUKA in those who meet the criteria for joint arthroplasty.

The main concern about the Decision Aid is that there were a few false positives (2.3%) where the Decision Aid suggested an OUKA should be done yet the surgeon did not do an OUKA. As an OUKA was not done we cannot know what the outcome would have been had one been implanted and therefore we have to assume that it might not have been good. Importantly in all of these false positives the contraindication to OUKA, such as a ruptured ACL, was readily identifiable during routine examination of the joint at the time of surgery. As inspection of the knee at the time of surgery is part of the surgical routine, with this stated to be necessary on the Decision Aid, we believe that it is safe to recommend the Decision Aid as the primary assessment for patient suitability for OUKA. The only proviso being that the patient must be consented for the possibility of a TKA, with TKA instrumentation being available should this be required.

In 3.3% of cases the Decision Aid did not support the use of an OUKA yet one was implanted. In these false negatives, although the clinical outcomes were satisfactory, the patients had significantly worse functional outcomes (flexion ($p < 0.001$), AKSS-Functional ($p < 0.001$), UCLA ($p =$

0.04)), and a lower implant survival 93.1% (95%CI 77.6 to 100) compared with those that had a OUKA that was supported by the Decision Aid. Whilst, due to the small number of knees, the data should be interpreted carefully, this would suggest that the Decision Aid does identify the optimal patients for OUKA and that surgeons should be cautious extending the indications beyond those recommended by the Decision Aid. The most common reason why the Decision Aid did not support an OUKA, that was implanted, was that there was PTCL in the medial compartment and not bone on bone which, in **Chapter 4** (**4.4.1 Partial-thickness Cartilage Loss in the Medial Compartment**), was identified as being associated with worse results[53,242].

Sensitivity analysis, investigating the role of skyline and stress radiographs, highlighted the importance of performing stress radiographs when identifying suitability for OUKA. In this series if stress radiographs were not performed the accuracy of the Decision Aid would be reduced by 5% (**Table 7.5**). In the absence of stress radiographs 10% of knees would be inappropriately identified as suitable for OUKA (PPV) as lateral compartment disease, demonstrated on valgus stress, would be missed. In addition 11% of knees would be inappropriately identified as not suitable for OUKA (NPV) due to medial bone on bone arthritis, demonstrated on varus stress, not being seen on standing extension view (SEV) radiographs which were identified in **Chapter 5** (**5.2.3.1 Assessment of the medial compartment**) as having a poor performance in assessment of the medial and lateral compartments in the workup for OUKA. This highlights the importance of performing stress radiographs in the workup for OUKA, particularly as during visual intra-operative examination it is often impossible to assess the cartilage thickness in the lateral compartment.

The sensitivity analysis demonstrated that not performing skyline radiographs only resulted in a 1% reduction in the accuracy of the Decision Aid. This finding, combined with the fact that bone loss and grooving in the lateral part of the PFJ is readily identified at the time of operation, suggests that skyline radiographs could be omitted as they do not significantly influence patient selection. The reason why skyline radiographs, and to certain extent stress radiographs, have been included in the

Decision Aid is different. The majority of surgeons currently restrict usage of OUKA to cases where the lateral compartment and PJF are virtually pristine, so as to avoid disease progression. This is incorrect, as providing the valgus stress radiograph shows full-thickness cartilage laterally, and there is not severe arthritis in the lateral part of the PFJ seen on skyline radiographs, this study demonstrates that excellent outcomes can be achieved. Indeed full-thickness ulceration is commonly seen on the medial side of the lateral femoral condyle, as well as in the PFJ, and these factors have previously been demonstrated not to compromise the outcomes[86,88,243]. If surgeons use the Decision Aid then they can complete an evidence-based document to determine whether an OUKA is indicated. Furthermore they can keep the document in the patient's record so if their decision to do an OUKA is ever questioned they will have evidence to support their decision making.

The recommended indications for OUKA are satisfied in about half of knees needing knee arthroplasty. In this study, which excluded lateral OUKA, it was used and its use was supported by the Decision Aid in 44% of cases and very good results were achieved. The results are consistent with the findings of **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**) which found where surgeons performed OUKA in a high-proportion, greater than 20%, of patients' excellent long-term results were seen. In series with mean follow-up of ten-years or more the revision rate was 0.63%pa (95%CI 0.46 to 0.83), which equates to a ten-year survival of 94% (95%CI 92% to 95). The use of the Decision Aid would ensure that surgeons use the recommended indications and therefore achieve optimal results. Under these circumstances the patients will have all the advantages of OUKA, including a faster recovery, lower morbidity and mortality compared to TKA, without the higher re-operation rate.

Importantly this radiological Decision Aid is implementable at all hospitals as it does not require specialist equipment or imaging modalities and enables surgeons to develop a patient management plan during a single clinic appointment and as it is simple it could not only be used by surgeons but also referring physicians.

There are certain limitations to this study. This decision aid and analysis is specific to OUKA and this study retrospectively analyses the mid-term outcome of patients treated by a single experienced OUKA surgeon with longer term data awaited. In the absence of a gold standard for patient selection for OUKA a single experienced OUKA surgeon series was chosen such that OUKA utilisation was high and that OUKA was being utilised in all appropriate cases in line with the current evidence. However, it is acknowledged that there may be variation even amongst experienced OUKA surgeons in terms of their patient selection and that the results seen in this high-volume user series may not be generalisable. Additionally, the association between high utilisation of OUKA and improved outcomes in patients undergoing this procedure has not been established to be causative. Whilst there is uncertainty as such whether increasing utilisation will result in improved outcomes, optimising patient selection by ensuring that patients meet the indications identified in **Chapter 4** would be expected to improve outcomes as the long-term results seen in published series reported in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**) that have adhered to these recommendations have reported similarly good outcomes to those seen in this series[164,185,244]. Further work is required to establish the effect of introducing the radiological Decision Aid into general use to assess the true impact of this decision tool.

7.5 Conclusions

The radiological Decision Aid has a high sensitivity and specificity for predicting suitability for medial OUKA and its use would be expected to be associated with excellent implant survival and functional outcomes. The Decision Aid is safe as it has a low false positive rate and, providing surgeons examine the knee at surgery where all false positive should be readily identifiable, no patient should have an inappropriate OUKA.

Chapter 8 Discussion

8.1 Summary of findings

This thesis identified that, in the hands of the developer surgeons, outcomes from OUKA are good with a survival of 94% (95%CI 92 to 96) at ten-years and 91% (95%CI 83 to 98) at fifteen-years with associated good functional outcomes. However, through meta-analysis of published series, it was also established that whilst the results seen in the hands of developer surgeons can be replicated elsewhere, globally outcomes are a lot more variable with estimates of ten-year survival ranging from 57% to 100%, mean 88% (95% CI 85 to 90%).

It was identified that both surgical caseload and usage influenced outcomes, but that surgical usage appeared more important, with good results following OUKA seen with high surgical usage, independent of the surgical caseload. It was identified that low-usage surgeons operated on significantly younger patients, and had a higher revision for unexplained pain than high-usage surgeons suggesting that low-usage surgeons may have different indications for OUKA, or revision of OUKA, compared to high-usage surgeons. Results from high-usage surgeons, indicating broad indications, were similar to those seen in the hands of the developer surgeons highlighting the importance of surgical selection for this procedure.

To establish the indications for OUKA the effect of different patient and disease factors on long-term outcomes was explored. It was found that the previously published patient factor contraindications based on the patient age (<60 years), weight (≥82kg) and activity level (high activity) do not influence outcomes, provided disease factors are standardised, with knees implanted in patients with these previously reported patient factor contraindications often actually doing better than those without these factors. Assessing disease factors it was also found that the

macroscopic status of the intact ACL, lateral osteophytes, PFJ disease, with the exception of lateral facet disease with bone loss and grooving, and/or anterior knee pain do not influence outcomes.

Knees with partial-thickness cartilage loss (PTCL) in the medial compartment at operation had significantly worse functional outcomes at one, two and five-years postoperatively with a quarter of knees with PTCL reporting fair or poor results, a fifth failing to achieve a clinically significant functional improvements from baseline status, and almost three times the reoperation rate, predominantly for unexplained pain compared to knees with FTCL. In knees with PTCL older age at operation and higher pre-operative function was associated with superior outcomes compared to knees with PTCL who did not possess these characteristics, however there was insufficient differentiation provided to support the use of OUKA in these groups. No prognostic MRI features were identified.

Having identified that it is the pathoanatomy of disease, in particular the requirement for bone on bone arthritis in the medial compartment and preserved full-thickness lateral compartment cartilage, as opposed to patient factors that have a significant effect on outcomes following OUKA, the optimum method of identifying these disease factors radiologically was assessed. It was identified that to assess for bone on bone arthritis in the medial compartment either a fixed-flexion 20° view (FFV20) radiograph or a varus stress radiograph at 20° flexion, both aligned to the joint surface, should be used as a standard standing extension view (SEV) AP knee radiograph does not accurately assess the medial compartment joint space width. When assessed in clinical practice in patients undergoing knee arthroplasty these techniques had an accuracy of 95% in identifying medial compartment bone on bone arthritis compared to an accuracy of 70% of the standard AP knee radiograph.

For the lateral compartment, to assess for preserved full-thickness cartilage, a valgus stress radiograph, aligned to the joint surface, was identified as the most appropriate technique. When

assessed in clinical practice in patients undergoing knee arthroplasty an AP Valgus stress radiograph at 20° flexion had an accuracy of 97% in identifying preserved full-thickness cartilage compared to an accuracy of 89% of the standard AP knee radiograph.

