Wear of Highly Cross-Linked Polyethylene in Primary Total Hip Replacement

The Effect of Manufacturing Method, Articulation Size and Age as Measured using Radiostereometric Analysis

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ABSTRACT

Background: The most common causes for revision of total hip replacement (THR) are periprosthetic osteolysis and loosening, both related to wear of the acetabular component. Acetabular components utilizing highly cross-linked polyethylene (XLPE) have been shown to wear less than earlier conventional polyethylene. Reported *in vivo* XLPE wear rates vary due to differing radiographic measurement techniques and methods of reporting results. XLPE liners are manufactured using different amounts of cross-linking, which may influence wear, as may articulation size and patient age.

Aims: The aims of this thesis were to (1) validate radiostereometric analysis (RSA) as the most accurate radiographic method to measure wear of XLPE acetabular components, (2) undertake a scoping review of RSA studies of XLPE wear, and (3) measure bedding-in and wear rate of XLPE using RSA to investigate the influence of: i) type of XLPE, ii) articulation size, and iii) patient age.

Methods: The validation study used a hip phantom to compare known two-dimensional (2D) movements of the femoral head within an acetabular component to movements measured radiographically using RSA, Hip Analysis Suite (HAS), PolyWare, Ein Bild Roentgen Analyse (EBRA) and Roentgen Monographic Analysis Tool (ROMAN).

The scoping review incorporated a systematic search of PubMed, Scopus and Cochrane databases to identify studies which used RSA to measure XLPE wear.

Patients in six cohorts, differing in XLPE type, articulation size or patient age, underwent regular RSA examinations to calculate XLPE wear rates between one and five years.

Results: RSA was significantly more accurate to measure 2D wear and had less variability in error than all other methods. Articulation size influenced accuracy of HAS and ROMAN measurements. Use of different acetabular reference segments did not influence accuracy of RSA.

The scoping review identified 14 publications by other authors that in combination reported XLPE wear at 2–10 years follow-up of 10 primary THR cohorts comprising 209 hips. Mean proximal wear rate ranged from 0.00 to 0.06 mm/yr. However, differences in how wear was determined limited comparability between studies. Recommendations were made to enhance standardization of reporting wear.

RSA studies undertaken as part of this thesis found that mean proximal bedding-in within the first year and the 2D and 3D wear rates between one and five years were higher in hips with a Marathon XLPE liner, which is manufactured with a lower radiation dose. Mean proximal wear rate was low for each of the six cohorts. Articulation size and age did not influence the wear rate at five years.

Conclusion: The superior accuracy of RSA wear measurements allow much smaller cohorts to be used in clinical wear studies. The scoping review and RSA studies confirmed the low early wear rates of XLPE components irrespective of articulation size and patient age. One type of XLPE liner had a higher wear rate at five years compared to other XLPE liners. Longer-term wear rates and the relationship between XLPE and periprosthetic osteolysis are yet to be determined.

DECLARATION

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DEDICATION

I would like to dedicate this work to my wife Kristy for her love and support during this time. She has patiently supported me throughout every step of this journey and we are now blessed to have Jack running between our feet and Ned on the way, both of whom have motivated me to complete this thesis.

"If I am a stranger now to you; I will always be, I will always be
Stronger now than me, stronger than you; Our love will always be
And if we let it go, I will try to be there for you; If I can, what if I can?" Ryan Adams

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"All the friends and family, all the memories going round, round, round
I have wished for so long, how I wished for you today
And the winds are blowing, and the skies keep turning grey
And the sun is setting, the sun will rise another day" Eddie Vedder

PUBLICATIONS ARISING FROM THIS THESIS

1. Campbell D, Mercer G, Nilsson KG, Wells V, Field JR, **Callary SA**. Wear of a highly cross-linked polyethylene liner: A preliminary RSA study. *European Journal of Orthopaedic Surgery and Traumatology* 2010: 20(1):23-27.

2. Campbell DG, Field JR, **Callary SA**. Second-generation highly cross-linked X3 polyethylene wear: A preliminary radiostereometric analysis study. *Clin Orthop Relat Res* 2010: 468(10):2704-2709.

3. **Callary SA**, Campbell DG, Mercer G, Nilsson KG, Field JR. Wear of a 5 megarad cross-linked polyethylene liner: A 6-year RSA study. *Clin Orthop Relat Res* 2013: 471(7): 2238-2244.

4. **Callary SA**, Field JR, Campbell DG. Low wear of a second-generation highly crosslinked polyethylene liner: A 5-year radiostereometric analysis study. *Clin Orthop Relat Res* 2013: 471:3596-3600.

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7. Howie DW, Holubowycz OT, **Callary SA**. The wear rate of highly cross-linked polyethylene is not increased by large articulations of total hip arthroplasties: A randomized controlled trial. *Journal of Bone and Joint Surgery - Am,* Accepted for publication on 6th June 2016.

8. **Callary SA**, Field JR, Campbell DG. The rate of wear of second-generation highly crosslinked polyethylene liners five years post-operatively does not increase if large femoral heads are used. *Bone and Joint Journal* 2016, Accepted for publication on 12th August 2016.

ABBREVIATIONS

THR	Total Hip Replacement
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
PE	Polyethylene
UHMWPE	Ultra-High Molecular Weight Polyethylene
XLPE,	Highly Cross-Linked UHMWPE (note: HXLPE, SQXL, SXPE, HXPE, HXLP, are all used to represent XLPE in the literature)
RSA	Radiostereometric Analysis (note: also known as Roentgen Stereophotogrammetric Analysis in literature)
HAS	Hip Analysis Suite
ROMAN	Roentgen Monographic Analysis Tool
EBRA	Ein Bild Rontgen Analyse
FHP	Femoral Head Penetration
2D	Two-Dimensional
3D	Three-Dimensional
yr	year
mm/yr	millimetres per year
MERBF	Mean Error of the Rigid Body Fitting
CN	Condition Number
SD	Standard Deviation
CI	95% Confidence Interval
BMI	Body Mass Index

THESIS OVERVIEW

The research included within this thesis had three aims.

The first aim was to validate RSA as the most accurate method to measure wear of XLPE liners in metal backed acetabular components. This was achieved by undertaking a phantom study and the results of that study are presented in Chapter 2.

The second aim was to undertake a scoping review of studies on wear of XLPE measured by RSA. The results of this scoping review, using a systematic search of all published literature, are presented in Chapter 3.

The third aim was to measure the bedding-in and wear rate of XLPE using RSA to investigate the influence of: i) type of XLPE, ii) articulation size, and iii) patient age. The results of six cohorts of patients, all monitored with RSA, which differed in respect to one or more of these factors, are presented in Chapter 4.

CHAPTER ONE

INTRODUCTION

1.1 Hip Replacement Surgery

During the early 1900’s there were a number of different surgical attempts to treat hip pain and restore mobility of the joint (Gomez et al., 2005). Total hip replacement (THR) surgery is an orthopaedic procedure that involves implanting prostheses to replace the articulating hip joint. The surgery, as we know it today, involves the patient’s hip joint being replaced with a combination of biocompatible components comprising metal, ceramic or polyethylene components. It is now one of the most commonly performed elective surgical procedures worldwide with over three million procedures performed annually worldwide (Kurtz, 2004).

The first attempt at hip replacement surgery was performed by Philip Wiles in 1938 using stainless steel components to replace both the femoral head and acetabulum (Wiles, 1958). In 1951 Kenneth McKee (McKee, 1951) began to use dental acrylic cement to fix femoral and acetabular implants but had a high rate of failure due to loosening (McKee et al., 1966). The discovery of a low friction bearing is credited to the work of Sir John Charnley who discovered that polytetrafluoroethylene (Teflon) was safe for use in the human body and first used it as a prosthetic material to replace the acetabulum in the late 1950’s (Charnley, 1961; Charnley, 1966). After early results showed prosthesis wear and soft tissue reaction to the Teflon particles, his research then lead to the use of ultra-high molecular weight polyethylene (UHMWPE). An acetabular prosthesis made of UHMWPE was first used in 1963 and demonstrated decreased wear rates compared to existing materials such as Teflon (Charnley, 1963). Although many bearing configurations have been trialled since then, a metal femoral head against a UHMWPE acetabular component has subsequently been the most popular choice of bearing.

There are now three categories of hip replacement surgery which the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) divides into primary partial, primary total and revision hip replacement (AOANJRR, 2016). Within primary THR, there are two further categories; total conventional hip replacement and total resurfacing hip replacement. The studies included within this thesis focus on patients undergoing primary total conventional hip replacement surgery.

Historically, the most common reason to have a THR is to relieve severe arthritis pain that is limiting the patient's activity. In Australia, osteoarthritis is currently the principal diagnosis for primary THR (89%) and more females than males undergo primary THR surgery with a ratio of 55:45 (AOANJRR, 2016). Other indications for primary THR are rheumatoid arthritis, fractured neck of femur, osteonecrosis and developmental dysplasia (AOANJRR, 2015). Primary THR is generally associated with high patient satisfaction rates and good functional outcomes (de Beer et al., 2012). As a result of good outcomes the use of primary THR continues to grow worldwide (Kurtz et al., 2014). Twenty five year projections of the use of primary THR in the United States indicated a likely increase of 174% between 2005 and 2030 (Kurtz et al., 2007). According to recent updated calculations, these projections are now expected to be exceeded with almost 500,000 primary THRs expected to be performed in 2020 in the US alone (Kurtz et al., 2014). Similarly in Australia, the number of primary THRs performed has increased by 70%, incrementally each year from 17,074 in 2003 to 33,904 in 2015 (AOANJRR, 2016).

1.2 Reasons for Revision THR Surgery

1.2.1 Common Reasons for Revision

Limitations in the survival of the prostheses result in the need for revision THR surgery (Collier et al., 1992). Traditionally, the reasons for revision surgery include implant loosening and osteolysis, dislocation of the prosthesis, fracture of the surrounding bone, and infection. The AOANJRR has identified the most common modes of failure as dislocation in the short term, within the first four postoperative years, and aseptic loosening and osteolysis in the mid- to long term (AOANJRR, 2015). Revision THR is more complex surgery than primary THR due to the reduced amount of bone within which to position a new prosthesis. There is also an increased risk of infection, dislocation, or fracture, all of which may require further revision surgery. Hence research has focussed on improving the survivorship of initial primary THR.

1.2.2 Loosening and Osteolysis

The results from the Swedish Total Hip Replacement Registry reported aseptic loosening as the reason for revision in 75% of all cases of first revision surgery between 1979-2000 (Malchau et al., 2002). In Australia, loosening and/or lysis was the principal cause for revision THR surgery in 56% of all cases up to 2009 (AOANJRR, 2009). Implant loosening and periprosthetic osteolysis remain the most common reason for revision of primary THRs included in the registry (28%) (AOANJRR, 2016). Loosening of THR implants is caused by the loss of adjacent bone, known as periprosthetic osteolysis (Howie et al., 2013) (Figure 1.1). The development of periprosthetic osteolysis is multifactorial, but most commonly accredited to the tissue response to prosthesis derived wear particles (Willert et al., 1972; Vernon-Roberts et al., 1976; Willert et al., 1977; Howie et al., 1988; Howie, 1990; Howie et al., 1990; Schmalzried et al., 1992; Harris, 1995; McGee et al., 1997; Holding et al., 2006; Howie et al., 2013). Polyethylene components, the material most commonly used in THR articulations, produce large numbers of wear particles, which initiate an inflammatory response and lead to osteolysis and subsequent component loosening (Howie et al., 2013).

Figure 1.1: A coronal computer tomography (CT) image showing extreme wear of the polyethylene liner, with the femoral head almost touching the metal backed shell. An osteolytic lesion is present around the screw which may compromise fixation of the acetabular prosthesis.

1.2.3 Dislocation

Dislocation of the femoral head from within the acetabular component (Figure 1.2) is the most common early complication after THR surgery with the majority of dislocations occurring within the first postoperative year (Amlie et al., 2010). Dislocation may require revision surgery if it becomes recurrent or the joint cannot be manually relocated. Including longer term follow-up, dislocation is currently the second most common reason for revision of primary THRs included in the Australian registry (24%) (AOANJRR, 2016). The use of larger articulations increase the distance required for complete dislocation of the femoral head outside of the acetabular component. The use of larger articulations has been limited in the past due to their association with larger amounts of wear of conventional UHMWPE liners (Livermore et al., 1990). The use of larger articulations in THR is discussed in more detail in Section 4.3.2.2.

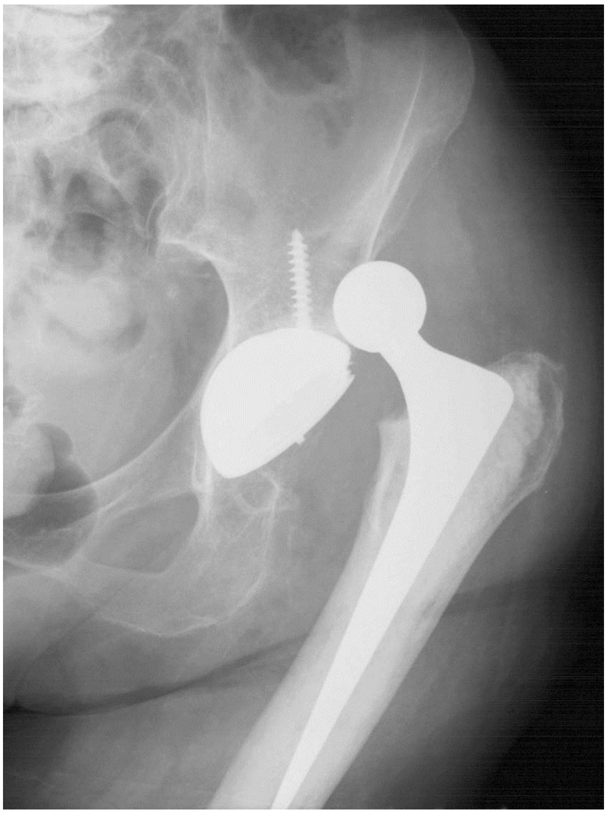

Figure 1.2: Radiograph of a dislocated femoral head outside of the acetabular component

1.2.4 Infection and Fracture

The two other most common reasons for revision of primary THR are fracture of the bone surrounding prostheses (19%) and infection (18%) (AOANJRR, 2016). Other less common reasons for revision THR include pain, leg length discrepancy, malposition of the implant, implant breakage, instability, wear of the acetabular insert and metal related pathology (AOANJRR, 2015).

1.3 Correlation Between Polyethylene Wear and Osteolysis

In a THR, it would take approximately a century to erode through a typical 10mm thick UHMWPE component with a linear wear rate of approximately 0.1 mm/yr. Hence, complete wear through of a UHMPWE liner is uncommon and, as described earlier in Section 1.2.2, it is the tissue response to polyethylene wear particles that leads to periprosthetic osteolysis and subsequent component loosening.