As stress radiographs can be time and resource consuming, which may be behind why their current utilisation is 17%, a novel stress device for the knee was developed. Following multi-disciplinary consultation the device was developed in line with the IDEAL-D framework and taken from pre-clinical testing through to regulatory approval and validation against the gold standard of manual, clinician performed, stress radiographs.

Finally, based on the findings of this thesis, it was hypothesised that the pattern and severity of disease, and as such suitability for OUKA could be reliably determined using a structured radiographic assessment together with structured Decision Aid. A radiological Decision Aid, based on the five disease factors identified as important in determining outcomes in OUKA was developed, and validated in an independent population of patients. Based on radiographs alone the Decision Aid was found to have a sensitivity and specificity of 92% and 88% respectively at predicting suitability for OUKA which increased to 93% and 96% respectively once pre-operative factors that influence implant selection, for example flexion too limited to implant a OUKA, were taken into account. Furthermore, in those patients who met Decision Aid criteria for OUKA and in whom OUKA was performed, excellent survival of 99% at five-years (95%CI 97 to 100) and functional outcomes were achieved, with evidence of worse outcomes in those who did not meet decision aid criteria for OUKA in whom OUKA was implanted.

8.2 Limitations

There are several limitations to this work. Firstly, much of this work from **Chapter 2**, **Chapter 3** and **Chapter 4** was performed in a consecutive series of patients operated on by the developer surgeons. This was chosen for several reasons. Firstly, this locally held dataset represents the largest consecutive series of patients with long-term follow-up for OUKA including demographic, intra-operative and outcomes data. Whilst consideration was made to using alternative dataset, in general, these did not hold intra-operative data and as such one would be reliant on the results of pre-operative clinical testing to infer the disease state. Whilst this approach is highly clinically relevant as it represents the challenges that surgeons are faced with in clinical practice, at present clinical tests that are 100% accurate at determining intra-operative findings pre-operatively do not exist and as such this approach would introduce uncertainty, as well as limit opportunity for further innovation in imaging techniques. Secondly, this dataset was chosen because it represents the outcomes of two experienced OUKA surgeons and as such the reproducibility of the surgical technique may be higher than that seen in other datasets which may result in a less variability in outcomes due to the influence of surgical technique than seen in other series. The inherent limitations in using this series operated on by the developer surgeons is that the results seen may not be representative of the outcomes of OUKA globally, as highlighted in **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**). Whilst the results of this thesis cannot be applied in isolation, and must be interpreted in the context of entire patient pathway, they are highly relevant to the practice of OUKA as one would predict that optimising patient selection using an evidence based approach is a key step to improving overall outcomes.

Whilst the findings presented in **Chapters 2**, **Chapter 3** and **Chapter 4** were also found to be valid at an independent centre during the validation of a Decision Aid in **Chapter 7** (**7.4 Validation of a radiological decision aid for OUKA**) as well as supported by reports from other centres, it must be

acknowledged that, in general, in the Decision Aid validation study, outcomes were good for both OUKA and TKA, and as such it has not been possible to assess whether there has been selection bias in selecting candidates for surgery who are more likely to have good outcomes. As such it remains to be seen whether applying the Decision Aid to the general orthopaedic population would result in improved global outcomes.

8.3 Future work

This thesis has reported several novel findings that require further confirmation. In **Chapter 2** (**2.2 Global Experience: Meta-analysis of published series of OUKA**) it was identified that, for OUKA, surgical usage appeared more important that surgical caseload in determining the risk of revision, with low-usage surgeons having a higher revision rate regardless of their overall caseload. Differences in patient characteristics, as well as failure mechanisms, for OUKA between groups highlighted that low-usage surgeons may be using different indications for OUKA than high-usage surgeons. Whilst both the relationship between usage and outcomes, and caseload and outcomes has been observed in the NJR the interplay between usage and caseload has not been investigated. Using NJR data this finding could be confirmed with analysis of patient characteristics as well as failure mechanisms providing further evidence to support, or refute, this hypothesis.

Chapter 3 reported that, when disease factors are standardised, age, weight and activity level do not effect long-term outcomes following OUKA and **Chapter 4** reported that the macroscopic status of the intact ACL, lateral osteophytes and, with the exception of bone loss with grooving to the lateral patella facet, PFJ disease does not affect long-term outcomes following OUKA. To improve our confidence in these observations where this data builds on short to medium-term data reported from other centres, in the first instance meta-analysis of this data could be performed, and where the observation is new further independent studies could be initiated. Currently NJR globally do not

collect data on disease factors however, through linking local databases in centres where disease factors are recorded or by linking imaging findings to NJR potential exists to evaluate these finding on a national scale. Finally, prospective cohort studies could be performed to evaluate these finding in consecutive series of patients.

The observation in **Chapter 5** that for the medial compartment of the knee fixed-flexion view (FFV20) radiographs and varus stress radiographs, both at 20° flexion, with the radiographic beam aligned to the tibial plateau, provided equivalent results needs to be confirmed externally and the performance of these techniques at confirming medial compartment bone on bone arthritis, identified in **Chapter 4** as important to achieve optimum outcomes, needs to be assessed in populations of knees with varying disease patterns and severities. Likewise for the lateral compartment the performance of valgus stress radiographs at identifying preserved full-thickness cartilage needs to be assessed independently in a large population of patients. In **Chapter 6** the novel stress device requires further external validation with its role in the workup of patients for OUKA confirmed in large independent studies.

Overall, based on the results reported in this thesis the standardisation of patient selection through the introduction of the Decision Aid, reported in **Chapter 7**, would be predicted to reduce the variability in outcomes of OUKA reported in **Chapter 2**. Whilst the evidence presented in this thesis is supported by other reports in the literature the causality of these findings cannot be established and as such prospective, independent, validation studies of the Decision Aid need to be performed in different regions of the world, together with the assessments of short and long-term functional outcomes and implant survival to support its widespread use.

Once the optimum population for OUKA has been defined it would then seem pertinent to perform comparative trials to assess outcomes of OUKA against other contemporary treatments for medial compartment OA, including fixed-bearing UKA or TKA, in this population to establish the true clinical

and cost-effective of this procedure, as well as to assess whether OUKA has a role in patients who are not optimal for OUKA, such as knees with partial-thickness cartilage loss, and how in these populations knees that are most likely to benefit from this procedure are identified.

8.4 Conclusions

The key findings of this thesis are that:

- In the developer series excellent long-term functional outcomes are seen following OUKA with an implant survival of 94% (95%CI 92 to 96) at ten-years and 91% (95%CI 83 to 98) at fifteen-years with lateral compartment disease progression being the most common mode of failure.
- Whilst the results following OUKA seen in the hands of developer surgeons can be replicated elsewhere globally outcomes are a lot more variable with estimates of ten-year survival ranging from 57% to 100%, mean 88% (95%CI 85 to 90).
- Both surgical caseload and usage influence outcomes following OUKA, but surgical usage appears more important, with good results seen with high surgical usage, independent of the surgical caseload.
- Differences in patient selection and failure mechanisms were seen between usage groups, with low-usage surgeons operating on significantly younger patients, and having a higher revision for unexplained pain, suggesting that there may be different indications for OUKA between low and high-usage surgeons.
- Previously published patient factor contraindications based on the patient age (<60 years), weight (≥82kg) and activity level (high activity) do not influence outcomes, when disease factors are standardised, with knees implanted in patients with these previously reported

patient factor contraindications often actually doing better than those without these factors.

- The macroscopic status of the intact ACL, lateral osteophytes, PFJ disease (with the exception of lateral facet disease with bone loss and grooving), and anterior knee pain do not influence outcomes.
- Knees with partial-thickness medial compartment disease at operation have significantly worse functional outcomes with almost three times the reoperation rate, predominantly for unexplained pain compared to knees with full-thickness cartilage loss.
- To assess for bone on bone arthritis in the medial compartment either a fixed-flexion view (FFV20) or varus stress radiograph, both at 20° flexion aligned to the joint surface, should be used as a standard standing extension view (SEV) knee radiograph does not accurately assess the medial compartment joint space width.
- For the lateral compartment, to assess for preserved full-thickness cartilage, a valgus stress radiograph aligned to the joint surface, was identified as the most appropriate technique, with SEV radiographs performing poorly.
- Stress radiographs can be either clinician performed or performed using a novel stress device. A stress device has been developed and validated in line with the IDEAL-D framework, and following regulatory approval in independent clinical use it has been found to be accurate in identifying the status of the medial and lateral compartments of the knee patients undergoing arthroplasty.
- The pattern and severity of disease, and as such suitability for OUKA, can be reliably determined using a structured radiographic assessment together with structured Decision Aid which has been found to be have a sensitivity and specificity of 92% and 88% based on radiographs alone, increasing to 93% and 96% once pre-operative factors that influence

implant selection, for example flexion too limited to implant a OUKA, were taken into account in an independent population.

Appendices

Appendix 1: Awards, publications and intellectual property

A1.1 Awards

- Innovation Challenge Award, Oxford University Hospitals NHS Trust (£12,000 for Oxford Stress System for Knee Arthroplasty Radiographs (OSSKAR) product development and validation) 2014
- NIHR Biomedical Research Centre Clinical Training Fellowship (Full funding for DPhil in Musculoskeletal Sciences, University of Oxford) 2014 - 2016

A1.2 Publications

Eight publications have come directly from this thesis. In addition this work has been presented nationally to the British Orthopaedic Association and British Association of Surgeons of the Knee and internationally to the American Academy of Orthopaedic Surgeons, Combined Orthopaedic Associations International Meeting, European Federation of National Associations of Orthopaedics and Traumatology and the European Society of Sports Traumatology, Knee Surgery and Arthroscopy.

- *Pandit H, ***Hamilton TW*** (*joint first author), Jenkins C, Mellon SJ, Dodd CAF & Murray DW. Fifteen-year survival and functional outcome of 1000 Oxford phase 3 UKR. (2015) Bone and Joint Journal 97-B:1493-1500

- **Hamilton TW**, Rizkalla J, Kontochristos L, Marks B, Mellon S, Dodd CAF, Pandit HG & Murray DW. The interaction of caseload and usage in determining outcomes of unicompartmental knee arthroplasty: A meta-analysis. (2017) Journal of Arthroplasty. 32(10):3228-3237
- **Hamilton TW**, Pandit HG, Jenkins C, Mellon SJ, Dodd CA, Murray DW. Evidence-Based Indications for Mobile-Bearing Unicompartmental Knee Arthroplasty in a Consecutive Cohort of Thousand Knees. (2017) Journal of Arthroplasty. 32(6):1779-1785
- **Hamilton TW**, Pandit HG, Inabathula A, Ostlere SJ, Jenkins C, Mellon SJ, Dodd CAF & Murray DW. Unsatisfactory outcomes following unicompartmental knee replacement for partial-thickness cartilage loss: a medium-term follow-up. (2017) Bone and Joint Journal 99-B:475-482
- **Hamilton TW**, Pistritto C, Jenkins C, Mellon SJ, Dodd CAF, Pandit HG & Murray DW Unicompartmental Knee Replacement: Does The Macroscopic Status Of The Anterior Cruciate Ligament Affect Outcome? Knee (2016) 23(3):506-510
- **Hamilton TW**, Choudhary R, Jenkins C, Mellon SJ, Dodd CA, Murray DW, Pandit HG. Lateral osteophytes do not represent a contraindication to medial unicompartmental knee arthroplasty: a 15-year follow-up. (2017) KSSTA 25(3):*652-659*
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THE BONE & JOINT JOURNAL

■ KNEE

The clinical outcome of minimally invasive Phase 3 Oxford unicompartmental knee arthroplasty

A 15-YEAR FOLLOW-UP OF 1000 UKAS

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There have been concerns about the long-term survival of unicompartmental knee arthroplasty (UKA).

This prospective study reports the 15-year survival and ten-year functional outcome of a consecutive series of 1000 minimally invasive Phase 3 Oxford medial UKAs (818 patients, 393 men, 48%, 425 women, 52%, mean age 66 years; 32 to 88). These were implanted by two surgeons involved with the design of the prosthesis to treat anteromedial osteoarthritis and spontaneous osteonecrosis of the knee, which are recommended indications. Patients were prospectively identified and followed up independently for a mean of 10.3 years (5.3 to 16.6).

At ten years, the mean Oxford Knee Score was 40 (standard deviation (SD) 9; 2 to 48): 79% of knees (349) had an excellent or good outcome. There were 52 implant-related re-operations at a mean of 5.5 years (0.2 to 14.7). The most common reasons for re-operation were arthritis in the lateral compartment (2.5%, 25 knees), bearing dislocation (0.7%, seven knees) and unexplained pain (0.7%, seven knees). When all implant-related re-operations were considered as failures, the ten-year rate of survival was 94% (95% confidence interval (CI) 92 to 96) and the 15-year survival rate 91% (CI 83 to 98). When failure of the implant was the endpoint the 15-year survival was 99% (CI 96 to 100).

This is the only large series of minimally invasive UKAs with 15-year survival data. The results support the continued use of minimally invasive UKA for the recommended indications.

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Unicompartmental knee arthroplasty (UKA) has been reported to have significant benefits over total knee arthroplasty (TKA). A propensity-matched analysis of over 100 000 patients has shown that compared with TKA, patients undergoing UKA are half as likely to have a major complication such as myocardial infarction, stroke or deep infection and are one quarter as likely to die within the first 30 days of surgery. They also have a significantly lower mortality within eight years of surgery.[1] Furthermore, it has been shown that patients who undergo UKA have a faster recovery, more normal knee kinematics, an increased range of movement (ROM) and better patient-reported outcome measures compared with those who have undergone TKA.[2,3] However, there are concerns about long-term implant survival. Variable survival is seen after UKA, and overall, it has a significantly higher rate of revision than TKA.[1] This higher incidence of revision is due to factors related to surgeon, patient and disease. The threshold for revision is also higher with TKA.[4]

The cemented Phase 3 Oxford medial UKA (Biomet, Swindon, United Kingdom) was introduced in 1998. It is implanted through a minimally invasive approach which avoids the need for disruption of the extensor mechanism and eversion of the patella required by previous designs. This enhances the speed of recovery and functional outcome.[3] Overall, however, the fundamental principles of the Oxford UKA remain unchanged. The articulation of the prosthesis has remained the same for the last 40 years, and incorporates a fully congruous mobile meniscal bearing which is designed to minimise wear and preserve the normal kinematics of the knee.

The Oxford UKA is indicated for patients with anteromedial osteoarthritis (AMOA) or spontaneous osteonecrosis of the knee (SONK).[5] In cases of AMOA the patient should have bone-on-bone arthritis in the medial compartment with full thickness cartilage in the lateral compartment, which is best seen on a valgus stress radiograph.[6] The medial collateral (MCL) and anterior cruciate ligaments (ACL) should be functionally normal, as

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Review

The Interaction of Caseload and Usage in Determining Outcomes of Unicompartmental Knee Arthroplasty: A Meta-Analysis

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ABSTRACT

Background: Outcomes after unicompartmental knee arthroplasty (UKA) are variable and influenced by caseload (UKA/y) and usage (percentage of knee arthroplasty that are UKA), which relates to indications. This meta-analysis assesses the relative importance of these factors.
Methods: MEDLINE (Ovid), Embase (Ovid), and Web of Science (ISI) were searched for consecutive series of cemented Phase 3 Oxford medial UKA. The primary outcome was revision rate/100 observed component years (% pa) with subgroup analysis based on caseload and usage.
Results: Forty-six studies (12,520 knees) with an annual revision-rate ranging from 0% to 4.35% pa, mean 1.21% pa (95% confidence interval [CI], 0.97-1.47), were identified. In series with mean follow-up of 10-years, the revision-rate was 0.63% pa (95% CI, 0.46-0.83), equating to a 94% (95% CI, 92%-95%) 10-year survival. Aseptic loosening, lateral arthritis, bearing dislocation, and unexplained pain were the predominant failure mechanisms with revision for patellofemoral problems and polyethylene wear exceedingly rare. The lowest revision-rates were achieved with caseload >24 UKA/y (0.88% pa; 95% CI, 0.63-1.61) and usage >30% (0.69% pa; 95% CI, 0.50-0.90). Usage was more important than caseload; with high usage (≥20%), the revision-rate was low, whether the caseload was high (>12 UKA/y) or low (≤12 UKA/y; (0.94% pa; 95% CI, 0.69-1.23 and 0.85% pa; 95% CI, 0.65-1.08), respectively); with low usage (<20%), the revision-rate was high, whether the caseload was high or low (1.58% pa; 95% CI, 0.57-3.05 and 1.76% pa; 95% CI, 1.21-2.41, respectively).
Conclusion: To achieve optimum results, surgeons, whether high or low caseload, should adhere to the recommended indications such that ≥20%, or ideally >30% of their knee arthroplasties are UKA. If they do this, then they can expect to achieve results similar to those of the long-term series, which all had high usage (>20%) and an average 10-year survival of 94%.

In appropriate patients, unicompartmental knee arthroplasty (UKA) has significant benefits over total knee arthroplasty (TKA) including faster recovery, better patient-reported outcome measures, and lower morbidity and mortality; however, it has been reported to be associated with a higher incidence of revision [1]. The causes of this higher incidence of revision are multifactorial and involve a complex interaction of patient, implant, and surgeon factors as well as differing thresholds for revision compared with TKA [2].

Surgeon factors associated with outcome include technical skills associated with the procedure itself as well as non-technical skills associated with decision-making around patient selection. Technical skills have been hypothesized to improve as surgical volume

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Primary Arthroplasty

Evidence-Based Indications for Mobile-Bearing Unicompartmental Knee Arthroplasty in a Consecutive Cohort of Thousand Knees

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ABSTRACT

Background: The indications for unicompartmental knee arthroplasty remain controversial. Previously recommended contraindications include the following: age under 60 years, weight 180 lb (82 kg) or over, patients undertaking heavy labor, chondrocalcinosis, and exposed bone in the patellofemoral joint. This study explores whether these contraindications are valid in mobile-bearing unicompartmental knee arthroplasty.

Methods: Using a prospective series of 1000 consecutive medial unicompartmental knee arthroplasties in which the reported contraindications were not applied, the functional outcome and survival in patients with or without contraindications were compared.

Results: Of the 1000 consecutive unicompartmental knee arthroplasties (818 patients), 68% (678 knees) would be considered contraindicated based on published contraindications. At a mean follow-up of 10 years (5-17), there was no difference in American Knee Society (AKS) Objective Scores ($P = .05$) or Oxford Knee Score ($P = .08$) between groups. However, knees with contraindications had significantly ($P = .02$) fewer poor outcomes and significantly better AKS Functional Scores ($P < .001$) and Tegner Activity Scores ($P < .001$). At 15 years, no difference in implant survival ($P = .33$) was observed. The 3% of unicompartmental knee arthroplasties performed in young men (age <60) weighing 180 lb or over with high activity levels, who have been reported to have poor outcomes after fixed-bearing unicompartmental knee arthroplasty, had significantly better AKS Functional Scores ($P < .001$), Oxford Knee Score ($P = .01$), and Tegner Activity Score ($P < .001$) at 10 years. No difference in AKS Objective Scores ($P = .54$) at 10 years or implant survival at 15 years ($P = .75$) was seen.