Two review articles have confirmed that a greater amount of wear of conventional UHMWPE liners is associated with a higher incidence of osteolysis (Oparaugo et al., 2001; Dumbleton et al., 2002). The first literature review found that osteolysis was rare in hips with a volumetric wear rate below 80 mm^3/yr (Oparaugo et al., 2001). The second review article suggested that osteolysis is infrequent when wear rates are less than 0.1 mm/yr and almost absent below 0.05 mm/yr (Dumbleton et al., 2002). A further study found that every 0.1 mm/yr increase in the linear wear rate increased a patient’s risk for the development of osteolysis by a factor of four (Orishimo et al., 2003). Hence, a person with a wear rate of 0.2 mm/yr was four times more likely to develop osteolysis than a person with a wear rate of 0.1 mm/yr. Furthermore they reported that for every 40 mm^3/yr increase in the volumetric wear rate resulted in a threefold increase in the risk of osteolysis (Orishimo et al., 2003). Another study with an average of 20 years follow-up reported a prevalence of osteolysis of 14%, and found that the risk of osteolysis, acetabular and femoral component loosening and revision rose significantly with increasing wear (Sochart, 1999). The 20-year survivorship of acetabular components with a wear rate greater than 0.2 mm/yr was below 30% compared to 90% for those with a wear rate less than 0.1mm/yr. Therefore, these findings all confirmed that conventional UHMWPE components used in the 1980’s and 1990’s were associated with wear and osteolysis.

Wear measurements of polyethylene components have subsequently been made as a surrogate method for predicting the likelihood of developing osteolysis and the need for revision surgery. Research within the orthopaedic community has therefore focussed on improving the wear properties of polyethylene and monitoring the *in vivo* wear of polyethylene components in THRs by using various radiographic methods.

1.4 Implant Options

1.4.1 Femoral Component

The metal femoral component (stem) may either be cemented or uncemented (press-fit) within the femoral canal. The majority of femoral stems are modular meaning the femoral head is independent of the stem and is attached to the stem via a taper design. The femoral head is made of either metal, ceramic or a ceramicised metal.

1.4.2 Acetabular Component

The acetabular component is implanted after the removal of cartilage and damaged bone and held in place either by cement or with the use of friction. Cemented acetabular components are usually made entirely of polyethylene, while cementless acetabular components are usually metal shells with an outer surface designed to allow boney ingrowth. In some cases, metal screws are inserted to improve the initial stability of the press-fit metal shell within the bone. Cementless press fit metal shells are usually used in combination with an insert (liner) made of either polyethylene, ceramic or metal and are most commonly modular modular allowing the liner to be exchanged easily, if required, at revision surgery.

The use of cementless fixation for both acetabular and femoral components in primary THR varies from a low prevalence of 15% in Sweden to a high of 82% in Canada (Troelsen et al., 2013). While the national joint registry in America is relatively new, studies suggest 86% of all THRs in the United States are cementless and less than 1% are cemented on both the femoral and acetabular side (Huo et al., 2011). The most recent data from the AOANJRR indicates that of primary THRs undertaken in Australia in 2015 96% of acetabular components had cementless fixation as did 64% of femoral components (AOANJRR, 2016). Currently, the top nine acetabular components used in Australia are all cementless and represent 76% of all those used in primary THR (AOANJRR, 2016). An additional 66 different types of acetabular components make up the remaining 24% of overall usage in Australia, highlighting the very large number of different components still used by orthopaedic surgeons (AOANJRR, 2016).

1.4.3 Bearing Articulation

As a result of the different femoral and acetabular implant options available, surgeons currently have a choice of different bearing articulations. Currently a combination of either a metal or ceramic femoral head can be used with a metal, polyethylene or ceramic liner or acetabular component. Optimal choice of bearing remains a constant debate within the orthopaedic community. All types of bearing surfaces are associated with a varying degree of wear debris that may cause osteolysis (Dumbleton et al., 2002). The proven biocompatibility and biomechanical properties of UHMWPE make it a desirable bearing surface for use in joint prostheses (Dumbleton et al., 2002). With over 40 years clinical experience with metal against polyethylene bearings, which have been shown to improve survivorship and treatment options for failed hips, metal on polyethylene articulations remain the most common choice of bearing internationally (Grover, 2005).

1.5 Ultra High Molecular Weight Polyethylene

1.5.1 Early Use of UHMWPE

Ultra high molecular weight polyethylene (UHMWPE) is a semi crystalline polymer that has been used for over four decades as a bearing surface in total joint replacements (Sobieraj et al., 2009). UHMWPE was first introduced to be used in THR in 1962 by Sir John Charnley (Kurtz, 2004). His concept of a low friction arthroplasty has been adopted by the orthopaedic community since 1958. UHMWPE has good mechanical bearing properties, a low coefficient of friction against metal or ceramic and is non-toxic (Schmidig et al., 2010). However, in the challenging biomechanical environment of THR, deterioration of the polymer component still occurs, resulting in wear particles. Radiographic measurements of UHMWPE liners identified the relatively high amount of wear occurring in these bearings in the 1970’s (Charnley et al., 1975). As a result of clinically significant wear, orthopaedic research continued to investigate alternative bearing surfaces including various manufacturing methods to improve the wear resistance of UHMWPE. A reduction in wear was hoped to result in a reduction in periprosthetic osteolysis and increased survivorship (Collier et al., 1998). However, improvements to UHMWPE performance *in vitro* have not always translated to improvements when used clinically. This is illustrated by for example, the poor *in vivo* performance of a modified UHMWPE component (Hylamer) which was eventually recalled from further clinical use due to its excessive wear and associated periprosthetic osteolysis (Livingston et al., 1997; Norton et al., 2002; Kurtz, 2004). In the early 1990's, a different manufacturing process was used to produce the Hylamer acetabular component under high pressure and temperature in an effort to increase the wear resistance of the material. Unfortunately the Hylamer component was prone to oxidation and clinical results varied depending how long the component was stored on the shelf prior to implantation (Kurtz, 2004). There was also pattern of backside liner deformation and burnishing was consistent with relative motion between the liner and the shell which may have generated fluid pressure and contributed to the development of retroacetabular osteolysis (Scott et al., 2000). Examples such as this highlight the need to evaluate new materials and implants in clinical studies to confirm improved *in vitro* performance, particularly where any change to the manufacturing process of UHMWPE can affect the mechanical behaviour of the material (Sobieraj et al., 2009).

1.5.2 Clinical Use of Irradiated Polyethylene

The first UHMWPE acetabular component intentionally gamma irradiated at a very high level (100mRad) was used in Japan in 1971 (Oonishi et al., 2001). Similarly, researchers in South Africa introduced a UHMWPE that was gamma irradiated with up to 70mRad in the presence of acetylene (Dowson, 1967). Despite this early discovery that irradiation increased the wear resistance of UHMWPE, almost all UMWMPE components used in the 1980's were non-irradiated and sterilized in an inert atmosphere. Sterilization techniques using irradiation in air were found to oxidise the material and changes in manufacturing techniques did not always translate to expected improved clinical performance (Sobieraj et al., 2009). Hence, further specific research studies into the optimal gamma irradiation dose, sterilization method and effect on wear properties of conventional UHMWPE were performed in the 1990's. Manufacturing methods were developed to cross-link polyethylene by exposing it to doses of gamma or electron beam irradiation and then annealing or remelting the material by thermal treatments to eliminate free radicals created during the irradiation process (Oonishi et al., 1997; Sun et al., 1997).

1.5.3 In Vitro Studies of Improved Wear Properties of XLPE

In vitro gravimetric wear measures the loss of material from the polyethylene liner when tested in a biomechanical simulator. *In vitro* hip simulator studies were able to show that XLPE components exhibit significantly reduced wear compared to UHMWPE components (Kurtz et al., 1999; Muratoglu et al., 2001; Bragdon et al., 2003). For example, two types of XLPE liners tested in a wear simulator, demonstrated very low wear rates of 1.5 and -1.4 mg/million cycles compared to wear rates of 15.7 and 12.5 mg/million cycles of two controls of non-crosslinked polyethylene liners (D'Lima et al., 2003). Similarly XLPE components have also been shown to generate significantly fewer wear particles and a up to a 96% reduction in the wear volume generated compared to conventional UHMWPE components (Ries et al., 2001).

1.5.4 Introduction of XLPE

Highly Cross-Linked Polyethylene (XLPE) components were introduced for use in THR surgery in 1998 (Kurtz et al., 2011) and by 2003 XLPE was used in two thirds of hip arthroplasties in the United States (Kurtz, 2004). More recently in Australia, the 2015 annual report of the joint replacement registry reported that XLPE was used in 95% of all primary THRs incorporating a PE bearing (AOANJRR, 2016). XLPE has been used in 174,409 procedures reported to the AOANJRR up until 2015 (AOANJRR, 2016). Of the 33,954 primary THRs undertaken in Australia in 2015, 72% involved a XLPE bearing surface against either metal (40%), ceramic (25%) of ceramicised metal (7%) femoral head (AOANJRR, 2016). This pattern of usage is similar worldwide. The studies included within this thesis investigate the use of metal on XLPE bearings unless otherwise stated.

1.5.5 Different Methods of Manufacture

The manufacture of XLPE components involves a number of different aspects including the type of polyethylene resin, level of irradiation, subsequent annealing or melting, and sterilization; all of which may influence the wear properties of the specific XLPE liner. Different companies continue to use different manufacturing methods for XLPE components aimed at balancing resistance to wear, oxidation and fatigue fracture (Pruitt et al., 2013). The individual manufacturing methods of XLPE acetabular components available for clinical use are described in Table 1.1. These methods may have certain advantages and disadvantages. Cross-linking UHMWPE with gamma irradiation is a slower process with less dose control compared to electron beam irradiation. Minimising free radicals produced during the cross-linking treatment by annealing leaves free radicals the material which, if combined by packaging in air, could lead to oxidation. Remelting reduces the free radicals to non-detectable levels improving oxidative resistance. Final sterilisation of the component with gamma irradiation may create more free radicals while sterilisation with gas plasma or ethylene oxide do not. Each step of manufacture may influence the *in vivo* mechanical properties of liners. For example, one study of conventional UHMWPE liners investigated the effect of sterilization on wear rates at 10 years (Engh et al., 2012b). Liners sterilized with gas plasma demonstrated a higher mean wear rate (0.20 ± 0.09 mm/yr) compared to liners sterilized with gamma irradiation in air (0.13 ± 0.07 mm/yr) and liners sterilized with gamma irradiation with barrier packaging without oxygen (0.09 ± 0.04 mm/yr) (Engh et al., 2012b).

Acetabular components are defined as XLPE when intentionally treated using a total irradiation dose ranging from 50 to 105 kGy (Kurtz et al., 2002). Melted XLPE may be susceptible to fatigue cracking and annealed XLPE may be susceptible to *in vivo* oxidation. More recent “second generation” XLPE use a sequential irradiation and annealing process which may reduce the free radical content while preserving the mechanical strength properties of first generation XLPE liners. Second generation XLPE liners include Arcom, X3 and Altrx (Table 1.1). Ideally, like all new prosthetic components, new XLPE liners should be rigorously tested in clinical trials before being released for general use because of potential variation in manufacturing methods that may lead to possible failure (Rohrl et al., 2005; Malchau et al., 2011).

Table 1.1: The manufacturing method XLPE components available for clinical use.

Trademark Name	Company and Year Introduced	PE Stock	Crosslinking	Thermal Treatment	Final Sterilisation
Marathon™	DePuy Orthopaedics Inc, Warsaw, IN, USA, 1998	GUR 1050 extruded rod	50kGy gamma irradiation	Melted at 155°C for 24 hours and then annealed at 120°C for 24 hours	Gas plasma
Crossfire™	Stryker Orthopaedics, Mahwah, NJ, USA, 1998	GUR 1050 extruded rod	75kGy gamma irradiation	Annealed (130°C)	30kGy gamma sterilization (in nitrogen)
Durasul®	Zimmer, Inc, Warsaw, IND, USA, 1998	GUR 1050 molded sheet	95kGy electron beam irradiation	Remelted at 150°C for 2 hours	Ethylene Oxide
Longevity™	Zimmer, Inc, Warsaw, IND, USA, 1999	GUR 1050 molded sheet	100kGy electron beam irradiation	Remelting >135°C	Gas plasma or Ethylene oxide
Aeonian	Kyocera Corp, Kyoto, Japan	GUR 1050 molded	30kGy gamma irradiation bar stock	Annealed 110°C in nitrogen for 12 hours	25 to 40kGy gamma sterilization (in nitrogen)
XLPE™	Smith and Nephew, Memphis, TN, USA, 2001	GUR 1050 extruded rod	100kGy gamma irradiation	Remelted at 147°C for at least 5 hours	Ethylene Oxide
Mechanically or sequential annealed XLPE					
Arcom®	Biomet, Inc. Warsaw, IND, USA, 2005	GUR 1050 isostatically compression molded	50kGy gamma irradiation	Mechanically annealed followed by 130°C thermal annealing	Gas plasma
X3™	Stryker Orthopaedics, Mahwah, NJ, USA, 2005	GUR 1020 molded sheet	Three steps of 30kGy gamma irradiation	Annealed at 130°C at each step of gamma irradiation	Gas plasma
AltrX™	DePuy Orthopaedics Inc, Warsaw, IN, USA, 2005	GUR 1020 ram extruded rod	75kGy gamma irradiation	Melted at 155°C and then annealed at 120°C for 24 hours	Gas plasma

1.5.6 In Vivo Studies of Improved Wear Properties of XLPE

Three literature reviews have established that the wear of XLPE liners *in vivo* is less than conventional UHMWPE liners (Mu et al., 2009; Kurtz et al., 2011; Kuzyk et al., 2011). A meta-analysis of randomised controlled trials found that the pooled mean linear wear rates were significantly reduced for XLPE at 2 to 8 years follow-up (Kuzyk et al., 2011). The mean linear wear of XLPE reported in studies within this meta-analysis varied between 0.01 to 0.12 mm/yr. Similarly, a review of all first generation XLPE studies found variable linear wear rates between 0.002 and 0.120 mm/yr (Kurtz et al., 2011). All eight studies included in a systematic review found XLPE had a significantly lower wear or penetration than conventional UHMWPE groups at 3 to 5 years follow-up (Mu et al., 2009).

There are now at least five separate randomised controlled trials with a minimum of five years follow-up demonstrating a reduced *in vivo* wear rate of XLPE compared to conventional UHMWPE (McCalden et al., 2009; Mutimer et al., 2010; Engh et al., 2012a; Johanson et al., 2012; Glyn-Jones et al., 2015) (Table 1.2). Firstly, the Longevity™ XLPE liner was shown to have a significantly reduced mean wear rate 0.003 mm/yr compared to 0.051 mm/yr at five years (McCalden et al., 2009). Secondly, the Marathon™ XLPE liner was shown to have a significantly reduced mean wear rate of 0.05 mm/yr compared to 0.26 mm/yr at 5 years (Mutimer et al., 2010). Thirdly, the Marathon™ XLPE liner was shown to have a significantly reduced mean wear rate of 0.04 mm/yr compared to 0.22 mm/yr at 10 years (Engh et al., 2012a). Fourth, the Durasul® XLPE liner was shown to have significantly reduced linear wear rate of 0.005 mm/yr versus 0.056 mm/yr at ten years (Johanson et al., 2012). Fifth, the Longevity™ XLPE liner was shown to have a significantly reduced mean wear rate of 0.003 mm/yr compared to 0.030 mm/yr at ten years (Glyn-Jones et al., 2015).