Conclusion: This large case series provides evidence that patients with the previously reported contraindications do as well as, or even better than, those without contraindications. Therefore these contraindications should not apply to mobile-bearing unicompartmental knee arthroplasty.

Unicompartmental knee arthroplasty has significant patient benefits over total knee arthroplasty, including improved functional outcomes and significantly lower morbidity and mortality [1]. Despite the benefits of unicompartmental knee arthroplasty, it remains relatively underutilized and this in part is due to controversies in the indications. In their seminal paper on unicompartmental knee arthroplasty, Kozinn and Scott [2] highlighted the benefits of unicompartmental knee arthroplasty including retained normal knee kinematics and proprioception, improved range of movement, preserved bone stock, and, in the case of failure, ability to revise to a primary total knee arthroplasty. However to optimize outcomes, primarily based on their experience with a fixed-bearing device, they advised strict patient and disease criteria for the procedure [2].

The Oxford unicompartmental knee arthroplasty (Zimmer Biomet, Warsaw, IN) employs a fully congruous freely mobile-bearing articulating with a spherical femur and a flat tibia. In contrast to the

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THE BONE & JOINT JOURNAL

■ KNEE

Unsatisfactory outcomes following unicompartmental knee arthroplasty in patients with partial thickness cartilage loss

A MEDIUM-TERM FOLLOW-UP

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Aims

While medial unicompartmental knee arthroplasty (UKA) is indicated for patients with full-thickness cartilage loss, it is occasionally used to treat those with partial-thickness loss. The aim of this study was to investigate the five-year outcomes in a consecutive series of UKAs used in patients with partial thickness cartilage loss in the medial compartment of the knee.

Patients and Methods

Between 2002 and 2014, 94 consecutive UKAs were undertaken in 90 patients with partial thickness cartilage loss and followed up independently for a mean of six years (1 to 13). These patients had partial thickness cartilage loss either on both femur and tibia (13 knees), or on either the femur or the tibia, with full thickness loss on the other surface of the joint (18 and 63 knees respectively). Using propensity score analysis, these patients were matched 1:2 based on age, gender and pre-operative Oxford Knee Score (OKS) with knees with full thickness loss on both the femur and tibia. The functional outcomes, implant survival and incidence of re-operations were assessed at one, two and five years post-operatively. A subgroup of 36 knees in 36 patients with partial thickness cartilage loss, who had pre-operative MRI scans, was assessed to identify whether there were any factors identified on MRI that predicted the outcome.

Results

Knees with partial thickness cartilage loss had significantly worse functional outcomes at one, two and five years post-operatively compared with those with full thickness loss. A quarter of knees with partial thickness loss had a fair or poor result and a fifth failed to achieve a clinically significant improvement in OKS from a baseline of four points or more; double that seen in knees with full thickness loss. Whilst there was no difference in implant survival between the groups, the rate of re-operation in knees with partial thickness loss was three times higher. Most of the re-operations (three-quarters), were arthroscopies for persistent pain.

Compared with those achieving good or excellent outcomes, patients with partial thickness cartilage loss who achieved fair or poor outcomes were younger and had worse pre-operative functional scores. However, there were no other differences in the baseline demographics. MRI findings of full thickness cartilage loss, subchondral oedema, synovitis or effusion did not provide additional prognostic information.

Conclusion

Medial UKA should be reserved for patients with full thickness cartilage loss on both the femur and tibia. Whilst some patients with partial thickness loss achieve a good result we cannot currently identify which these will be and in this situation MRI is unhelpful and misleading.

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Patients with early arthritis of the knee are said to account for over a quarter of secondary care consultations for osteoarthritis (OA).[1] Having failed conservative treatment, in three-quarters of cases the pain and functional scores are the same, if not worse than in those with more advanced changes.[2] In randomised studies, arthroscopic surgery has been shown not to help these patients and there is uncertainty over the role of corticosteroids, hyaluronic acid and platelet rich plasma.[3-6] The optimum form of treatment in this large group of patients, including the role of expectant management, therefore, remains unclear.

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The Knee

Unicompartmental knee replacement: Does the macroscopic status of the anterior cruciate ligament affect outcome?

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ABSTRACT

Purpose: ACL damage is associated with progression of arthritis and whilst in the population undergoing joint replacement in the majority of cases the ACL is intact there is a wide spectrum of ACL disease. This study investigated whether the macroscopic status of the ACL affected functional outcome or survival following UKR.
Methods: The macroscopic status of the ACL was recorded in 820 cemented Oxford UKRs implanted by two surgeons for the recommended indications. The ACL was considered functionally normal in the setting of anteromedial tibial wear and macroscopically the ACL visually appeared normal or had synovial damage or longitudinal splits. The patients were followed up independently with a mean follow-up of 10.3 years (range 5.3 to 16.6).
Results: More marked ACL macroscopic damage was significantly associated with increasing age, male gender and a more extensive anteromedial tibial defect. Patients with more ACL damage had a significantly lower preoperative AKSS Objective Score, however no difference in AKSS-Functional or OKS was detected between groups. At 10 years no difference in functional outcome or activity level was found between groups. Compared to those with a macroscopically normal ACL at 10 years a significantly greater improvement from baseline OKS score was seen in patients with macroscopic ACL abnormalities. At 15 years no difference in implant survival, or failure mechanism, was detected between groups.
Conclusion: The macroscopic status of the ACL does not affect long term functional outcomes or implant survival and in the setting of an intact ACL macroscopic status is not a contraindication to mobile bearing UKR.
Level of evidence: Level IV.

1. Introduction

In patients with moderate to severe osteoarthritis who fail non-operative management unicompartmental knee replacement (UKR) is a clinical and cost effective treatment [11,30]. UKR provides significant functional benefits over total knee replacement (TKR), including increased range of movement, preserved knee kinematics and preserved proprioception [9,22,21]. These benefits have, in part, been attributed to the fact that UKR is minimally invasive retaining the native structures of the joint, including the knee ligaments, in particular the anterior cruciate ligament (ACL).

In the native knee the intact ACL plays a pivotal role in knee kinematics and is important for femoral rollback, the screw-home mechanism and normal gait [14]. In addition the mechanoreceptors within the ACL play a key role in proprioception, loss of which is associated with poor knee function [23]. ACL degeneration is strongly associated with osteoarthritis and a correlation exists between radiological grade of osteoarthritis and degree of degeneration of the ACL [15].

The ACL has been reported to be intact in up to two thirds of patients undergoing TKR (range 25% to 68%) and it is known that the macroscopic status of the ACL is associated with the pathoanatomy of knee arthritis within the joint, with progressive ACL damage associated with an increasing size of anteromedial tibial defect [7,25].

A functional ACL is a requirement for mobile bearing UKR. When mobile bearing UKR is used in ACL deficient knees a significantly higher failure rate, predominantly due to tibial loosening, is observed compared to ACL intact knees or ACL deficient knees treated with simultaneous or sequential ACL reconstruction and UKR [12]. In addition where mobile bearing UKR is performed in ACL deficient knees this is associated with abnormal knee kinematics and bearing movement [19].

Whilst a functionally intact ACL is a requirement for mobile bearing UKR, not all patients have a macroscopically normal ACL. Furthermore it is known that even in a macroscopically normal ACL high levels of histological abnormalities exist. The outcome of UKR in these patients who have macroscopic abnormalities in the ACL is unknown. As a significant number of patients presenting with anteromedial arthritis have an abnormal, yet intact, ACL it is important to establish whether it is safe to perform a UKR in these cases. This study investigated the relationship between the macroscopic status of the ACL and the

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KNEE

Lateral osteophytes do not represent a contraindication to medial unicompartmental knee arthroplasty: a 15-year follow-up

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Abstract
Purpose Lateral osteophytes have been reported to be associated with lateral compartment disease and as such it is unclear whether medial unicompartmental knee arthroplasty should be performed if these are present.
Methods Using the OARSI classification system, 0 (no osteophyte) to 3 (large osteophyte), radiographs from a series of cemented meniscal-bearing unicompartmental knee arthroplasty implanted in the setting of full-thickness lateral cartilage where lateral osteophytes were not considered a contraindication were identified and factors associated with the presence and size of lateral osteophytes, and their impact on clinical outcomes and implant survival were assessed.
Results Pre-operative radiographs from 458 knees (392 patients), independently followed up for a mean 10.5 years (range 5.3–16.6), were assessed. Lateral osteophytes were present in 62 % of knees with 18 % scored as Grade 3. Inter-observer reliability was good (kappa = 0.70). The presence and size of lateral osteophytes was associated with younger age at joint replacement ($p = 0.01$) and increasing BMI ($p = 0.01$). No association was seen with gender, pre-operative status, assessed using the Oxford Knee Score (OKS), American Knee Society (AKSS) Objective or Functional Score, Tegner activity score, or size of medial tibial lesion. Subgroup analysis of Grade 3 Osteophytes revealed that these were associated with a greater degree of macroscopic ACL damage. At 10 years there was no difference in function (n.s.), and at 15 years no difference in implant survival or mechanism of failure between groups (n.s.). Subgroup analysis of Grade 3 osteophytes found no significant difference in functional outcome at 10 years or implant survival at 15 years.
Conclusion The presence of lateral osteophytes is not a contraindication to medial meniscal-bearing unicompartmental knee arthroplasty. The clinical relevance of this study is that it highlights the importance of an appropriate pre-operative assessment of the lateral compartment as in the setting of full-thickness cartilage at operation lateral osteophytes do not compromise long-term functional outcome or implant survival.
Level of evidence IV.