Hence, in just these five studies the reported mean wear rate of XLPE varied between 0.003 and 0.050 mm/yr. There are potentially a number of reasons for such variation, including the radiographic wear measurement technique and reporting method used; component factors including the type of XLPE liner and articulation size; and patient factors including age and activity. It is therefore difficult to compare the results of *in vivo* wear studies. For example, wear studies of only the Marathon™ XLPE liner at greater than five years, revealed the reported mean 2D wear rates of 0.01 (Engh et al., 2006), 0.014 (Callary et al., 2013), 0.031 (Bitsch et al., 2008), 0.04 (Engh et al., 2012a) and 0.05 mm/yr (Mutimer et al., 2010). In these five studies the main reasons for the variation in the reported wear rates were the different radiographic measurement techniques used and the different methods of reporting of wear results, including the variation in the time allowed for early bedding in and creep.

Table 1.2: Separate randomised controlled trials with a minimum of five years follow-up demonstrating a reduced in vivo wear rate of XLPE compared to conventional UHMWPE acetabular components

Publication	**XLPE Acetabular Component**	**Follow-up (years)**	**Mean Annual Wear Rate (mm/year)**	
			XLPE	**Conventional UHMWPE**
(McCalden et al., 2009)	Longevity	5	0.003	0.051
(Mutimer et al., 2010)	Marathon	5	0.050	0.260
(Engh et al., 2012a)	Marathon	10	0.040	0.220
(Johanson et al., 2012)	Durasul	10	0.005	0.056
(Glyn-Jones et al., 2015)	Longevity	10	0.003	0.030

1.6 *In Vivo* Measurement of Wear

1.6.1 Femoral Head Penetration on Radiographs

Clinical wear studies of THR bearing surfaces use serial radiographs to measure the amount of femoral head penetration (FHP) within the acetabular component as a representation of wear of the bearing surface. Various methods have been used clinically, both to monitor patients closely as new bearing surfaces have been introduced and also by clinicians to assess the amount of wear at long term follow-up. Penetration of the femoral head within the acetabular component over time occurs in two phases, namely the initial 'bedding-in' of the liner into the metal shell and creep, followed by true wear which is the loss of polyethylene particles from the polyethylene liner (McCalden et al., 2005; Campbell et al., 2010).

1.6.2 Bedding-In and Creep

Bedding-in and creep occur early after implantation within the first year following THR. Bedding-in is the settling of a PE liner within the metal acetabular shell and creep is the initial plastic deformation of the PE liner that occurs over time under cyclic loading (Sychterz et al., 1999). While these are separate processes, radiographic measurements are unable to differentiate the two. In the remaining of this thesis the term bedding-in is used to represent a combination of bedding-in and creep. An *in vitro* study demonstrated that the majority of bedding-in occurs within the first 2.5 million cycles (Estok et al., 2005). Given that the average walking activity of patients after THR approaches 2 million cycles at one year (Silva et al., 2002) the bedding-in is likely to be completed within the first postoperative year. To exclude bedding-in from measurement of true wear, radiographic studies have omitted the early FHP and then calculated an annual wear rate thereafter (McCalden et al., 2005; Callary et al., 2015). The time allowed for the bedding-in process varies from two months to two years between studies (Callary et al., 2015).

1.6.3 Radiographic Wear Measurement Methods

Traditionally, methods such as the Livermore method (Livermore et al., 1990) and Dorr and Wan method (Dorr et al., 1995) utilised supine anteroposterior (AP) radiographs taken at regular postoperative time points to measure manually the centre of the femoral head ellipse relative to the centre of the acetabular component ellipse. Computerised software programs were developed in the 1990's to analyse digitized plain radiographs and improve the identification of the centre of each ellipse. Commonly used programs include Hip Analysis Suite (HAS, University of Chicago, Chicago, IL) (Martell et al., 1997); PolyWare (Draftware Developers Inc., Vevay, IN) (Devane et al., 1995a; Devane et al., 1995b), Ein Bild Roentgen Analyse (EBRA, University of Innsbruck, Innsbruck, Austria) (Krismer et al., 1995) and, more recently, Roentgen Monographic Analysis Tool (ROMAN, Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, UK) (Geerdink et al., 2008). The accuracy and precision of these methods varies in the literature (Rahman et al., 2012). Measurements made from standard clinical radiographs were sensitive enough to measure wear of conventional UHMWPE. However, due to the improved wear properties of XLPE, measurement of the lower amounts of *in vivo* wear associated with XLPE is more challenging, ideally requiring a more sensitive radiographic measurement method, namely Radiostereometric Analysis (RSA).

1.6.4 Radiostereometric Analysis

Radiostereometric analysis (RSA), also known as roentgen stereophotogrammetric analysis, is widely regarded as the gold standard of measuring three-dimensional prosthesis migration *in vivo* (Karrholm et al., 1997; Karrholm et al., 2006). RSA uses dual simultaneous radiographs taken over a calibration cage to calculate the three dimensional movement of one skeletal body segment relative to another (Karrholm et al., 2006). The traditional RSA method relies on the implantation of small spherical tantalum beads of either 0.5, 0.8 or 1.0mm diameter to represent each skeletal body of interest (Karrholm et al., 1997). The patient then undergoes consecutive radiographic examinations at set time points to monitor movement of one body relative to another.

The RSA method was first introduced in 1972 by Goran Selvik (Selvik et al., 1983; Selvik, 1989). Due to its superior sensitivity the main use of RSA is in total joint replacement to measure prosthetic wear and migration relative to the surrounding bone over time. To measure polyethylene wear, tantalum markers are usually implanted in the peripheral rim of the polyethylene liner or on the backside of the cemented polyethylene components at the time of surgery or, for a small number of studies, at the time of manufacture. The centre of the femoral head ellipse is used as a marker and the penetration of the femoral head relative to the polyethylene segment is measured. RSA was first used to measure polyethylene wear in 1979 in a study of four hips under the guidance of creator Selvik (Baldursson et al., 1979). The method has subsequently been used in numerous other orthopaedic applications including monitoring bone growth (Alberius et al., 1990), spinal fusion (Humadi et al., 2013), cartilage wear (Field et al., 2009; Field et al., 2016), tendon healing (Solomon et al., 2011a) and fracture stability during healing (Chehade et al., 2009; Solomon et al., 2011b).

Accuracy and precision are important factors in any measurement system. The accuracy of RSA can only be assessed by comparing measurements to known movements of an *in vitro* phantom model connected to micrometers. Precision is easier to determine and can be calculated *in vivo* by performing double examination of patients within a short time interval in which it is assumed no additional wear occurs (Valstar et al., 2005) Accuracy of RSA to measure medial, proximal, anterior and 3D polyethylene wear in optimal conditions, using a phantom model, was reported to be 33, 22, 86 and 55 microns respectively (Bragdon et al., 2002). Precision was reported to be 8.4, 5.5 and 16 microns in the x-, y- and z-axes respectively (Bragdon et al., 2002).

Many variables may influence the accuracy and precision of RSA measurements when applied in different settings, including intraoperative bead positioning, method of acquisition of RSA radiographs and the specific RSA software used. Quality control measures have been included within recommendations on how to report RSA results (Valstar et al., 2005). The condition number (CN) represents the spatial spread of beads in all three dimensions with a lower CN representing a superior spread. Guidelines proposed by Valstar et al suggest RSA examinations are deemed adequate if the CN is less than 150 and the mean error of rigid body fitting is below 0.3mm (Valstar et al., 2005). Developments of the RSA method have led to measurements now being undertaken using digitally which are more precise than manual RSA measurements (Borlin et al., 2002). A number of different software packages are available to analyse RSA radiographs including UmRSA software (RSA Biomedical, Umea, Sweden) and RSA-CMS software (Leiden University Medical Centre, Netherlands).

The most recent development of UmRSA software (version 6.0, RSA Biomedical) includes novel algorithms for better identification of the centre of the femoral head and acetabular component which when used in combination with beaded RSA measurements improves both the accuracy and precision of RSA (Borlin et al., 2006). The use of this ellipse algorithm has also allowed studies of acetabular components to be undertaken without the attachment of beads in the polyethylene liner saving time, money, and reducing safety concerns of beads implanted within the liner (Borlin et al., 2006). In addition this algorithm has decreased the number of RSA examinations previously thought to be unusable (Borlin et al., 2006).

1.7 References

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CHAPTER TWO

Accuracy of Methods to Measure Femoral Head Penetration within Metal-Backed Acetabular Components

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A number of different software programs are used to investigate the *in vivo* wear of polyethylene bearings in total hip arthroplasty. With wear rates below 0.1 mm/yr now commonly being reported for highly cross-linked polyethylene (XLPE) components, it is important to identify the accuracy of the methods used to measure such small movements. The aims of this study were to compare the accuracy of current software programs used to measure two-dimensional (2D) femoral head penetration (FHP) and to determine whether the accuracy is influenced by larger femoral heads or by different methods of representing the acetabular component within radiostereometric analysis (RSA).

The findings are presented in the form of the published manuscript.

Statement of Authorship

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Principal Author

Name of Principal Author (Candidate)	Stuart Callary
Contribution to the Paper	First author on the paper. Planned and performed the study including taking all radiographs of phantom model. Analysed all resultant radiographs and collated results. Reviewed all literature, prepared all tables, wrote initial draft and edited manuscript through review process. Acted as corresponding author.
Overall percentage (%)	80%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.

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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Accuracy of Methods to Measure Femoral Head Penetration Within Metal-Backed Acetabular Components

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ABSTRACT: A number of different software programs are used to investigate the in vivo wear of polyethylene bearings in total hip arthroplasty. With wear rates below 0.1 mm/year now commonly being reported for highly cross-linked polyethylene (XLPE) components, it is important to identify the accuracy of the methods used to measure such small movements. The aims of this study were to compare the accuracy of current software programs used to measure two-dimensional (2D) femoral head penetration (FHP) and to determine whether the accuracy is influenced by larger femoral heads or by different methods of representing the acetabular component within radiostereometric analysis (RSA). A hip phantom was used to compare known movements of the femoral head within a metal-backed acetabular component to FHP measured radiographically using RSA, Hip Analysis Suite (HAS), PolyWare, Ein Bild Roentgen Analyse (EBRA), and Roentgen Monographic Analysis Tool (ROMAN). RSA was significantly more accurate than the HAS, PolyWare, and ROMAN methods when measuring 2D FHP with a 28 mm femoral head. Femoral head size influenced the accuracy of HAS and ROMAN 2D FHP measurements, EBRA proximal measurements, and RSA measurements in the proximal and anterior direction. The use of different acetabular reference segments did not influence accuracy of RSA measurements. The superior accuracy and reduced variability of RSA wear measurements allow much smaller cohorts to be used in RSA clinical wear studies than those utilizing other software programs. © 2016 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res

Keywords: polyethylene wear; total hip arthroplasty; radiostereometric analysis; accuracy

Studies investigating the in vivo wear of polyethylene following total hip arthroplasty (THA) use a number of different methods to measure the femoral head penetration (FHP) within the acetabular component.[1,2] Traditionally, supine anteroposterior (AP) radiographs of the hip are taken at sequential postoperative time points and the FHP measured within the first year is assumed to be part of the bedding-in/creep process and the rate of FHP after the first year is then assumed to represent actual wear of the polyethylene.[1,3] Computerized software programs have been developed to measure FHP within the acetabular component using a variety of edge-detection techniques to improve identification of the ellipse outline of both the femoral head and metal-backed shell. Commonly used computer software programs include Hip Analysis Suite (HAS, University of Chicago, Chicago, IL),[4] PolyWare (Draftware Developers, Inc., Vevay, IN),[5–7] Ein Bild Roentgen Analyse (EBRA, University of Innsbruck, Innsbruck, Austria),[8] and more recently, Roentgen Monographic Analysis Tool (ROMAN, Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, UK).[9] In contrast to the other methods of analysis which use standard clinical radiographs, radiostereometric analysis (RSA) utilizes a specialized radiographic set-up of two tubes above a calibration cage, thereby requiring patients to be enrolled in clinical studies.[10] It offers the advantage of simultaneous measurement of FHP in three dimensions, namely the medial–lateral, proximal–distal, and anterior–posterior directions. All measurement methods have improved over time with the enhanced digitization of radiographs and improvements in the software programs.[11,12]

The amount of polyethylene wear of THA articulations involving highly cross-linked polyethylene (XLPE) is significantly less than that of articulations with conventional ultra-high molecular weight polyethylene (UHMWPE).[13] With wear rates below 0.1 mm/yr now commonly being reported, it is important to identify the accuracy of the methods used to measure such small movements. Accuracy, also referred to as bias,[14] is usually defined as the closeness of agreement between a test result and the accepted reference or "true" value.[14,15] Reports of accuracy are difficult to interpret because of variations between studies in the reference measurement techniques utilized, which include phantom models, scans of retrieved liners,[16] or even comparison against other radiographic measurements methods such as RSA.[17,18] Accuracy studies also differ in the specific axis investigated, be it proximal, 2D or 3D, as well as in the statistical parameter used to represent error which varies between the mean, median, standard deviation (SD), 95% confidence interval (CI), and root mean square error (RMSE) across studies. As a result of these methodological and reporting differences, the reported accuracy of the measurement methods vary within the literature. For example, the mean error of 3D FHP measurements ranges from 0.005[19] to

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Conflicts of interest: None.

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0.24 mm[20] for HAS and from 0.022[7] to 0.34 mm[5] for PolyWare. While RSA is widely regarded as the gold standard measurement method,[21] only one study has compared the accuracy of RSA to that of another software program, namely PolyWare, using an in vitro phantom model.[22] A review of some radiographic wear measurement methods attempted to adjust for the different statistical presentations of accuracy by calculating the RMSE for each method from each study's data, reporting an RMSE of 0.065 for RSA, 0.033 for HAS, and 0.025 mm for PolyWare.[1]

Two important variables that may influence the accuracy of wear measurements are the use of larger femoral heads and the different representation of the acetabular component within RSA methodology. Larger articulations involving UHMWPE have been shown to have increased volumetric wear rates compared to standard articulations[23] but to date few studies have examined the differences in wear between large and standard articulations involving XLPE.[24,25] The accuracy of RSA wear measurements were found not to be influenced by head size using a 22 or 28 mm femoral head[26] but larger articulations may influence the accuracy of radiographic measurement methods due to reduced visibility of the acetabular ellipse and, for RSA, fewer beads being visible in the peripheral rim to represent the acetabular component. RSA methodology has evolved over time and there are now a variety of different acetabular reference segments used, including beads in the peripheral edge of the liner, the outer ellipse of the acetabular component, or a combination of both beads and the ellipse.[27]

The aims of this study were to use a phantom model: (1) to compare the accuracy of software programs currently used to measure 2D FHP; (2) to determine whether accuracy of these methods is influenced by larger femoral heads; and (3) to determine whether accuracy of RSA measurements are influenced by using different acetabular reference segments.

METHODS

Phantom Model

An acetabular component (56 mm outer diameter, Trilogy, Zimmer, Warsaw, IN) was implanted within a left plastic hemi-pelvis (Sawbones, Vashon Island, WA) with an orientation of 40° inclination and 15° anteversion. This hemi-pelvis was attached to a plexi-glass platform (Fig. 1a). The polyethylene liner (36 mm diameter, Longevity, Zimmer) was reamed to increase the inner diameter to approximately 40 mm prior to implanting 12 RSA tantalum beads (1.0 mm diameter, RSA Biomedical, Umea, Sweden) in the peripheral edge and locking the liner within the acetabular component. A femoral stem (CPT 12/14, Zimmer) with modular 28 mm head was cemented to a brass rod and attached to the translational stage (Models M-460A-xyz and M-UTR-80, Newport Corporation, Irvine, CA). The stage could be moved in three axes with three separate micrometers (DMH-1 Digital Micrometer, Newport Corporation). According to the manufacturer, this translation system is accurate to 1 μ and backlash is eliminated by spring loading the moving assemblies against the tips of the actuators. The femoral stem was carefully moved so that the femoral head was initially positioned in the center of the acetabular component. The femoral head was then moved through a series of 17 0.050 mm increments, between 0.000 and 0.200 mm in each of the proximal, medial, and anterior directions as per the methodology used by Iopollo et al.,[28] Crockarell et al.,[29] and Bragdon et al.[30] Each series of 17 increments was then repeated five times. Plain AP pelvic radiographs and RSA examinations were taken after every movement of the femoral head. The 28 mm femoral head was then replaced with a 36 mm femoral head and the five series of 17 increments were repeated, with radiographic examinations again undertaken after every movement.

RSA Methodology

For all RSA radiographic examinations, a uniplanar RSA set-up with two radiographic tubes was used (Fig. 1b). A room-mounted unit (Siemens Ysio Digital System, Siemens AG,

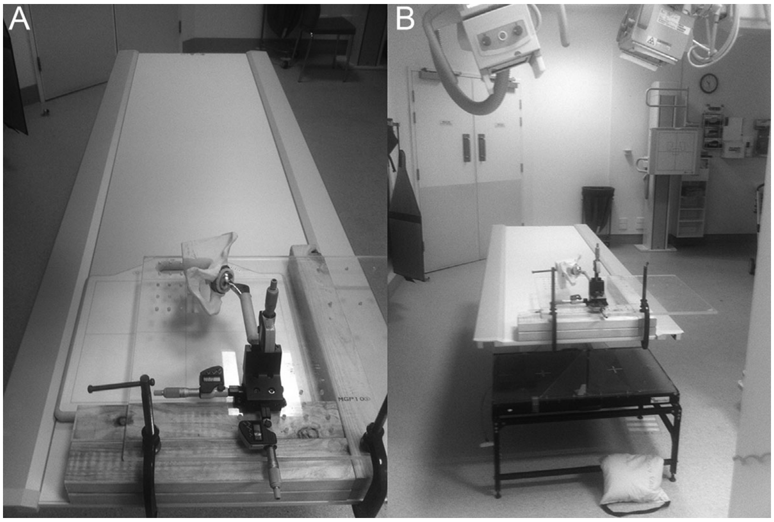

Figure 1. Accuracy phantom jig on table for: (A) AP pelvis radiographs with digital cassette able to be pulled in and out underneath plexiglass platform and (B) RSA radiographs using the room and mobile radiographic tubes above the calibration cage beneath the table.

Germany) and a mobile radiographic unit (Shimadzu Art analogue mobile machine, Shimadzu Medical Systems Ltd., Tokyo, Japan) were positioned with a 40° angle between the tubes. The calibration cage (Cage 43; RSA Biomedical) contained two 35 cm × 43 cm high-resolution digital radiographic cassettes (Agfa CR General plates, Agfa Healthcare, Mortsel, Belgium) each with a 1.6 m focal length to the film. The RSA calibration cage containing both cassettes was aligned to be parallel with the end of the table. The radiographic tubes were exposed simultaneously at 100 kV and 5 mAs. The exposures were digitized with an AGFA Centricity CR SP1001 processor (AGFA Healthcare). Radiographs were analyzed using UmRSA software (v6.0 and UmRSA DICOM link; RSA Biomedical) by one author (SAC). FHP was determined in relation to the acetabular reference segment. There were six different acetabular reference segments used in the study (Fig. 2): (1) the ellipse of both the outer diameter and circular opening of the acetabular component in combination with five beads (RSA Combined 5); (2) ellipse in combination with three beads (RSA Combined 3); (3) ellipse in combination with one bead (RSA Combined 1); (4) the rigid body created by five beads (RSA Beaded 5); (5) the rigid body created by three beads (RSA Beaded 3); and (6) only the ellipse itself (RSA Ellipse). In the context of the current study, use of each of these six different reference segments represents a different set of RSA measurements. The medial, proximal, anterior, 2D and 3D FHP was recorded for each different acetabular reference segment used.

Plain AP Pelvis Radiographs

The room-mounted radiographic tube (Siemens Ysio Digital System) was centered on the pubic symphysis and exposed with 60 kV and 5 mAs (Fig. 1a). The focus film distance was 1.1 m. The collimation included the whole pelvis as per the current clinical protocol (Fig. 1a). The AP pelvis radiographs were then analyzed using PolyWare (Rev 5, v5.14, Draftware Developers, Inc.),[5–7] HAS (v8.0.4.3, University of Chicago),[4] ROMAN (v1.70, Robert Jones and Agnes Hunt Orthopaedic Hospital),[9] and EBRA (EBRA-Cup Rel 2003, University of Innsbruck).[8] The 2D FHP was recorded for each method. EBRA measurements of medial and proximal FHP were also recorded. The radiographic cassette for plain radiographs was aligned to be parallel with the end of the table.

Statistical Analysis

Accuracy (bias) was calculated as the difference between the radiographic measurement of FHP and the known micrometer movement of the phantom femoral head. The accuracy of each method and for each head size was summarized using the mean accuracy of the five series of seventeen increments (80 increments in total, with five starting positions). The mean and standard deviation (SD) are presented as per current ASTM recommendations[14] as well as root mean square error (RMSE) to enable comparison with earlier publications. The effects of head size and method on accuracy in each axis were investigated using ordinary least squares regression. Interaction terms were assessed in all models. Overall effects were assessed at the 5% level, whereas the post hoc comparisons were assessed at $p < 0.001$ due to the large number of comparisons. All tests were two-tailed. All analyses were undertaken using SAS v9.3 (SAS Institute, Inc., Cary, NC). Only the EBRA measurements were compared to RSA measurements in the proximal and medial directions.

RESULTS

2D FHP

The mean accuracy and variability of each of the RSA, PolyWare, HAS, EBRA, and ROMAN methods used to measure 2D FHP with either a 28 or 36 mm femoral head is summarized in Table 1 and Figure 3.

The interaction of head size by method was significant ($p < 0.0001$). The p-values for post hoc comparisons between each method for each head size used are in Table 2. There was no difference between any of the six RSA methods irrespective of whether a 28 or 36 mm head was used (Table 2). When used with a 28 mm femoral head, all RSA methods showed a superior accuracy compared to the HAS ($p < 0.0001$), PolyWare ($p \leq 0.0003$), and ROMAN ($p < 0.0001$) methods (Table 2), whereas there was no difference between the RSA methods and EBRA. The RMSE of each of RSA measurements using the six different acetabular reference segments ranged between 0.018 and 0.033 mm, whereas that of all other methods ranged between 0.076 and 0.152 mm (Table 1), indicating less

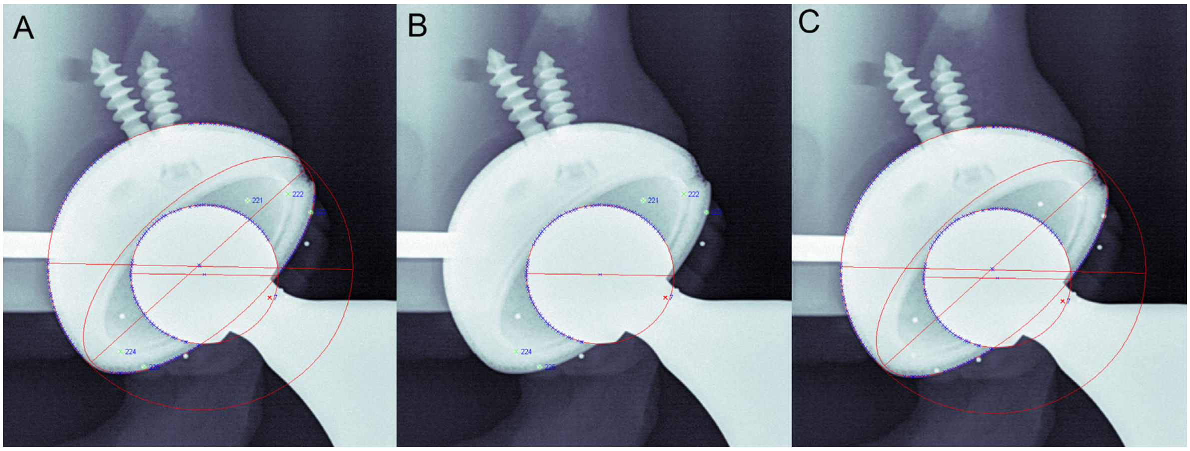

Figure 2. Different representation of the acetabular reference segment: (A) combined; (B) Beaded; (C) Ellipse.

Table 1. The Accuracy (mm) of Software Methods Used to Measure 2D FHP According to Head Size

	28 mm Articulation			36 mm Articulation			28 vs. 36
	Mean	SD	RMSE	Mean	SD	RMSE	*p*-Value
RSA Combined 5	0.005	0.029	0.030	0.009	0.017	0.019	0.676
RSA Combined 3	0.004	0.023	0.023	0.009	0.018	0.019	0.599
RSA Combined 1	0.007	0.026	0.026	0.011	0.025	0.027	0.704
RSA Beaded 5	0.004	0.033	0.033	0.009	0.015	0.018	0.594
RSA Beaded 3	0.000	0.020	0.020	0.010	0.017	0.019	0.327
RSA Ellipse	0.008	0.027	0.028	0.011	0.022	0.025	0.787
EBRA	0.006	0.095	0.105	−0.002	0.088	0.076	0.466
HAS	0.058	0.088	0.095	0.031	0.070	0.087	0.006
PolyWare	0.045	0.077	0.089	0.027	0.078	0.081	0.083
ROMAN	−0.100	0.093	0.136	−0.006	0.153	0.152	<0.0001

measurement variability with RSA, irrespective of the specific acetabular reference segment used. Measurements made using the ROMAN method showed the largest variability, with an RMSE of 0.136 and 0.152 mm for 28 and 36 mm femoral head measurements, respectively.

With a 36 mm head, RSA had a superior accuracy to HAS, PolyWare, and ROMAN measurements although the difference was not statistically significant. EBRA had a significantly superior accuracy to measure 2D FHP than HAS for both head sizes ($p \leq 0.001$) but a similar variability (Table 1). HAS and PolyWare had a significantly superior accuracy compared to ROMAN with either head size ($p \leq 0.0003$), whereas EBRA was superior only when using a 28 mm femoral head ($p < 0.0001$).

For each of the RSA measurements using the six different acetabular reference segments, there were no significant differences in the mean accuracy of 2D FHP between the 28 and 36 mm head sizes (Table 1, Fig. 3). Femoral head size significantly influenced the mean accuracy of HAS ($p = 0.006$) and ROMAN ($p < 0.0001$) 2D FHP measurements (Table 1).

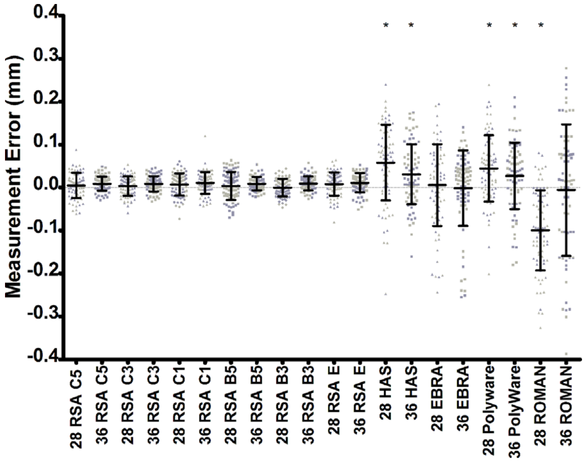

Figure 3. The mean measurement 2D FHP error (mm) for each radiograph analyzed for each method using either a 28 or 36 mm femoral head. Error bars indicate standard deviation.

Proximal FHP

The mean accuracy and variability of each of the RSA and EBRA methods used to measure proximal FHP with either a 28 or 36 mm femoral head is summarized in Table 3.

The interaction between head size and method was not significant ($p = 0.684$). However, the accuracy of proximal FHP measurements was independently associated with head size ($p < 0.0001$) and with method ($p = 0.0009$). Proximal measurements of a 28 mm femoral head had a superior accuracy compared to a 36 mm femoral head independent of method used ($p < 0.0001$). EBRA had an inferior accuracy compared to five of the six RSA measurements independent of femoral head size ($p < 0.0001$). The variability (RMSE) of proximal measurements was similar across all RSA measurements using different acetabular reference segments. The variability of all RSA measurements were lower than that of EBRA measurements for both femoral head sizes (Table 3).

Medial FHP

The mean accuracy and variability of each of the RSA and EBRA methods used to measure medial FHP with either a 28 or 36 mm femoral head is summarized in Table 3.

The interaction of head size by method was significant ($p = 0.0003$). All RSA measurements had a significantly superior accuracy compared to EBRA using a 28 mm femoral head ($p < 0.0001$), but not when using a 36 mm head. The variability (RMSE) of medial measurements was similar across all RSA measurements and lower than that of EBRA measurements for both femoral head sizes. Head size significantly influenced the mean accuracy only of EBRA medial measurements ($p < 0.0001$).

Anterior FHP

The mean accuracy and variability of RSA measurements with different acetabular reference segments used to measure anterior FHP with either a 28 or 36 mm femoral head is summarized in Table 3. The interaction between head size and method was not

Table 2. Post Hoc Comparisons (*p*-Value) of Different Methods Used to Measure 2D FHP for 28 and 36 mm Articulations

	RSA C5	RSA C3	RSA C1	RSA B5	RSA B3	RSA E	EBRA	HAS	PolyWare
28 mm articulation									
RSA C5									
RSA C3	0.896								
RSA C1	0.834	0.733							
RSA B5	0.905	0.989	0.743						
RSA B3	0.615	0.710	0.476	0.700					
RSA E	0.740	0.643	0.903	0.653	0.403				
EBRA	0.929	0.826	0.904	0.837	0.554	0.808			
HAS	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001		
PolyWare	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0003	0.0001	0.170	
ROMAN	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
36 mm articulation									
RSA C5									
RSA C3	0.981								
RSA C1	0.864	0.846							
RSA B5	0.998	0.983	0.862						
RSA B3	0.954	0.935	0.910	0.952					
RSA E	0.854	0.852	0.990	0.836	0.900				
EBRA	0.290	0.300	0.219	0.291	0.264	0.214			
HAS	0.031	0.029	0.046	0.030	0.035	0.048	0.001		
PolyWare	0.070	0.066	0.101	0.069	0.079	0.103	0.004	0.726	
ROMAN	0.144	0.145	0.103	0.151	0.129	0.100	0.688	0.0003	0.001

RSA C5 is Combined 5; RSA C3 is Combined 3; RSA C1 is combined 1; RSA B5 is Beaded 5; RSA B3 is Beaded 3; RSA E is Ellipse.

significant ($p = 0.387$). However, the mean accuracy of anterior FHP measurements with a 28 mm femoral head was superior to that with a 36 mm head independent of method ($p < 0.0001$). There was no statistical difference between any of the RSA measurements using different acetabular reference segments when measuring anterior FHP. The variability (RMSE) of anterior FHP measurements was similar, irrespective of femoral head size or specific acetabular reference segment used.