Keywords Meniscal-bearing unicompartmental knee arthroplasty · Implant survival · Functional outcome · Osteophytes · Patient selection

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THE BONE & JOINT JOURNAL

■ KNEE

Anterior knee pain and evidence of osteoarthritis of the patellofemoral joint should not be considered contraindications to mobile-bearing unicompartmental knee arthroplasty

A 15-YEAR FOLLOW-UP

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Correspondence should be sent to D. W. Murray; email: David.Murray@ndorms.ox.ac.uk

doi:10.1302/0301-620X.99B5.BJJ-2016-0695.R2 $2.00

Bone Joint J 2017;99-B:632–9.
Received 18 July 2016; Accepted after revision 1 December 2016

Aims
It is not clear whether anterior knee pain and osteoarthritis (OA) of the patellofemoral joint (PFJ) are contraindications to medial unicompartmental knee arthroplasty (UKA). Our aim was to investigate the long-term outcome of a consecutive series of patients, some of whom had anterior knee pain and PFJ OA managed with UKA.

Patients and Methods
We assessed the ten-year functional outcomes and 15-year implant survival of 805 knees (677 patients) following medial mobile-bearing UKA. The intra-operative status of the PFJ was documented and, with the exception of bone loss with grooving to the lateral side, neither the clinical or radiological state of the PFJ nor the presence of anterior knee pain were considered a contraindication. The impact of radiographic findings and anterior knee pain was studied in a subgroup of 100 knees (91 patients).

Results
There was no relationship between functional outcomes, at a mean of ten years, or 15-year implant survival, and pre-operative anterior knee pain, or the presence or degree of cartilage loss documented intra-operatively at the medial patella or trochlea, or radiographic evidence of OA in the medial side of the PFJ. In 6% of cases there was full thickness cartilage loss on the lateral side of the patella. In these cases, the overall ten-year function and 15-year survival was similar to those without cartilage loss; however they had slightly more difficulty with descending stairs. Radiographic signs of OA seen in the lateral part of the PFJ were not associated with a definite compromise in functional outcome or implant survival.

Conclusion
Severe damage to the lateral side of the PFJ with bone loss and grooving remains a contraindication to mobile-bearing UKA. Less severe damage to the lateral side of the PFJ and damage to the medial side, however severe, does not compromise the overall function or survival, so should not be considered to be a contraindication. However, if a patient does have full thickness cartilage loss on the lateral side of the PFJ they may have a slight compromise in their ability to descend stairs. Pre-operative anterior knee pain also does not compromise the functional outcome or survival and should not be considered to be a contraindication.

Cite this article: *Bone Joint J* 2017;99-B:632–9

Anterior knee pain and osteoarthritis (OA) in the patellofemoral joint (PFJ) are common in patients with OA of the knee and have previously been reported as contraindications for fixed-bearing unicompartmental knee arthroplasty (UKA).[1,2] Whether symptomatic, radiological or intra-operative evidence of OA of the PFJ represent contraindications for mobile-bearing UKA remains uncertain. Long-term follow-up of series of the mobile-bearing Oxford UKA (Zimmer Biomet, Bridgend, United Kingdom) have reported few revisions for anterior knee pain or progression of OA to the PFJ.[3-8] However, PFJ problems are a common cause of failure in the second decade after fixed-bearing UKA.[9-11] There are several reasons why this may be the case. Most designs of fixed-bearing UKA have a polyradial femoral component which can sit proud of the native femoral surface and impinge on the patella,

■ KNEE

Radiological Decision Aid to determine suitability for medial unicompartmental knee arthroplasty

DEVELOPMENT AND PRELIMINARY VALIDATION

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H. G. Pandit,
A. V. Lombardi,
J. B. Adams,
C. R. Oosthuizen,
A. Clavé,
C. A. F. Dodd,
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doi:10.1302/0301-620X.98B10.BJJ-2016-0432.R1 $2.00

Bone Joint J 2016;(10 Suppl B):3–10.

Aims

An evidence-based radiographic Decision Aid for meniscal-bearing unicompartmental knee arthroplasty (UKA) has been developed and this study investigates its performance at an independent centre.

Patients and Methods

Pre-operative radiographs, including stress views, from a consecutive cohort of 550 knees undergoing arthroplasty (UKA or total knee arthroplasty; TKA) by a single-surgeon were assessed. Suitability for UKA was determined using the Decision Aid, with the assessor blinded to treatment received, and compared with actual treatment received, which was determined by an experienced UKA surgeon based on history, examination, radiographic assessment including stress radiographs, and intra-operative assessment in line with the recommended indications as described in the literature.

Results

The sensitivity and specificity of the Decision Aid was 92% and 88%, respectively. Excluding knees where a clear pre-operative plan was made to perform TKA, i.e. patient request, the sensitivity was 93% and specificity 96%. The false-positive rate was low (2.4%) with all affected patients readily identifiable during joint inspection at surgery.

In patients meeting Decision Aid criteria and receiving UKA, the five-year survival was 99% (95% confidence intervals (CI) 97 to 100). The false negatives (3.5%), who received UKA but did not meet the criteria, had significantly worse functional outcomes (flexion $p < 0.001$, American Knee Society Score - Functional $p < 0.001$, University of California Los Angeles score $p = 0.04$), and lower implant survival of 93.1% (95% CI 77.6 to 100).

Conclusion

The radiographic Decision Aid safely and reliably identifies appropriate patients for meniscal-bearing UKA and achieves good results in this population. The widespread use of the Decision Aid should improve the results of UKA.

Cite this article: *Bone Joint J* 2016;98-B(10 Suppl B):3–10.

Unicompartmental knee arthroplasty (UKA) provides significant benefits to patients, healthcare providers and healthcare payers.[1-3] Compared with total knee arthroplasty (TKA), patients undergoing UKA recover faster, achieve better functional outcomes, have a lower morbidity and mortality and report higher patient satisfaction.[1,2,4,5] Furthermore, UKA has been reported to be more cost effective than TKA in both the short- and long-term.[3,6,7] One concern with UKA however is the more variable long-term implant survival, with UKA having a higher overall revision rate than TKA.[1] This higher incidence of revision is multi-factorial, although it is known to be related to patient selection, surgical caseload, as well as a lower threshold for revision than with TKA.[8]

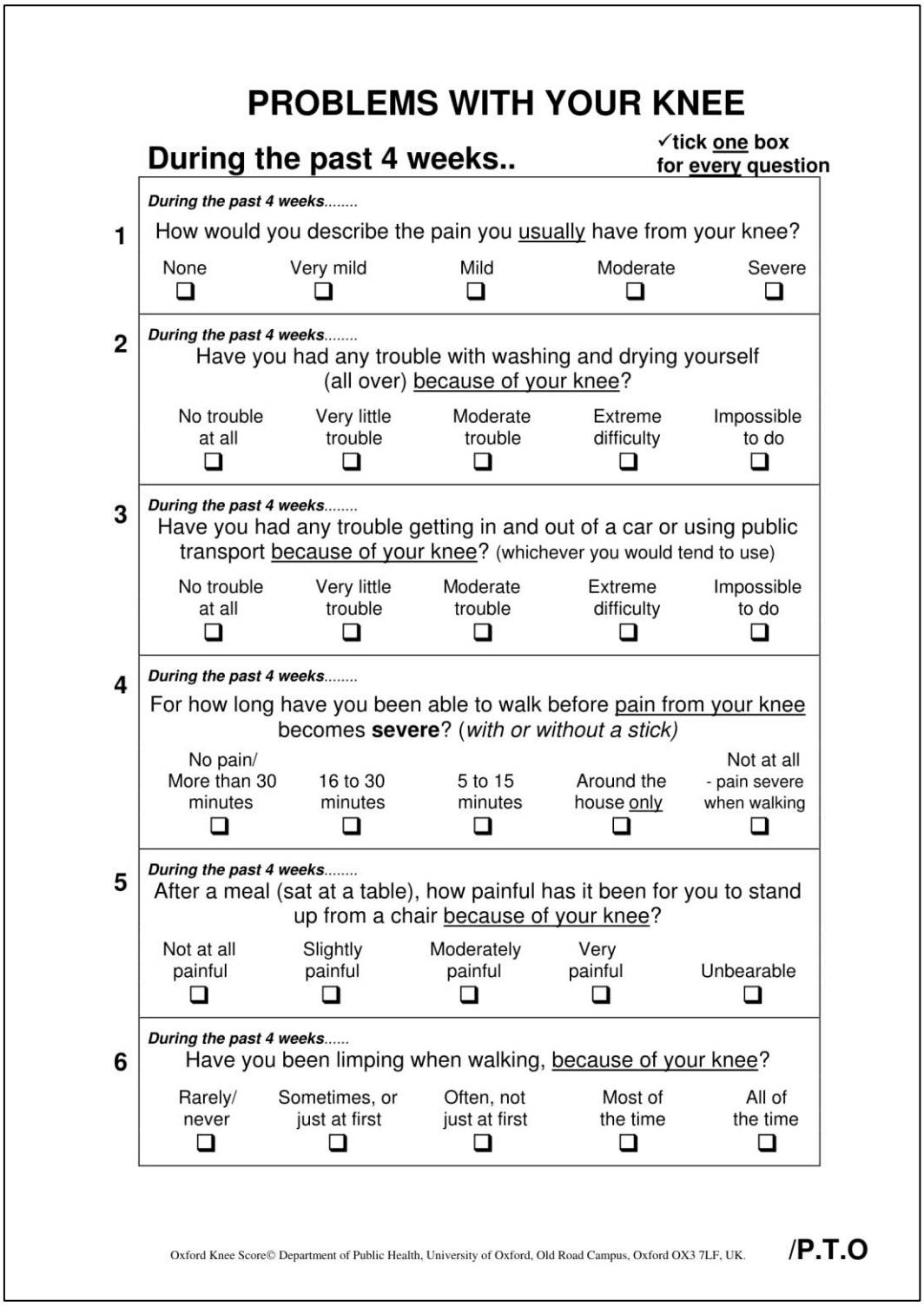
Despite meniscal-bearing UKA being appropriate in up to half the patients receiving treatment with knee arthroplasty, UKA is used in only 8% with large variation in usage between surgeons.[9] One proposed reason for this variation is the lack of recognition of indications for UKA. The primary indication for meniscal-bearing UKA is anteromedial osteoarthritis (AMOA), with spontaneous osteonecrosis of the knee (SONK) representing another important indication.[10] Patient factors including age, weight and level of activity; radiographic factors including chondrocalcinosis and lateral osteophytes; and operative factors including the presence of a chondral ulcer on the medial side of the lateral femoral condyle, have been demonstrated not to compromise outcomes