3D FHP

The mean accuracy and variability of RSA measurements with different acetabular reference segments used to measure 3D FHP with either a 28 or 36 mm femoral head is summarized in Table 3. The interaction between head size and method was not significant ($p = 0.330$). 3D FHP was not significantly associated with head size ($p = 0.234$) or RSA measurements using different acetabular reference segments ($p = 0.071$).

DISCUSSION

Due to the low in vivo wear being reported for XLPE liners,[13] it is important to understand the differences in the accuracy of the software programs currently used to measure wear. The reported accuracy for each method in the literature varies due to studies using different reference measurements, different directions of wear investigated, diverse statistical presentation of the error, and continuously updated versions of the software methods that incorporate different methods to identify the ellipse. This is the first study that utilizes a phantom hip model to compare the accuracy of the most common software programs, including RSA, to measure FHP. In contrast to the review of radiographic methods by McCalden et al.,[1] our study has found RSA measurements of 2D FHP to be significantly more accurate than those of HAS, PolyWare, and ROMAN.

Our results are compared to those of studies that examined the accuracy of radiographic measurements of FHP by comparing these to known movements of hip phantom models with a metal-backed acetabular component (Tables 4 and 5). The only other study that has compared the accuracy of RSA to other methods found two model-based RSA software programs to be more accurate and precise than PolyWare 2D FHP measurements.[22] Our results confirm that the accuracy of RSA is superior to that of PolyWare but we found that the variability (RMSE) of PolyWare 2D FHP measurements (0.08 mm) is much lower than that previously reported by Stilling et al. (0.47 mm).[22] Of the five other reports of the accuracy of PolyWare,[5,7,20,31,32] only one investigated the accuracy of 2D FHP measurements and reported a mean accuracy of 0.15 mm[32] (Table 5). This is inferior to our mean accuracy of 0.05 mm but we found a similar variability of measurement error within 0.4 mm.[32] The reported mean accuracy of HAS to measure 2D FHP varies

Table 3. The Accuracy (mm) of Each RSA Method and EBRA Measurements in Each Axis of Measurement, According to Head Size Used

	Medial						Proximal						Anterior						3D					
	28			36			28			36			28			36			28			36		
	Mean	SD	RMSE	Mean	SD	RMSE	Mean	SD	RMSE	Mean	SD	RMSE	Mean	SD	RMSE	Mean	SD	RMSE	Mean	SD	RMSE	Mean	SD	RMSE
RSA Combined 5	−0.002	0.030	0.030	−0.007	0.011	0.013	−0.004	0.021	0.021	0.010	0.017	0.020	0.003	0.059	0.059	−0.024	0.023	0.034	0.005	0.035	0.029	0.009	0.022	0.019
RSA Combined 3	−0.002	0.018	0.018	−0.009	0.011	0.014	0.000	0.017	0.017	0.011	0.019	0.022	0.008	0.032	0.033	−0.020	0.025	0.033	0.004	0.028	0.023	0.009	0.023	0.020
RSA Combined 1	0.001	0.022	0.022	−0.013	0.013	0.018	0.001	0.020	0.020	0.013	0.026	0.029	0.009	0.040	0.040	−0.012	0.041	0.043	0.007	0.033	0.026	0.011	0.033	0.027
RSA Beaded 5	−0.006	0.037	0.038	−0.004	0.011	0.012	−0.010	0.023	0.025	0.010	0.016	0.019	0.005	0.078	0.078	−0.032	0.030	0.044	0.004	0.043	0.033	0.009	0.024	0.018
RSA Beaded 3	−0.006	0.015	0.016	−0.005	0.010	0.011	−0.003	0.016	0.016	0.011	0.018	0.021	0.007	0.031	0.032	−0.029	0.031	0.043	0.000	0.025	0.020	0.010	0.024	0.019
RSA Ellipse	0.002	0.024	0.024	−0.012	0.016	0.020	0.003	0.021	0.021	0.012	0.023	0.025	0.009	0.042	0.043	−0.012	0.046	0.047	0.008	0.035	0.028	0.011	0.033	0.025
EBRA	0.030	0.081	0.086	0.000	0.067	0.067	−0.011	0.066	0.067	−0.003	0.071	0.070												

between 0.01 and 0.08 mm in four studies.[4,19,29,33] While the correction of elliptical distortion in the later version of HAS (v8.0.3.0) has been found to significantly improve the accuracy of linear and volumetric wear measurements compared to previous versions,[33] our mean error of 0.03 and 0.06 mm for 36 and 28 mm heads, respectively, was similar to previous reports. In the only report of the accuracy of the ROMAN method, Crockarell et al.[29] reported the median error of HAS (0.075 mm) to be superior to that of ROMAN (0.137 mm) to measure 2D FHP. Our results support that HAS was superior to ROMAN when using a 28 mm femoral head and that ROMAN had a higher variability (RMSE) independent of head size. This is important for users to consider because two studies have reported that ROMAN is more precise than HAS.[9,34] There is only one previous study that reports the mean accuracy of EBRA to be 0.004 and 0.005 mm in the medial and proximal axes which are similar to our results. However the variability of EBRA 2D FHP measurements was similar to PolyWare and HAS measurements.

Femoral head size significantly influenced 2D FHP measurements using ROMAN and HAS measurements in our study. Head size also significantly influenced the accuracy of EBRA proximal measurements and RSA measurements in the proximal and anterior directions. The accuracy of methods using different sized articulations should be considered when using these software programs to investigate the wear of larger heads. A potential cause for the apparent differences in accuracy between 28 and 36 mm articulations is the projection of the femoral head within the metal backed acetabular component. Therefore, the observed differences may not translate to acetabular components with different densities, such as either less dense cemented components or denser tantalum components, where the visualization of the femoral head ellipse may be compromised. Although the differences in mean accuracy were statistically significant, it should be noted that the mean accuracy was still relatively small. For example, the largest mean accuracy of proximal measurements using EBRA or any of the six RSA methods was 0.013 mm.

RSA methodology measures the center of the femoral head relative to either beads in the polyethylene liner or beads attached to the metal-backed shell, both of which can be used in conjunction with an ellipse algorithm for the acetabular component. The RMSE reported for the medial and proximal axes in our study were very low and similar to four other studies that used UmRSA[27,30,35] and a model-based RSA software[22] (Table 4). The model-based RSA software had higher errors in the anterior axis and resultant 3D measurements.[22] Previously, the accuracy of the RSA method was improved when more markers were used to represent the acetabular component[30,36] but this was not the case in our study. Only one study has

Table 4. Existing Reports of RSA Accuracy Against Known Movements of the Femoral Head Within a Metal-Backed Acetabular Component in a Phantom Hip Model

	Statistical Presentation	RSA Methodology	Axis of Measurement				
			x	y	z	2D	3D
Borlin et al. 2006[27]	RMSE	Beaded	0.024	0.037	0.048		
	RMSE	Combined (Beads + Ellipse)	0.024	0.037	0.035		
	RMSE	Ellipse	0.039	0.050	0.062		
Bragdon et al. 2004[35]	95%CI	Beaded (7 liner)	0.050	0.021	0.038		0.044
	95%CI	Beaded (5 tower)	0.036	0.023	0.041		0.036
Bragdon et al. 2002[30]	95%CI	Beaded (5 tower)	0.033	0.022	0.086		0.055
Stilling et al. 2012[22]	RMSE	MBRSA	0.056	0.042	0.209	0.073	0.487
Von Schewelov et al. 2004[26]	Mean (SD)						0.01 (0.15)
Current study	RMSE	Combined (Beads + Ellipse)	0.018	0.017	0.033	0.023	0.023

compared the accuracy of different acetabular reference segments with and without ellipse algorithms[27] and our study confirmed that there was no significant difference in the accuracy using different representations of the acetabular component (Table 4). Using the ellipse outlines alone does not require the intraoperative insertion of beads with advantages of reduced operation time as well as reduced risk of affecting the mechanical properties of the liner.[37] However, the appearance of beads and the ellipse on clinical RSA radiographs are often not as optimal as on RSA radiographs in our phantom study. As a result, the precision of RSA wear measurements using different acetabular reference segments should be validated for clinical studies. For example, Nebergall et al.[38] have recently reported that precision of RSA is improved if the ellipse of the shell is used in combination with markers in the liner. Future improvements in radiographic acquisition, software, or calibration cage design[39] may further improve accuracy of RSA measurements.

This study has a number of limitations. First, only 2D FHP measurements were compared across all methods because the majority of wear has been reported to occur in the proximal–distal and medial–lateral directions, within the anteroposterior plane.[16,40,41] Medial, proximal, anterior, and 3D measurements were undertaken and compared between RSA measurements made using six different acetabular reference segments, whereas EBRA measurements were compared to RSA measurements in the proximal and medial directions only. Although PolyWare and HAS also have the ability to measure FHP in the proximal and medial directions, this requires manually adjusting each individual result according to the inclination and version of the acetabular component due to the automated output being oriented with the face of the acetabular component.

Table 5. Existing Reports of HAS, PolyWare, and ROMAN Accuracy Against Known 2D and 3D FHP Movements Within a Metal-Backed Acetabular Component in a Phantom Hip Model

	Statistical Presentation	HAS		PolyWare		ROMAN
		2D	3D	2D	3D	2D
Crockarell et al. 2012[29]	Median	0.075				0.137
Devane et al. 1995[5]	Mean (SD)				0.34 (0.12)	
Devane et al. 1999[7]	Mean (SD) ABS*				0.022 (0.012)	
Ebramzadeh et al. 2003[47]	Median		0.10		0.10	
Kang et al. 2003[32]	Mean			0.15	0.21	
Kray et al. 2010[33]	Mean (SD) ABS*	0.007 (0.015)				
Martell et al. 1997[4]	Mean (SD)	0.01 (0.21)				
Martell et al. 2003[19]	Mean (SD)	0.011 (0.149)	0.005 (0.125)			
Stilling et al. 2012[22]	RMSE			0.467	0.471	
Sychterz et al. 2001[20]	Mean (SD)		0.24 (0.14)		0.15 (0.08)	
Current study	Mean (SD)	0.058 (0.088)		0.045 (0.077)		−0.100 (0.093)

*Absolute error values used.

HAS and PolyWare can measure 3D FHP but require AP pelvis and lateral radiographs taken at different times on the same day. Clinical lateral radiographs have often been found to be inadequate and uneven in exposure[42] and the patient moves between exposures of AP and lateral views. This is likely to result in the femoral head changing position within the acetabular component, leading to a slight difference in the FHP measurement. Recent clinical studies using HAS have not used the lateral radiographs and only measured 2D wear.[25] Second, the precision (reproducibility and repeatability) of measurements were not examined. Double in vivo radiographic examinations taken on the same day, with the assumption no further FHP has occurred between examinations, better represent these measures and should be undertaken in each clinical study as per the guidelines for RSA studies suggested by Valstar et al.[43] Thirdly, the accuracy in our study was measured under ideal conditions with no soft tissue or substitute for soft tissue used. Water was used to simulate soft tissue in a previous study and found to make a negligible difference.[44] Fourth, only one design of acetabular component in one size was used throughout the study. Different coatings and radiodensities of acetabular components have recently been shown to influence the precision of model-based RSA measurements.[45] Furthermore, the orientation of acetabular component was only investigated in one position in our study, which may influence the accuracy of methods due to identification of the ellipse.[31] The positioning of the rim of the metal-backed shell was important as this design has a "cut-out" of the rim to allow the locking mechanism of the liner to be reached. The position of this cut-out may mean that very little of the rim is able to be marked on the lateral edge of the acetabular component. Fifth, the position of the acetabular component and femoral head on the radiograph was consistent with the radiographic tube being centered on the pubic symphysis, as higher and lower positioning has previously been shown to influence accuracy of PolyWare and HAS.[46]

In conclusion, the accuracy of any given software program influences the sample size required for clinical wear studies. The superior accuracy and reduced variability of RSA wear measurements allow much smaller cohorts to be used in RSA clinical wear studies than those utilizing other software programs. RSA methodology is able to measure wear in all three axes accurately from radiographs taken simultaneously. In clinical studies, RSA therefore reduces the likelihood of additional error being introduced compared to other methods that measure 3D FHP from AP and lateral radiographs where patient movement is likely to occur between radiographs. The specific acetabular reference segment used did not influence accuracy of RSA measurements in our study. Finally, differences between femoral head sizes in the accuracy of FHP measurements made using software programs should be considered prior to using these methods in studies comparing the wear of different sized articulations.

AUTHORS' CONTRIBUTIONS

SAC contributed to conception, study design, data acquisition and analysis, drafting of manuscript. LBS contributed to data acquisition, data analysis, drafting of manuscript. OTH contributed to study design, data analysis, critical review of manuscript. DGC contributed to conception, critical review of manuscript. DWH contributed to conception, study design, critical review of manuscript.

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CHAPTER THREE

Wear of Highly Crosslinked Polyethylene Acetabular Components: A Review of RSA Studies

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Since establishing that RSA was the most accurate method to measure polyethylene wear, as described in Chapter Two, a systematic literature search was undertaken to include RSA studies of XLPE wear. The aims were to identify the *in vivo* wear rates of XLPE and to investigate factors that had previously been known to influence wear rates of conventional UHMWPE liners.

Despite the almost universal acceptance of the use of XLPE in acetabular components, to date publications reporting *in vivo* wear of XLPE measured using RSA have been based on 12 cohorts, comprising a total of only 260 hips. This scoping review identified variation in both the methodology and manner of reporting results of RSA studies. A number of recommendations to enhance the reporting of RSA wear results were made.

The findings are presented in the form of the published manuscript.

Statement of Authorship

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Contribution to the Paper	First author on the paper. Performed systematic literature search and scoping review. Reviewed all literature and collected data from publications included. Prepared all tables, wrote initial draft and edited manuscript through review process. Acted as corresponding author.
Overall percentage (%)	75%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.

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Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Wear of highly crosslinked polyethylene acetabular components

A review of RSA studies

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Background and purpose — Wear rates of highly crosslinked polyethylene (XLPE) acetabular components have varied considerably between different published studies. This variation is in part due to the different techniques used to measure wear and to the errors inherent in measuring the relatively low amounts of wear in XLPE bearings. We undertook a scoping review of studies that have examined the in vivo wear of XLPE acetabular components using the most sensitive method available, radiostereometric analysis (RSA).

Methods — A systematic search of the PubMed, Scopus, and Cochrane databases was performed to identify published studies in which RSA was used to measure wear of XLPE components in primary total hip arthroplasty (THA).