A1.3 Intellectual property

- **Hamilton TW,** Pandit HG, Mellon SJ & Murray DW. Patent application for 'Patient positioning apparatus' (Oxford Stress System for Knee Arthroplasty Radiographs (OSSKAR)). Patent Application Number: 1507059.2. Filed: 24 April 2015. A medical device for performing valgus and varus stress imaging of the knee.
- **Hamilton TW,** Pandit HG & Murray DW. Copyright for 'Radiological Decision Aid to Determine Suitability for Medial Unicompartmental Knee Arthroplasty'. Registered: 25 June 2015.
- **Hamilton TW,** Pandit HG, Mellon SJ & Murray DW. CE marking for 'Oxford Stress System for Knee Arthroplasty Radiographs (OSSKAR)'. Application Number: CA014935. Filed: 10 July 2015.

Appendix 2: Scoring Systems

A2.1 Oxford Knee Score



PROBLEMS WITH YOUR KNEE

During the past 4 weeks.. ✓**tick one box for every question**

1 *During the past 4 weeks.....*
How would you describe the pain you usually have from your knee?

None	Very mild	Mild	Moderate	Severe
❑	❑	❑	❑	❑

2 *During the past 4 weeks.....*
Have you had any trouble with washing and drying yourself (all over) because of your knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❑	❑	❑	❑	❑

3 *During the past 4 weeks.....*
Have you had any trouble getting in and out of a car or using public transport because of your knee? (whichever you would tend to use)

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❑	❑	❑	❑	❑

4 *During the past 4 weeks.....*
For how long have you been able to walk before pain from your knee becomes **severe**? (*with or without a stick)*

No pain/ More than 30 minutes	16 to 30 minutes	5 to 15 minutes	Around the house only	Not at all - pain severe when walking
❑	❑	❑	❑	❑

5 *During the past 4 weeks.....*
After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
❑	❑	❑	❑	❑

6 *During the past 4 weeks.....*
Have you been limping when walking, because of your knee?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
❑	❑	❑	❑	❑

Oxford Knee Score© Department of Public Health, University of Oxford, Old Road Campus, Oxford OX3 7LF, UK. **/P.T.O**

During the past 4 weeks...

✓tick one box for every question

7 *During the past 4 weeks.....*

Could you kneel down and get up again afterwards?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

8 *During the past 4 weeks.....*

Have you been troubled by pain from your knee in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
❑	❑	❑	❑	❑

9 *During the past 4 weeks.....*

How much has pain from your knee interfered with your usual work *(including housework)*?

Not at all	A little bit	Moderately	Greatly	Totally
❑	❑	❑	❑	❑

10 *During the past 4 weeks.....*

Have you felt that your knee might suddenly 'give way' or let you down?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
❑	❑	❑	❑	❑

11 *During the past 4 weeks.....*

Could you do the household shopping on your own?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

12 *During the past 4 weeks.....*

Could you walk down one flight of stairs?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

A2.2 American Knee Society Score

PART B (American Knee Soc. Score): For Doctor/Clinician to Complete

DIAGNOSIS: Date:

Evaluator (Surname) ☐☐☐☐☐☐☐☐☐☐☐☐☐☐ Centre:

Pain	points
None	50
Mild or Occasional	45
Mild - Stairs only	40
Mild Walking and Stairs	30
Moderate - Occasional	20
Moderate - Continual	10
Severe	0

Stability: (maximum movt in any position)

AP	*points*	*Med-lat*	*points*
< 5 mm	10	<5°	15
5-10 mm	5	6-9°	10
>10 mm	0	10-14°	5
		15°	0

ROM	
degrees	points
≥125	25
120	24
115	23
110	22
105	21
100	20
95	19
90	18
85	17
80	16
75	15
70	14
65	13

degrees	points
60	12
55	11
50	10
45	9
40	8
35	7
30	6
25	5
20	4
15	3
10	2
5	1
0	0

Extension: ☐☐ Maximum Flexion ☐☐☐

subtotal ☐☐☐/100

Flexion contracture:		Extension Lag		Alignment	
	points		points	ASIS – Knee - Ankle	points
0	0	0	0	5-10°Valgus (normal)	0
5-9°	2	0-9°	5	0-4°Valgus	10
10-15°	5	10-20°	10	11- 15°Valgus	10
16-20°	10	>20°	15	Other	20
>20°	15			Measurement	degrees
				Note varus / valgus	

DEDUCTIONS (minus)

Deductions Total ☐☐/50

Knee Score ☐☐☐/100

FUNCTION SCORE

Walking		Stairs		Support (deductions)	
	points		points		points
Unlimited	50	normal	50	Stick	5
500m-1km	40	down with rail	40	2 sticks	10
100-500m	30	up & down with rail	30	crutches/walker	20
<100m	20	unable down	15		
Housebound	10	unable	0		
Unable	0				

Function Total ☐☐☐/100

COMMENTS & CHARNLEY ABC:

A: knee only B: other joints C: systemic illness

Please file safely in patient notes

PhysioResearch11/02/03MK4

A2.3 Tegner Activity Scale

Please circle the number which best describes the activity you are able to do:

Level 10	Competitive sports: football/rugby – national and international.
Level 9	Competitive sports: football (lower divisions), ice hockey, wrestling, gymnastics.
Level 8	Competitive sports: bandy, squash/badminton, athletics (jumping etc.) downhill skiing.
Level 7	Competitive sports: Tennis, athletics (running), motocross, speedway, handball, basketball Recreational sports: football, badminton, ice hockey, squash, athletics (jogging), cross-country.
Level 6	Recreational sports: tennis, badminton, handball, basketball, downhill skiing, jogging at least five times per week.
Level 5	Work: Heavy labour (eg building, forestry). Competitive sports: Cycling, cross-country skiing. Recreational sports: Jogging on uneven ground at least twice a week.
Level 4	Work: Moderate heavy labour (eg lorry driving, heavy domestic work). Recreational sports: cycling, cross-country skiing, jogging on even ground at least twice a week.
Level 3	Work: Light labour eg nursing. Competitive and recreational sports: swimming, walking in forest possible.
Level 2	Work: Light labour Walking on uneven ground possible but walking in forest impossible.
Level 1	Work: Sedentary. Walking on even ground possible.
Level 0	Sick leave or disability pension due to knee problems.

A2.4 University California Los Angeles Activity Score

UCLA Activity Score	ID:
	Study: ☐ Left ☐ Right
	Examination Date (MM/DD/YY): / /
	Subject Initials: |____|____|____|
	Medical Record Number:

Interval: _____

Check one box that best describes current activity level.

☐ 1: Wholly Inactive, dependent on others, and can not leave residence

☐ 2: Mostly Inactive or restricted to minimum activities of daily living

☐ 3: Sometimes participates in mild activities, such as walking, limited housework and limited shopping

☐ 4: Regularly Participates in mild activities

☐ 5: Sometimes participates in moderate activities such as swimming or could do unlimited housework or shopping

☐ 6: Regularly participates in moderate activities

☐ 7: Regularly participates in active events such as bicycling

☐ 8: Regularly participates in active events, such as golf or bowling

☐ 9: Sometimes participates in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor or backpacking

☐ 10: Regularly participates in impact sports

Appendix 3: Data Collection Forms

A3.1 Oxford Surgical Data Collection Form

Please attach patient sticky label here

NOC

Completed forms in top red tray on Vicky's desk (Bone Bank office) please

OXFORD UKA OPERATION FORM

Patient's name **Hospital Number** **Side: R / L** **Medial / Lateral**

Operation Date: / / 201 Operation type: Primary / Revision **Diagnosis:** OA / AVN

Operating surgeon: Operating surgeon grade:

Assistant surgeon: Assistant surgeon grade:

Consultant surgeon: Operation approach: MIS UKA Funded: NHS

Aanesthesia: 1.GA 2.Femoral block 3.Sciatic block 4.Single shot spinal 5.Epidural 6.Combined spinal and epidural 7.Intra-articular infiltration 8a.Intra-articular epidural catheter top-up with saline 8b.Intra-articular epidural catheter top-up with 0.5% bupivicaine

---

SURGICAL FINDINGS

ACL: Normal / Synovial Damage / Longitudinal splits / Friable and Fragmented / Absent / Absent and Reconstructed simultaneously / Absent and staged Reconstruction

	PTCL *	Focal (<2cm^2) FTCL**	Extensive (>2cm^2) FTCL	Bone loss < 5 mm	Bone loss > 5mm
Involved Femur					
Involved Tibia					