Results — 18 publications examined 12 primary THA cohorts, comprising only 260 THAs at 2–10 years of follow-up. The mean or median proximal wear rate reported ranged from 0.00 to 0.06 mm/year. However, differences in the manner in which wear was determined made it difficult to compare some studies. Furthermore, differences in RSA methodology between studies, such as the use of supine or standing radiographs and the use of beaded or unbeaded reference segments, may limit future meta-analyses examining the effect of patient and implant variables on wear rates.

Interpretation — This scoping review confirmed the low wear rates of XLPE in THA, as measured by RSA. We make recommendations to enhance the standardization of reporting of RSA wear results, which will facilitate early identification of poorly performing implants and enable a better understanding of the effects of surgical and patient factors on wear.

■

The clinical problem

Implant loosening and periprosthetic bone loss remain the most common reasons for revision of primary total hip arthroplasty (THA) in the medium to long term (AOANJRR 2013). The tissue response to polyethylene wear particles is an important cause of periprosthetic bone loss – osteolysis – behind acetabular components (Dumbleton et al. 2002). Review articles on THAs with conventional polyethylene have confirmed that the greater the amount of polyethylene wear, the higher the incidence of osteolysis (Oparaugo et al. 2001, Dumbleton et al. 2002) and that osteolysis is rare below a linear wear rate of 0.1 mm/year (Dumbleton et al. 2002). Research has therefore been focussed on improving the wear properties of polyethylene and on monitoring the in vivo wear of polyethylene liners of acetabular components of THAs by using various radiographic methods.

The introduction of XLPE

The first ultra-high-molecular-weight polyethylene (UHMWPE) that was intentionally gamma irradiated at a high level (100mRad) was first used clinically in 1971 (Oonishi et al. 2001). However, further research into the optimal dose of gamma radiation and its effect on the wear properties of conventional UHMWPE was not performed until the 1990s. Manufacturing methods were developed to crosslink polyethylene by exposing it to gamma or electron beam irradiation and then annealing or remelting the material by thermal treatments (Oonishi et al. 1997, Sun et al. 1997). In vitro hip simulator studies were able to show that highly crosslinked polyethylene (XLPE) components show significantly reduced wear compared to UHMWPE components (Kurtz et al. 1999,

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Muratoglu et al. 2001). Thus, XLPE components were introduced for use in THA surgery in 1998 (Kurtz et al. 2011), and by 2003 XLPE was used in two-thirds of hip arthroplasties in the USA (Kurtz 2004). More recently in Australia, the 2013 annual report of the joint replacement registry reported that XLPE was used in 94% of all primary THAs incorporating a PE bearing (AOANJRR 2013). When used in primary THA, XLPE has a lower rate of revision for any reason than conventional PE (AOANJRR 2013). Different companies continue to use different manufacturing methods for each XLPE product, aiming to balance resistance to wear, oxidation, and fatigue fracture (Pruitt et al. 2013). Ideally, as with all new prosthetic components, new XLPEs should be rigorously tested in clinical trials before being released for general use because of potential variation in manufacturing methods, which may lead to possible failure (Rohrl et al. 2005, Malchau et al. 2011).

The in vivo wear rate of XLPE acetabular components has been shown to be less than that of conventional UHMWPE components (Mu et al. 2009, Kurtz et al. 2011, Kuzyk et al. 2011). However, the wear rates reported for XLPE components have varied considerably between different published studies (Kurtz et al. 2011). For example, the mean 2D wear rate of one type of XLPE liner, using different measurement techniques after 5 years or more, has varied between 0.01 and 0.05 mm/year (Engh et al. 2006, Bitsch et al. 2008, Mutimer et al. 2010, Engh et al. 2012, Callary et al. 2013a).

Methods of wear measurement

Clinical studies of bearing surfaces use serial radiographs to measure the amount of femoral head penetration within the acetabular component as a representation of wear of the bearing surface. Traditionally, plain anteroposterior and/or lateral radiographs have been taken at regular time points postoperatively and the measurements have been made either manually (Livermore method (Livermore et al. 1990); Dorr and Wan method (Dorr and Wan 1995)) or using a software program that analyzes digitized radiographs (Martell's "Hip Analysis Suite" (Martell and Berdia 1997); Devane's "PolyWare" (Devane et al. 1995a, Devane et al. 1995b)). Measurements made from plain radiographs were sensitive enough to measure wear of conventional UHMWPE. However, due to the improved wear properties of XLPE, measurement of the lower amounts of in vivo wear associated with XLPE is more challenging, ideally requiring a more sensitive measurement method—namely radiostereometric analysis (RSA) (Bragdon et al. 2006a, Stilling et al. 2012) .

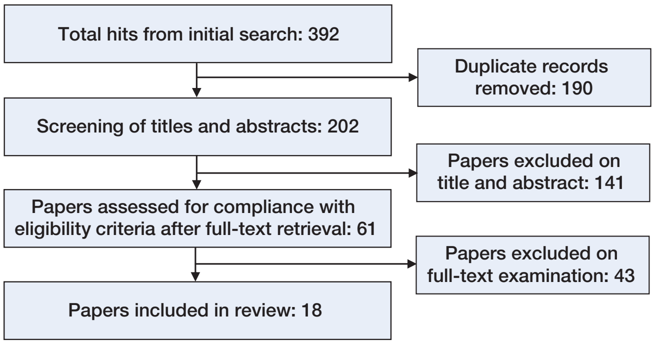
Radiostereometric analysis

RSA uses dual simultaneous radiographs taken over a calibration cage to calculate the 3D movement of one skeletal body segment relative to another (Karrholm et al. 2006). The traditional RSA method relies on the implantation of small spherical tantalum markers (0.8 and 1.0 mm diameter) to represent each skeletal body of interest (Karrholm et al. 1997). RSA was first used to measure polyethylene wear in 1976 (Baldursson et al. 1979). To measure polyethylene wear, tantalum markers are usually implanted in the peripheral rim of the polyethylene liner or on the back side of the cemented polyethylene components at the time of surgery, or (for a small number of studies) at the time of manufacture. The patient then undergoes consecutive radiographic examinations at set time points to measure the penetration of the femoral head within the polyethylene component. Accuracy of RSA under optimal conditions has been reported to 33, 22, 86, and 55 µm for measurement of medial, proximal, anterior, and 3D wear, respectively (Bragdon et al. 2002).

If the influences of patient and implant factors on wear rates of XLPE are to be investigated in detail, ideally it should be through meta-analysis of RSA studies. Before a meta-analysis, the published literature must be surveyed to determine whether the data reported in primary studies are sufficient to enable comparison of such factors. Scoping review is a method of inquiry similar to a systematic review but with the distinct aim of assessing the quantity and scope of the research studies conducted on a certain topic (Grant and Booth 2009, The Joanna Briggs Institute 2011). We therefore undertook a scoping review of studies on wear of XLPE acetabular components measured by RSA, using a systematic search to identify these studies.

Methods

A systematic search of the published literature in PubMed, Scopus, and Cochrane databases was performed on December 19, 2013. Title, abstract, and keyword fields were queried using the following keywords and index terms in the databases where applicable: "radiostereometric" AND "wear"; "radiostereometric" AND "polyethylene"; "radiostereometry" AND "wear"; "radiostereometry" AND "polyethylene"; "rsa" AND "wear"; "rsa" AND "polyethylene"; "stereophotogrammetric" AND "wear"; "stereophotogrammetric" AND "polyethylene" (Figure 1). These search terms were chosen based on the different names used to describe RSA studies. Publications in English were included if they reported the wear of XLPE, as measured by RSA, in either cemented or uncemented acetabular components in primary THAs. All such studies were included in this review, as the aim of scoping reviews is to determine the extent of the literature on a certain topic and therefore, unlike meta-analyses or systematic reviews, exclusion based on critical appraisal of methodological quality is not required. Polyethylene components were defined as highly crosslinked when intentionally treated using a total radiation dose ranging from 50 to 105 kGy (Kurtz et al. 2002). Duplicate publications, theses, case reports, conference proceedings, and abstracts were all excluded. Data extracted from the studies included details of the patient cohort, the RSA methodology used, precision, total femoral head penetration, bedding-in/creep, and wear.



Flow chart of the systematic search performed of the PubMed, Scopus, and Cochrane databases.

Results

We found 18 publications (Table 1) that fitted the criteria (Figure), representing 12 independent cohorts of patients. 9 of the 18 publications (Digas et al. 2004, Digas et al. 2007, Rohrl et al. 2007, Glyn-Jones et al. 2008b, Thomas et al. 2011, Johanson et al. 2012, Rohrl et al. 2012, Callary et al. 2013a,b) were longer-term follow-up reports of these cohorts. The wear of 7 different XLPE components was measured, incorporating 3 designs of cemented XLPE acetabular components and 4 designs of XLPE liners of uncemented acetabular components, as detailed in Table 1. 10 of the 12 cohorts received 28-mm articulations, and 2 cohorts involved larger articulations (32-mm and 36-mm). The material of the femoral head was cobalt chromium in 8 cohorts and oxidized zirconium in one. The material was not reported for 3 cohorts.

Collectively, RSA results have been reported for a maximum of 260 THAs (Table 2). The initial report of each cohort was published at either 2 or 3 years, and the longest follow-up was 10 years. The age of each cohort at THA varied between a mean or median of 48 and 72 years.

The specific RSA methodology used varied between cohorts (Table 2). For example, supine radiographs were used for RSA examinations in 6 cohorts, standing in 4, and a combination of both supine and standing in 2. All but 1 of the RSA studies used the UmRSA software package (RSA Biomedical, Umea, Sweden), but with different versions over time. The remaining study used software described by Gill et al. (1998). Tantalum beads were implanted within the XLPE component in 11 of 12 cohorts, to represent the acetabular segment. In most cases, RSA radiographs within the first postoperative week were used as the reference examination.

The precision of proximal wear measurements was reported for 6 cohorts and varied from 0.02 to 0.11 mm (Table 3). Both proximal and 3D head penetrations were reported for almost all cohorts, but the time over which the wear rate was calculated varied due to the time period allowed for bedding-

Table 1. Implants used in each patient cohort

Cohort	Publication	XLPE component	Head size, mm	Head material	Femoral component
1	Digas et al. 2003; Digas et al. 2004; Digas et al. 2007; Johanson et al. 2012	Durasul (Zimmer)	28	CoCr	Spectron (Smith & Nephew)
2	Digas et al. 2004; Digas et al. 2007	Longevity liner within Trilogy shell (Zimmer)	28	CoCr	Spectron (Smith & Nephew)
3	Rohrl et al. 2005; Rohrl et a.l 2007; Rohrl et a.l 2012	Osteonics Cup made of Crossfire PE (Stryker Orthopaedics)	28	CoCr	Exeter Femoral Stem (Stryker Orthopaedics)
4	Zhou, et al. 2006	XLPE 10 within Reflection Shell (Smith and Nephew)	28	CoCr	Spectron (Smith & Nephew)
5	Bragdon et al. 2007	Longevity liner within Trilogy Shell (Zimmer)	28	NR	NR
6	Bragdon et al. 2007	Longevity liner within Trilogy Shell (Zimmer)	36	NR	NR
7	Glyn-Jones et al. 2008a; Glyn-Jones et al. 2008b; Thomas et al. 2011	Longevity liner within Trilogy Shell (Zimmer)	28	CoCr	CPT (Zimmer)
8	Ayers et al. 2009	Longevity liner within Trilogy Shell (Zimmer)	28	NR	ML Taper (Zimmer)
9	Campbell et al. 2010a; Callary et al. 2013a	Marathon liner within Pinnacle Shell (Depuy Orthopaedics)	28	CoCr	Corail (Depuy Orthopaedics)
10	Campbell et al. 2010b; Callary et al. 2013b	X3 liner within Trident Shell (Stryker Orthopaedics)	32	CoCr	Accolade (Stryker Orthopaedics)
11	Kadar et al. 2011	Reflection All-Poly XLPE (Smith & Nephew)	28	CoCr	Spectron EF (Smith & Nephew)
12	Kadar et al. 2011	Reflection All-Poly XLPE (Smith & Nephew)	28	Oxinium	Spectron EF (Smith & Nephew)

NR: not reported.

Table 2. Details of RSA studies

Cohort	Age (range)	Number of patients	Follow-up, months	Report	Years of follow-up	Number of patients included in RSA results	Software	Acetabular reference	Standing/ Supine
1	Median 54 (35–68)	31	within 7 days, 3, 6, 12, 24, 36 60, 84, 120	1st 2nd 3rd 4th	2 3 5 10	(Digas et al. 2003); 23 supine, 21 standing (Digas et al. 2004); 20 supine, 18 standing (Digas et al. 2007); 28 supine, 22 standing (Johanson et al. 2012); 23 supine	UmRSA	B	Supine [a]
2	Median 48 (29–70)	32	within 7 days, 3, 6, 12, 24, 36, 60	1st 2nd	2 5	(Digas et al. 2004); 22 supine, 20 standing (Digas et al. 2007); 19 supine, 12 standing	UmRSA	B	Supine [a]
3	Mean 58 (49–79)	10	within 7 days, 2, 12, 24, 36, 60, 72, 120	1st 2nd 3rd	3 6 10	(Rohrl et al. 2005); 10 (Rohrl et al. 2007); 9 (Rohrl et al. 2012); 8	UmRSA	B	Supine
4	Mean 68 (53–83)	30	3 to 7 days, 2, 12, 24	1st	2	(Zhou et al. 2006); 28	UmRSA 6.0	B+E	Supine
5	Mean 56 (36–77)	16	6 weeks, 6, 12, 24, 36	1st	3	(Bragdon et al. 2007); 16(25/30 [b])	UmRSA 6.0	B; B+E; E	Standing
6	Mean 56 (36–77)	14	6 weeks, 6,12, 24, 36	1st	3	(Bragdon et al. 2007); 14 (25/30 [b])	UmRSA 6.0	B; B+E; E	Standing
7	Mean 68 (52–76)	27	PO, 3, 6, 12, 24, 36, 60, 84	1st 2nd 3rd	2 3 7	(Glyn-Jones et al. 2008a); 26 (Glyn-Jones et al. 2008b); 26 (Thomas et al. 2011); 22	Gill et al. 1998	Un-bedead	Standing
8	Mean 58 (SD 8)	24	6 weeks, 6, 12, 24	1st	2	(Ayers et al. 2009); 24	UmRSA	B	Standing
9	Median 72 (55–80)	30	4–6 days, 6, 12, 24, 72	1st 2nd	2 6	(Campbell et al. 2010a); 25 (Callary et al. 2013a); 24	UmRSA 6.0	B+E	Supine
10	Median 63 (47–76)	21	Within 7 days, 6, 12, 24, 60	1st 2nd	2 5	(Campbell et al. 2010b); 19 (Callary et al. 2013b); 18	UmRSA 6.0	B+E	Supine
11	Mean 70 (SD 5)	30	9–15 days, 3, 6, 12, 24	1st	2	(Kadar et al. 2011); 29	UmRSA 5.0	B	Supine
12	Mean 70 (SD 5)	30	9–15 days, 3, 6, 12, 24	1st	2	(Kadar et al. 2011); 24	UmRSA 5.0	B	Supine

[a] Supine and standing from 3 months.
[b] Combined number of patients included in wear results for cohorts 5 and 6.
B: beaded; B+E: beaded plus ellipse; E: ellipse

in, which ranged from 2 to 24 months (Table 4). The proximal wear rate calculated after this period of assumed bedding-in ranged from a mean or median of 0.00 to 0.06 mm/year.

Discussion

New materials, such as XLPE components used in THA, need to be closely monitored as part of their stepwise introduction into clinical use (Malchau 1995, Malchau et al. 2011). The wear rates reported for XLPE components varied between studies. Some of this variation is likely to be due to the different measurement methods used (Kurtz et al. 2011). However, some variation could also be due to variables that include patient factors such as BMI and activity;

Table 3. Precision of RSA from double examinations in each cohort

Cohort	Publication in which precision was reported	Original calculation method	Number of double examinations	Adjusted precision (95% CI = 1.96 × SD) x	y	z	3D
1	Digas et al. 2003	99% CI	45	0.10	0.08	0.15	0.17
2	Digas et al. 2004	99% CI	45	[a]	[a]	[a]	[a]
3	Rohrl et al. 2007	95% CI	99	[b]	0.08	[b]	0.16
	Rohrl et al. 2012	1.96 × SD	[b]	[b]	0.09	[b]	0.31
4	Zhou et al. 2006	Beaded 1.96 × SD	28	[b]	0.08	[b]	0.22
		Ellipse 1.96 × SD	28	[b]	0.10	[b]	0.28
5 and 6	[b]	[b]	[b]	[b]	[b]	[b]	[b]
7	[b]	[b]	[b]	[b]	[b]	[b]	[b]
8	[b]	[b]	[b]	[b]	[b]	[b]	[b]
9	Campbell et al. 2010a	95% CI	22	0.03	0.02	0.07	[b]
10	[b]	[b]	[b]	[b]	[b]	[b]	[b]
11 and 12	Kadar et al. 2011	2.009 × SD	50	0.11	0.11	0.33	0.21

[a] Precision not specified for each axis, “between 0.07 and 0.32 mm”.
[b] Not reported.

Table 4. Proximal and 3D femoral head penetration, bedding-in, and wear rate reported for each cohort in each follow-up report

Cohort	Follow-up years		Femoral head penetration [a] (mm)	Bedding-in [b] mm	Wear rate [c] mm/year
Proximal					
1	2	(Digas et al. 2003)	0.13 (0.03 to 0.31) [d]	0.1 [d]	0.03 [f] (3–24 m) [e]
	3	(Digas et al. 2004)	0.13 (-0.02 to 0.30) [d]	0.1 [d, g]	0.03 [f] (3–36 m) [e]
	5	(Digas et al. 2007)	0.15 (-0.10 to 0.86) [d]	0.1 [d, g]	0.02 [f] (3–60 m) [e]
	10	(Johanson et al. 2012)	0.15 [g]	0.1 [d, g]	0.01 (SE 0.00) (2–10 yr) [d]
2	2	(Digas et al. 2004)	0.08 (-0.03 to 0.28) [d]	0.08 [d]	0.03 [f] (3–24 m) [e]
	5	(Digas et al. 2007)	0.08 (-0.02 to 0.24) [d]	0.08 [d, g]	0.02 [f] (3–60 m) [e]
3	3	(Rohrl et al. 2005)	NR	0.05 (0–2 months)	0.01 (2–24 m)
	6	(Rohrl et al. 2007)	0.08 (CI 0.02 to 0.13)	0.06 [g]	0.01 (2–72 m)
	10	(Rohrl et al. 2012)	0.07 (CI -0.02 to 0.15)	0.06 [g]	0.00 (2–120 m)
4	2	(Zhou et al. 2006)	0.07 [g]	0.06 [g]	0.01 (2–24 m)
5	3	(Bragdon et al. 2007)	0.06 [h] (SE 0.03)	0.06 [h] (SE 0.04)	0.03 [h] (SE 0.02)
6	3	(Bragdon et al. 2007)	0.06 [h] (SE 0.06)	0.07 [h] (SE 0.02)	0.00 [h] (SE 0.06)
7	2	(Glyn-Jones et al. 2008a)	NR	NR	0.06 (SD 0.07) (3–24 m)
	3	(Glyn-Jones et al. 2008b)	NR	0.17 [g]	0.02 [g]
	7	(Thomas et al. 2011)	NR	NR	0.01 (CI ±0.03)
8	2	(Ayers et al. 2009)	0.07 [h] (-0.04 to 0.19)	0.07 [h] (-0.14 to 0.16)	0.02 [g]
9	2	(Campbell et al. 2010a)	0.12 (-0.10 to 0.38)	0.11 (-0.01 to 0.39)	0.01
	6	(Callary et al. 2013a)	0.19 (0.00 to 0.51)	0.11 (-0.01 to 0.39)	0.01 (-0.02 to 0.06)
10	2	(Campbell et al. 2010b)	0.02 [h] (-0.07 to 0.16)	0.01 [h] (-0.09 to 0.12)	0.02 [h]
	5	(Callary et al. 2013b)	0.02 (-0.11 to 0.13)	0.01 (-0.09 to 0.12)	0.00 (-0.03 to 0.03)
11	2	(Kadar et al. 2011)	0.09 (CI 0.06–0.12)	0.06 [g]	0.03
12	2	(Kadar et al. 2011)	0.08 (CI 0.04–0.12)	0.06 [g]	0.02
3D					
1	2	(Digas et al. 2003)	0.18 (0.07–0.35) [d]	0.15 [d]	0.11 [f] (3–24 m) [e]
	3	(Digas et al. 2004)	0.23 (0.04–0.41) [d]	0.18 [d, g]	0.09 [f] (3–36 m) [e]
	5	(Digas et al. 2007)	0.23 (0.02–0.91) [d]	NR	0.04 [f] (3–60 m) [e]
	10	(Johanson et al. 2012)	0.22 [d, g]	0.18 [d, g]	0.01 [f] (SE 0.00) (2–10 yr) [d]
2	2	(Digas et al. 2004)	0.22 (0.05–0.40) [d]	0.25 (supine)	0.19 [f] (3–24 m) [e]
	5	(Digas et al. 2007)	0.20 (0.10–0.61) [d]	0.24 (supine)	0.07 [f] (3–60 m) [e]
3	3	(Rohrl et al. 2005)	0.17 (CI 0.06–0.28)	NR	NR
	6	(Rohrl et al. 2007)	0.23 (CI 0.10–0.35)	NR	0.03 (2–72 m)
	10	(Rohrl et al. 2012)	0.20 (CI 0.03–0.36)	0.19 [g]	0.00 [f] (2–120 m)
4	2	(Zhou et al. 2006)	0.19 [g]	0.15 [g]	0.03 [f] (2–24 m)
5	3	(Bragdon et al. 2007)	NR	NR	NR
6	3	(Bragdon et al. 2007)	NR	NR	NR
7	2	(Glyn-Jones et al. 2008a)	0.31 (SD 0.18)	0.30 [g]	0.06 (SD 0.06) (3–24 m)
	3	(Glyn-Jones et al. 2008b)	0.35 (SD 0.14)	0.26 (SD 0.17)	0.03 (SD 0.06)
	7	(Thomas et al. 2011)	0.33 (CI ± 0.10)	0.29 (95% CI ±0.07)	0.01 (CI ± 0.02)
8	2	(Ayers et al. 2009)	NR	NR	NR
9	2	(Campbell et al. 2010a)	0.23 (0.02–0.84)	0.23 (0.06 to 0.93)	0.00 [f]
	6	(Callary et al. 2013a)	0.32 (0.05–0.60)	0.23 (0.06 to 0.93)	0.018 (-0.11 to 0.08)
10	2	(Campbell et al. 2010b)	0.16 [h] (0.07–0.26)	0.16 [h] (0.02 to 0.32)	-0.04 [h]
	5	(Callary et al. 2013b)	0.15 (0.04–0.32)	0.19 (0.02 to 0.32)	-0.01 (-0.06 to 0.04)
11	2	(Kadar et al. 2011)	0.19 (CI 0.15–0.23)	NR	NR
12	2	(Kadar et al. 2011)	0.18 (CI 0.13–0.22)	NR	NR

CI: 95% confidence interval
NR: not reported.
[a] Initial to final follow-up unless otherwise noted; mean (range).
[b] Initial examination to 1-year follow-up unless otherwise noted; mean (range).
[c] Annual rate from 1-year follow-up to final follow-up unless otherwise noted; mean (range).
[d] Supine
[e] Standing
[f] Manually calculated to be rate/year from a reported value given after bedding-in.
[g] Visualized from graph
[h] Median

implant factors such as femoral head material, liner thickness, and manufacturing methods for XLPE; and surgical factors such as inclination angle of the acetabular component. Thus, while the wear rate of XLPE acetabular components has been shown to be substantially less than that of conventional UHMWPE components (Kurtz et al. 2011, Kuzyk et al. 2011, Mu et al. 2009), the possible influence of the above variables remains unclear. Although a meta-analysis would be required to investigate the influence of these variables on wear rates of XLPE, the number of patients required for a meta-analysis would greatly exceed that included in the current literature, due to the low wear of XLPE and the relatively weak effect of such variables on wear. Our scoping review identified a relatively small number of studies that had measured the wear of XLPE components using the most sensitive measure available, namely RSA. Overall, the studies examined 12 cohorts involving only 260 THAs. By recommending further guidelines to standardize the reporting of RSA wear studies, we hope that this will assist retrospective analysis of the influence of these factors in the future.

Methodology of RSA studies

Cohort size

All of the cohorts had a sample size of between 10 and 32 at recruitment. As RSA has been demonstrated to have high sensitivity (Bragdon et al. 2002), statistical power can be achieved with fewer observations and therefore a small sample size is not, in itself, necessarily a methodological limitation. However, most studies had decreasing sample sizes over time. Missing or poor-quality RSA examinations further reduced the size of the originally recruited cohort, after exclusions for death and other reasons for loss to follow-up. This common problem of decreasing availability of RSA data over time must be considered when designing RSA-based clinical trials, especially if longer-term follow-up is required.

Follow-up time points

Follow-up time points within the first year varied between the RSA studies, thereby potentially influencing the amount of femoral head penetration recorded. The first reference RSA examination was usually performed within the first week postoperatively. However, some studies used 11–15 days, 2 weeks, or 6 weeks as their baseline examination. This may influence both bedding-in and femoral head penetration measurements. How bedding-in and wear varies between different types of XLPE components remains unknown. The amount of initial plastic (permanent) deformation of the polyethylene liner may differ due to design, manufacturing error, fit of the liner within the shell, elasticity of the metal shell, and surface of the inner shell. Bedding-in may also differ between cemented XLPE components and XLPE liners within uncemented metal shells.

RSA software and acetabular reference segment

The specific manner in which RSA was undertaken also varied between the studies, and may therefore also affect the outcome of meta-analyses. Early versions of the UmRSA software required the implantation of tantalum markers in the polyethylene, and subsequently measured the movement of the center of the femoral head within the rigid body defined by the markers in the polyethylene. A recent modification to the UmRSA software allows metal-backed hemispherical acetabular components to be measured using an ellipse algorithm (Borlin et al. 2006). Therefore, the movement of the femoral head can be measured within the ellipse of the metal acetabular components or by using beads in the liner, or by using a combination of both methods (beaded plus ellipse) (Borlin et al. 2006). The study that used Gill's software (Gill et al. 1998) used the known dimensions of the prostheses and measured the femoral head penetration relative to the center of the metal acetabular component, this approach being similar to the ellipse-only method. Studies that do not use beads have the potential to save time and money, and also eliminate safety concerns relating to the implantation of beads. Furthermore, there is no exclusion of patients due to insufficiently marked components, which is a common reason for exclusion of hips in beaded analysis (Borlin et al. 2006). RSA wear measurements in the proximal direction using the ellipse algorithm alone are less precise than those using a beaded reference segment: 0.10 mm and 0.08 mm, respectively (Zhou et al. 2006). A combination of beads and the ellipse algorithm was found to have the smallest error (Borlin et al. 2006) and the least amount of variance (Bragdon et al. 2007). To date, only 1 study has presented the results of all 3 different reference segments (beaded, beaded plus ellipse, and ellipse only), and showed only slight variation in the results (Bragdon et al. 2007). However, these different representations of the acetabular reference segment may influence the measurement of early creep and bedding-in if there is early movement between the liner and the metal-backed shell.

Patient positioning

Another methodological difference between studies was the use of standing and/or supine positioning during RSA examinations (Table 2). Standing radiographs are thought to position the femoral head in the deepest part of its wear track within the polyethylene liner. However, standing radiographs may have poorer image quality due to different soft tissue exposure (stomach overhang) and different pelvic positioning. Patients have also reported that standing examinations caused discomfort at the initial postoperative examination (Digas et al. 2003). 3 RSA studies have investigated the differences in measurements made using standing and supine radiographs. Specifically, von Schewelov et al. (2006) reported that 3D wear measurements made from supine and standing (i.e. weight-bearing) examinations taken on the same day had a high correlation and there was no difference in the magnitude of penetration. Digas et al. (2004) also found no difference in the proximal head penetration recorded, while Bragdon et al. (2006b) found small differences in some wear measurements between standing and supine examinations, but the occurrence was low and did not affect the average results.

Precision reported in RSA studies

Given the typically low amounts of XLPE wear reported in RSA clinical studies, determination of the precision of the RSA method is important. Despite the RSA-reporting guidelines recommending the inclusion of precision measurements in clinical studies (Valstar et al. 2005), double examinations to determine precision were undertaken for only 6 of the 12 cohorts. While double examinations give a slight increase in radiation exposure of patients, the precision of RSA measurements cannot be determined using a phantom model (Borlin et al. 2006). Proximal wear measurements were more precise (range: 0.02–0.11 mm) than 3D wear measurements (range: 0.16–0.28 mm). The RSA method is more precise in the x- and y-axes relative to the z-axis because the latter measurements are made "out of plane" in the uniplanar setup (Karrholm et al. 1997). This will in turn affect the precision of the 3D measurement, namely the vectorial sum of all 3 axes.

Reporting of RSA wear results

To summarize the wear rate derived from studies identified in this review, the reported results were described using 3 terms: (1) "femoral head penetration" (initial examination to latest follow-up), (2) "bedding-in" (initial examination to the 1-year examination), and (3) "wear rate" (the annual wear rate between the 1-year examination and latest follow-up). RSA provides measurements in 3 axes: proximal-distal, medial-lateral, and anterior-superior. Proximal and 3D (vectorial sum) femoral head penetration and wear rates were most commonly reported, although the axis of measurement was not defined in some publications. Interpretation of the results was further complicated by the use of a number of different terms to denote the same concept. For example, proximal measurements were variously referred to as superior, longitudinal, or linear—and 3D measurements as total, linear, or maximum total point motion (MTPM). Interestingly, the 2D wear rates, which allow comparison of results to those of studies using less sophisticated techniques and plain radiographs, were only reported in 2 cohorts (Callary et al. 2013a, Callary et al. 2013b).