* Partial thickness cartilage loss ** Full Thickness cartilage loss

	Normal	Superficial Damage	PTCL*	Focal (<2cm^2) FTCL**	Extensive (>2cm^2)FTCL
Lateral facet patella					
Medial facet patella					
Trochlea					
Uninvolved femur (Non-weight bearing)					
Uninvolved femur (Weight bearing)					

IMPLANT PARAMETERS

Bearing: Phase 2 /3 Bearing thickness: 0 /1/ 2/ 3 /4 /5 /6 /7 /8 /9

Bearing type: Mark 1 /Mark 2/ Anatomic / Lateral domed /Lateral Fixed

---

Femur: Phase 3 / Phase 3 Hiflex/Cementless femur

Femur Size: Ex-Small / Small / Medium (Standard) / Large / Ex-Large

Last Spigot Size: 0 / 1 / 2 / 3 / 4 / 5 / 6 / 7

Tibia: Phase 3 (new) / Phase 3 (old) / phase 2/Domed lateral

Tibia Size: AA / A / B / C / D / E / F or 26x38 / 26x41 / 28x44 / 30x47 / 32x50 / 34x53 0r 28x40 / 28x44 /28x48 /31x48 /31x52

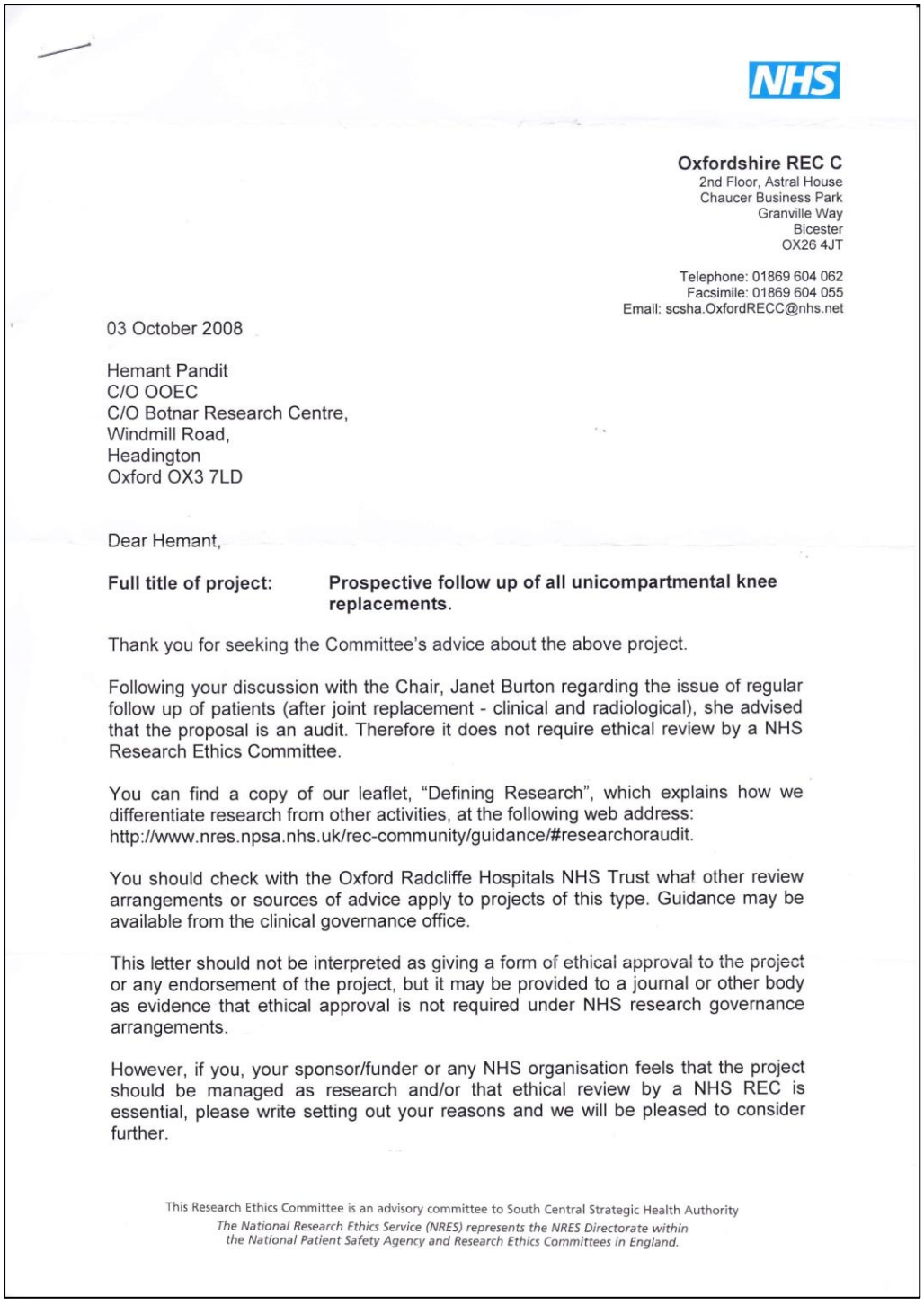
Cement: CMW1 / CMW3 / Palacos/ Optipac **CEMENTED** **CEMENTLESS**

Additional procedures: 1. RSA Y / N **2. Mosaicplasty** Y / N

PLEASE ATTACH IMPLANT STICKERS ON REVERSE - THANK YOU

Appendix 4: Ethics

A4.1 Prospective follow-up of all OUKA



NHS

Oxfordshire REC C
2nd Floor, Astral House
Chaucer Business Park
Granville Way
Bicester
OX26 4JT

Telephone: 01869 604 062
Facsimile: 01869 604 055
Email: scsha.OxfordRECC@nhs.net

03 October 2008

Hemant Pandit
C/O OOEC
C/O Botnar Research Centre,
Windmill Road,
Headington
Oxford OX3 7LD

Dear Hemant,

Full title of project: **Prospective follow up of all unicompartmental knee replacements.**

Thank you for seeking the Committee's advice about the above project.

Following your discussion with the Chair, Janet Burton regarding the issue of regular follow up of patients (after joint replacement - clinical and radiological), she advised that the proposal is an audit. Therefore it does not require ethical review by a NHS Research Ethics Committee.

You can find a copy of our leaflet, "Defining Research", which explains how we differentiate research from other activities, at the following web address: http://www.nres.npsa.nhs.uk/rec-community/guidance/#researchoraudit.

You should check with the Oxford Radcliffe Hospitals NHS Trust what other review arrangements or sources of advice apply to projects of this type. Guidance may be available from the clinical governance office.

This letter should not be interpreted as giving a form of ethical approval to the project or any endorsement of the project, but it may be provided to a journal or other body as evidence that ethical approval is not required under NHS research governance arrangements.

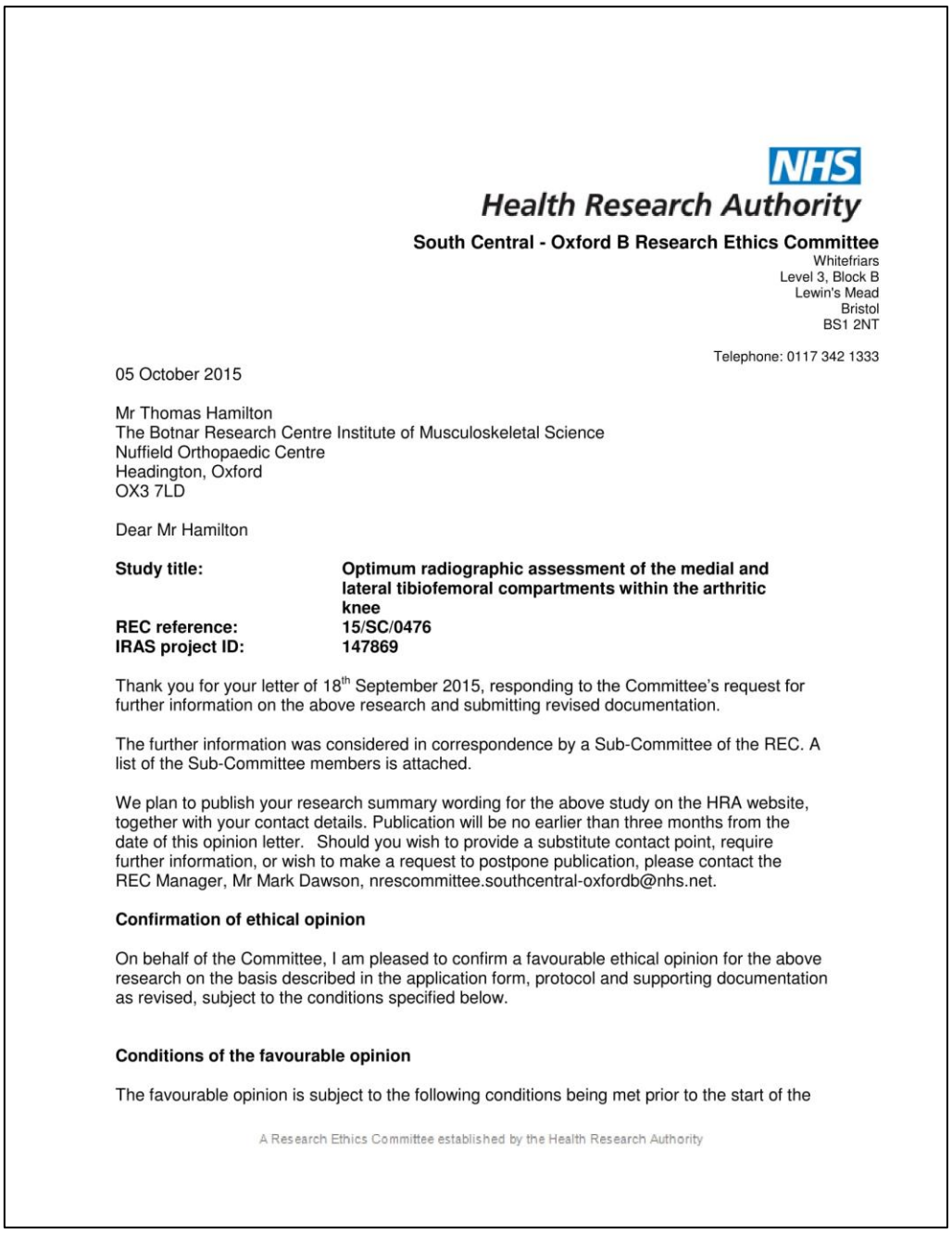
However, if you, your sponsor/funder or any NHS organisation feels that the project should be managed as research and/or that ethical review by a NHS REC is essential, please write setting out your reasons and we will be pleased to consider further.

Where NHS organisations have clarified that a project is not to be managed as research, the Research Governance Framework states that it should not be presented as research within the NHS.

Yours sincerely

Sabrina Harris
Committee Co-ordinator

A4.2 Optimum radiographic assessment of the arthritic knee



NHS
Health Research Authority

South Central - Oxford B Research Ethics Committee
Whitefriars
Level 3, Block B
Lewin's Mead
Bristol
BS1 2NT

Telephone: 0117 342 1333

05 October 2015

Mr Thomas Hamilton
The Botnar Research Centre Institute of Musculoskeletal Science
Nuffield Orthopaedic Centre
Headington, Oxford
OX3 7LD

Dear Mr Hamilton

Study title:	**Optimum radiographic assessment of the medial and lateral tibiofemoral compartments within the arthritic knee**
REC reference:	**15/SC/0476**
IRAS project ID:	**147869**

Thank you for your letter of 18th September 2015, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a Sub-Committee of the REC. A list of the Sub-Committee members is attached.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mr Mark Dawson, nrescommittee.southcentral-oxfordb@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the

A Research Ethics Committee established by the Health Research Authority

study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]	v1.0	06 July 2015
Covering letter on headed paper [Cover Letter]	1.1	14 September 2015
GP/consultant information sheets or letters [GP Letter]	1.1	14 September 2015
Interview schedules or topic guides for participants [Clinical Record Form]	1.1	14 September 2015
IRAS Checklist XML [Checklist_18092015]		18 September 2015
Letter from funder [Funding Letter]	v1.0	20 May 2015
Letters of invitation to participant [Participant Letter]	1.1	14 September 2015
Non-validated questionnaire [Intra-operative audit]	1.1	14 September 2015
Other [H Pandit CV]	v1.0	01 May 2015
Other [S Mellon CV]	v1.0	20 March 2015
Participant consent form [Consent Form]	1.1	14 September 2015
Participant information sheet (PIS) [Participant Information leaflet]	1.1	14 September 2015
REC Application Form [REC_Form_13072015]		13 July 2015
Referee's report or other scientific critique report [Peer Review]	v1.0	05 March 2014
Research protocol or project proposal [Protocol]	1.1	14 September 2015
Summary CV for Chief Investigator (CI) [T Hamilton CV]	v1.0	21 March 2015
Summary CV for student [T Hamilton CV]	v1.0	23 March 2015
Summary CV for supervisor (student research) [D Murray CV]	v1.0	01 May 2015
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Study Flow chart]	1.1	14 September 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

15/SC/0476	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

PP
Mr Chris Foy
Chair

Email:nrescommittee.southcentral-oxfordb@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
"After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Ms Heather House, Oxford University Hospitals NHS Trust*

South Central - Oxford B Research Ethics Committee

Attendance at Sub-Committee of the REC meeting in correspondence

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mr Chris Foy (Char)	Medical Statistician	Yes	
Dr Wilhelm Kueker	Consultant Neuroradiologist	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mr Stephan Ramey	REC Assistant

A4.3 Validation of a device for performing valgus and varus stress x-rays of the knee

NHS
Health Research Authority

South Central - Oxford B Research Ethics Committee
Whitefriars
Level 3, Block B
Lewin's Mead
Bristol
BS1 2NT

Telephone: 0117 342 1333

05 October 2015

Mr Thomas Hamilton
The Botnar Research Centre Institute of Musculoskeletal Science
Nuffield Orthopaedic Centre
Headington, Oxford
OX3 7LD

Dear Mr Hamilton

Study title:	**Validation of a device for performing valgus and varus stress x-rays of the knee**
REC reference:	**15/SC/0468**
Protocol number:	**v1.0**
IRAS project ID:	**160553**

Thank you for your letter of 18th September 2015, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a Sub-Committee of the REC. A list of the Sub-Committee members is attached.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mr Mark Dawson, nrescommittee.southcentral-oxfordb@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the

A Research Ethics Committee established by the Health Research Authority

study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter]	1.0	12 July 2015
Covering letter on headed paper [Cover letter]	v1.1	14 September 2015
GP/consultant information sheets or letters [GP Letter]	1.1	14 September 2015
Instructions for use of medical device [Product Information]	0.1	01 June 2015
IRAS Checklist XML [Checklist_18092015]		18 September 2015
Letter from funder [Funding]	1.0	20 May 2015
Letters of invitation to participant [Participant Letter]	1.1	14 September 2015
Non-validated questionnaire [Intra-operative Audit]	1.1	14 September 2015
Other [MHRA Letter]	v0.1	10 July 2015
Other [CE Certification]	v0.1	24 June 2015
Other [OSSKAR Technical File]	v1.0	07 July 2015
Participant consent form [Consent Form]	1.1	14 September 2015
Participant information sheet (PIS) [PIS]	1.1	14 September 2015
REC Application Form [REC_Form_13072015]		13 July 2015
Research protocol or project proposal [Protocol]	1.1	14 September 2015
Summary CV for Chief Investigator (CI) [CV]	1.0	20 March 2015
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Flow chart]	1.1	14 September 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at
http://www.hra.nhs.uk/hra-training/

15/SC/0468	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

PP
Mr Chris Foy
Chair

Email:nrescommittee.southcentral-oxfordb@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
"After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Ms Heather House, Oxford University NHS Trust*

South Central - Oxford B Research Ethics Committee

Attendance at Sub-Committee of the REC meeting in correspondance

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mr Chris Foy (Chair)	Medical Statistician	Yes	
Dr Wilhelm Kueker	Consultant Neuroradiologist	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mr Stephan Ramey	REC Assistant

Appendix 5: Meta-analysis

A5.1 Search strategy

Arthroplasty, Replacement, Knee/

Partial.ab

unicompartmental.ab

unicondylar.ab

uni.ab

UKA.ab

UKR.ab

UCA.ab

UCR.ab

PKA.ab

PKR.ab

PCA.ab

Oxford.ab

meniscal.ab

mobile.ab

OR/ 2-15

1 AND 16

17 (limited to humans)

Database searched	Date searched	Number of results
MEDLINE (OVID) & in Process 1946 to March 16, 2016	17/03/2016	1554
EMBASE (OVID) 1996 to Week 11 2016	17/03/2016	975
ISI Web of Science (SCI, SSCI, CPCI-S & CPCI-SSH) searched to 20/01/15	17/03/2016	1056
Total		**3585**

A5.2 Meta-analysis excluded studies

Study	Country	Reason excluded
Aldinger 2004[245]	Germany	No survival data
Catani 2012[246]	Italy	No survival data
Chatellard 2013[247]	France	Not cemented Oxford Phase 3
Daniilidis 2009[248]	Germany	No survival data
Emerson 2002[249]	USA	Not cemented Oxford Phase 3
Emerson 2008[250]	USA	Not cemented Oxford Phase 3
Gleeson 2004[251]	UK	Non-consecutive patients
Hooper 2015[252]	New Zealand	Not cemented Oxford Phase 3
Jahromi 2004[253]	Australia	No survival data
Kaczmarczyk 2003[254]	Poland	No survival data
Kendrick 2015[255]	UK	No survival data
Kubat 2011[256]	Czech Republic	No survival data
Langdown 2005[257]	UK	Non-consecutive patients
Li 2006[258]	Australia	Non-consecutive patients
Liddle 2013[259]	UK	Not cemented Oxford Phase 3
Ma 2013[260]	China	No survival data
Mascitti 2005 [261]	Italy	No survival data
Masri 2009[262]	Canada	Non-consecutive patients
Mercier 2010[263]	France	Not cemented Oxford Phase 3
Mullaji 2011[264]	India	No survival data
Muller 2004[265]	Germany	Not cemented Oxford Phase 3
Nassiri 2010[266]	Ireland	Non-consecutive patients
Pandit 2013[267]	UK	Not cemented Oxford Phase 3
Pandit 2015[268]	UK	Not cemented Oxford Phase 3
Parratte 2012[269]	France	Not cemented Oxford Phase 3
Pietschmann 2014[270]	Germany	No survival data
Rajasekhar 2004 [38]	UK	Not cemented Oxford Phase 3
Shakespeare 2012[271]	UK	No survival data
Skowronski 2005[272]	Poland	Not cemented Oxford Phase 3
Streit 2015[273]	Germany	Non-consecutive patients
Sun 2012[49]	China	Non-consecutive patients
Tang 2012[274]	China	No survival data
Tuncay 2015[275]	Turkey	Non-consecutive patients
Verdonk 2005[276]	Belgium	Not cemented Oxford Phase 3
Volpin 2006	Israel	No survival data
Vorlat 2006[277]	Belgium	Not cemented Oxford Phase 3
White 2012[278]	UK	Not cemented Oxford Phase 3
Zermatten 2012[279]	Switzerland	Not cemented Oxford Phase 3

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