Mean and median values were commonly reported, but for some publications these figures had to be estimated from graphs or calculated using other data provided in the publication (Table 4). Within any one cohort, varying numbers of patients were often included at different follow-up time points, possibly affecting the reported mean wear rate, particularly if patients with wear rates at either end of the range were differentially represented over time. The mean annual proximal wear rate did not exceed 0.06 mm/year for any cohort. Only 2 publications reported mean 3D wear rates above 0.06 mm/year (Digas et al. 2003, Digas et al. 2004). However, because the wear rate in both of these cohorts was calculated between 3 months and the latest follow-up, some of the penetration attributed to wear may in fact have been due to bedding-in. This is supported by the finding that a much lower mean 3D wear rate of 0.005 mm/year was reported for the same cohort between 2 and 10 years (Rohrl et al. 2012). It is therefore important to emphasize that if wear rate is calculated using a reference time point within the bedding-in phase, the reported rate may be an overestimation of the true wear rate. Although the majority of studies used 1 year as the baseline reference for wear rate calculations, the assumed end of bedding-in/creep and the beginning of wear has varied in the literature, ranging from 2 months to 2 years (McCalden et al. 2005).

Studies of UHMWPE identified that an annual wear rate exceeding 0.1 mm/year was associated with an increased risk of developing osteolysis (Dumbleton et al. 2002), and an increased risk of revision surgery due to loosening or lysis. This suggests that the percentage of THAs with wear exceeding certain thresholds is, in fact, of more clinical importance than a mean or median wear rate. It is important to emphasize that the threshold of XLPE wear possibly associated with osteolysis is unknown. Therefore, presentation of scatter plots of individual wear rates, coupled with long-term clinical follow-up of patients, will facilitate a better understanding of the relationship between XLPE wear and subsequent development of osteolysis. Only 4 publications in the current review have reported percentages of patients exceeding specified thresholds (Digas et al. 2007, Thomas et al. 2011, Callary et al. 2013a, Callary et al. 2013b). Specifically, 3 reported no patients with a wear rate greater than 0.1 mm/year (Thomas et al. 2011, Callary et al. 2013a, Callary et al. 2013b) and 1 reported that 24 of 28 patients in cohort 1 had a wear rate of less than 0.05 mm/year and that all patients in cohort 2 had a wear rate below 0.05 mm/year (Digas et al. 2007).

Recommendations to improve reporting of RSA wear results

13 guidelines were described by Valstar et al (2005) for standardization of RSA of implants. These guidelines have recently been incorporated within the ISO for measuring migration with RSA (ISO 16087:2013 (E)). The findings of the present scoping review have led to further recommendations of important items that should be included when reporting RSA wear results (Table 5). Standardization of the manner in which RSA wear results are presented will enable a better understanding of the effects of surgical and patient factors on wear. Most importantly, such standardization is also likely to facilitate early identification of poorly performing implants.

Future studies on wear using RSA

Our review has identified that the wear rates reported for XLPE components are low, which is encouraging for continued clinical use. With 1 exception, the mean proximal and 3D annual

Table 5. Recommendations to enhance reporting of RSA wear results

Recommendations to enhance reporting of RSA wear results	
Methodology	
1	Components used (femoral head size and material; description of XLPE component)
2	Patient positioning (supine or standing)
3	Software and acetabular reference segment used
Results	
4	Allow one year for bedding-in and creep, and report results using the terms: – femoral head penetration (initial examination to latest follow-up) – bedding-in (initial examination to the one-year examination) – wear rate (the annual wear rate between the one-year examination and latest follow-up)
5	Report axis of measurement (x, y, z, 2D or 3D)
6	Use scatter plots of wear results to allow identification of outliers

wear rates decreased when the length of follow-up increased. In the cohort in which this was not the case (Campbell et al. 2010a, Callary et al. 2013a), the liner was manufactured using an irradiation dose at the lower end of the range included as XLPE (50 kGy). Thus, new designs of XLPE components need to be monitored prospectively. Second-generation XLPEs are being introduced rapidly internationally and differ from first-generation XLPEs by being either sequentially irradiated and annealed, mechanically deformed or compressed, or diffused with vitamin E (Dumbleton et al. 2006). However, we identified only 1 cohort in which the bedding-in and wear of a second-generation XLPE liner had been investigated (Campbell et al. 2010b, Callary et al. 2013b). In this cohort, the mean proximal bedding-in was lower than that of all first-generation XLPE components (0.007 mm vs. 0.06–0.17 mm).

The low wear rates reported for XLPE have also encouraged the use of larger articulations, which have been shown to reduce the incidence of dislocation within the first year after THA (Howie et al. 2012). In Australia, head sizes of 32 mm or more have been increasingly used over the last 5 years in primary THAs with XLPE components (AOANJRR 2013). However, the effect of articulation size on XLPE wear rates is poorly understood. To date, only 1 RSA study has compared the wear rates of 28- and 36-mm articulations. Although that study reported no difference at 3 years (Bragdon et al. 2007), it is important to note that this non-randomized comparison included only 25 hips.

Identification of any potential association between patient-related factors such as age, sex, weight, or activity on the one hand and wear of XLPE on the other is desirable. However, such studies require relatively large samples, given the variability in these factors between patients. Individual RSA studies are limited in this regard due to the costly specialized equipment and analysis required, and to the need for prospective radiographs above a calibration cage. Conversely, although other measurement techniques, such as Martell's Hip Analysis Suite (Martell and Berdia 1997) and PolyWare (Devane et al. 1995a,b), are able to measure the wear rates of larger cohorts retrospectively using plain radiographs, they are limited by their lack of sensitivity. In future, meta-analyses of data pooled from existing RSA studies may provide a means of examining not only the effect of patient-related factors on XLPE wear, but also the relationship between XLPE wear and osteolysis.

Conclusion

Despite the almost universal acceptance of the use of XLPE in acetabular components, to date the publications reporting in vivo wear of XLPE measured using RSA have been based on 12 small cohorts covering only 260 hips. The present scoping review has identified variation in both the methodology and the manner of reporting results of RSA studies. We have made a number of recommendations to enhance the reporting of RSA-based wear results. Longer-term studies are required to determine whether the low wear of XLPE identified in the short term does indeed translate to a low incidence of osteolysis in the medium to long term and, importantly, to a reduction in the need for revision surgery.

SC: performed scoping review, collected data from publications included, and wrote the manuscript. LS: assisted with collection of data and proofread the manuscript. OH: analyzed the review data and contributed to the manuscript. DC: planned the study and proofread the manuscript. ZM: planned systematic search criteria and assisted with the scoping review. DH: planned the study and contributed to the manuscript.

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CHAPTER FOUR

IN VIVO WEAR OF XLPE AS MEASURED BY RSA

4.1 INTRODUCTION

4.1.1 Factors That Affect Wear

Patient, implant, and surgical factors have been shown to affect the wear rate of conventional UHMWPE liners. The studies undertaken as part of this thesis have examined how such factors affect the wear rate of XLPE liners.

Specifically, Chapter Four addresses the third aim of this thesis, namely to measure the bedding-in and wear rate of XLPE using RSA to investigate the influence of i) type of XLPE, ii) articulation size and iii) patient age.

Six different cohorts, described in Table 4.1, underwent regular RSA examinations up to six years follow-up. The results of five of these six individual cohorts have been published or accepted for publication. These manuscripts are presented in this Chapter, as shown in Table 4.1. The results of Cohort D were not published prior to submission of this thesis and are presented in Section 4.7.

A summary of the combined results from all six cohorts are presented in Section 4.10.

4.1.2 Patient Related Factors

Polyethylene wear is related to the patient specific contact stress in THR (Kosak et al., 2011). Patient related factors that are therefore hypothesised to influence the wear rate of XLPE include age, activity, and weight or body mass index (BMI, kg/m^2). Wear is acknowledged to be related to number of cycles of use and therefore more active patients could possibly have higher prosthesis wear (Schmalzried et al., 2000). The increased activity and higher demands of younger patients are both thought to increase wear rates. This was confirmed in one study of conventional UHMWPE liners in patients under 50 where the amount of wear was inversely related to the patient's age (Berger et al., 1997). However it is important to recognise that a younger patient age may not be the best surrogate of higher activity and that ideally patient activity would be measured with activity monitors (Keeney et al., 2015). Studies of younger patient cohorts have confirmed low wear rates of XLPE liners at early follow-up but often do not have an older control group (Ayers et al., 2009; Shia et al., 2009; Mall et al., 2011; Ranawat et al., 2012; Ayers et al., 2015). Furthermore, the measurement methods used in these studies are frequently not able to detect the small amounts of XLPE wear (Shia et al., 2009; Mall et al., 2011; Ranawat et al., 2012). For example Shia et al. (2009) used Hip Analysis Suite to analyse plain radiographs and reported a mean wear of 0.033 mm/yr but did not report the range of wear. The wear of XLPE has only been measured with RSA in one cohort of younger patients and that study did not have a control group of older patients. Specifically, the median proximal wear rate of XLPE was 0.02 mm/yr between one and two years after THR (Ayers et al., 2009) and 0.004 mm/yr at five years (Ayers et al., 2015), much lower than conventional UHMWPE (0.04 mm/year at five years).

Increased patient weight or BMI are commonly thought to potentially increase wear rates of XLPE as the load through the hip joint is increased. For example, one large clinical study of conventional UHMWPE liners found that the age and weight of the patient were important predictors of proximal wear (Digas et al., 2003b). Clinical studies investigating the influence of BMI on XLPE wear rate have been limited by the use of measurement methods less sensitive than RSA (Sandgren et al., 2014). However, one study did find an inverse relationship between increasing BMI and risk of revision for bearing wear (Wagner et al., 2016). This may be due to patients with a lower BMI being more active or conversely patients with a higher BMI having higher comorbidities preventing further surgery. In the same study, increased BMI was however associated with increased rates of reoperation, increased rates of early hip dislocation, wound infection and deeper peri-prosthetic infection.

4.1.3 Implant Factors

4.1.3.1 XLPE Manufacture

The manufacturing method of each type of XLPE liner is slightly different, as described earlier in Section 1.5.5. For example, liners included as XLPE are intentionally treated with a total irradiation dose ranging from 50 to 105 kGy (Kurtz et al., 2002). Manufacturing differences may influence the mechanical properties of the liner. For example, the accelerated wear observed with conventional UHMWPE liners sterilised with ethylene-oxide caused concerns about long-term problems and particularly their use in younger patients (Digas et al., 2003b). Comparisons of different XLPE liners are limited by the small amounts of wear occurring. One *in vitro* hip simulator study has shown that a second-generation XLPE liner (X3™; Stryker Orthopaedics, Mahwah, NJ, USA) demonstrated 97% wear reduction compared to a conventional UHMWPE liner and 62% wear reduction compared to a first-generation XLPE (Crossfire, Stryker Orthopaedics, Mahwah, NJ) (Dumbleton et al., 2006). It would be of interest to investigate the wear rates of different XLPE liners *in vivo*. However, only two clinical studies have addressed the effect of manufacturing method on XLPE wear. The wear of two different types of XLPE acetabular components (Durasul and Longevity) measured using RSA were reported at two years (Digas et al., 2004) and again at five years (Digas et al., 2007). While both XLPE components had low mean proximal wear rates of 0.02 mm/yr at five years, the Durasul was a cemented component and the Longevity liner was implanted within a metal backed-shell which limits the comparison. More recently Takada et al (2016) compared the wear rates of an annealed XLPE liner (Crossfire) to a remelted XLPE liner (Longevity). Both XLPE liners had a mean 2D wear rate of 0.03 mm/yr (SD ±0.02) at 7 to 10 years follow-up which is slightly higher than reported in other studies, possibly due to the use of less sensitive PolyWare measurements from plain radiographs (Takada et al., 2016). Similarly, For example, an 2D wear rate of 0.026 and 0.025 mm/yr was reported for Reflection and Longevity XLPE components respectively at 6-7 years in a study using Martells method (Whittaker et al., 2010).

4.1.3.2 Articulation Size

The first THR prostheses introduced by Charnley used an articulation with a 42.8mm femoral head that was aimed at replicating the size of the native femoral head (Charnley, 1961). This was hypothesised to retain hip stability and range of motion while avoiding component-on-component impingement. Due to problems associated with large amounts of wear and loosening of prostheses, the size of articulation used was reduced over time to 22.25mm (Charnley et al., 1975).

In vivo wear of conventional UHMWPE was increased with larger articulations. For example, 32mm articulations had an increased wear rate of 0.18 mm/yr compared to that of 22mm articulations, at 0.15 mm/yr (Kesteris et al., 1996). This increase in linear wear rate resulted in a large difference in mean volumetric wear rates, specifically 1239 mm^3/yr compared to 420 mm^3/yr for 32 and 22mm articulations respectively. (Kesteris et al., 1996). Similarly, at a minimum follow-up of nine years the mean volumetric wear rate of 32mm articulations (911 mm^3/yr) was higher than that of 28mm (521 mm^3/yr) and 22mm (513 mm^3/yr) articulations, although the linear wear rates were not statistically significantly different between head sizes, being 0.10, 0.08 and 0.13 mm/yr for the 32, 28 and 22mm articulations respectively (Livermore et al., 1990). The volumetric wear rate is usually an extrapolation of the linear wear rate measured on radiographs proportional to the spherical diameter of the articulation used. Higher volumetric wear rates are therefore expected for larger articulations with the same linear wear rate as smaller articulations. The limitations of volumetric estimations from linear wear rates are discussed further in Section 4.11.7.5.

Larger articulations provide greater range of movement, joint stability and almost complete elimination of component-to-component impingement (Burroughs, 2005). Femoral head size was found to be a risk factor for total hip dislocation in the Norwegian Arthroplasty Register, with 28mm articulations leading to revision more often than 32mm articulations (Bystrom et al., 2003). A large multicentre international randomised controlled trial has shown that a 36mm articulation is associated with a significantly lower early dislocation rate after primary THR than a 28mm articulation (Howie et al., 2012). Specifically, the incidence of dislocation at one year after primary THR was 0.8% with 36mm articulations and 4.4% with 28mm articulations. Cohort studies have also found a decreased risk of revision THR for dislocation or instability when larger articulations were used (Berry et al., 2005; Peters et al., 2007; Conroy et al., 2008; Amlie et al., 2010).

Improvement in manufacture of polyethylene liners and reduced early wear of XLPE has allowed re-consideration of larger articulations which had become less popular due to the potential for accelerated volumetric wear (Livermore 1990, Maloney 2010). The use of large-diameter articulations in primary THR has increased in an effort to reduce the risk of dislocation, the most common cause of early failure of THRs (AOANJRR, 2016). As a result, the AOANJRR reports an increasing use of large femoral head sizes in THR since 2003 and an increasing use of head sizes of 32mm or more in the last five years with XLPE liners (AOANJRR, 2013). If these large articulations are associated with increased XLPE wear, this will result in increased periprosthetic bone loss, prosthesis loosening and revision surgery.

One *in vitro* hip simulator study found that the wear rate of an unspecified XLPE liner (Howmedica Osteonics, Rutherford, NJ) was greater for 32mm articulations compared to 28mm articulations, 2.57 and 1.51 mg/million cycles respectively

(Hermida et al., 2003). A more recent *in vitro* study of a second-generation XLPE liner (X3™, Stryker) showed an increased amount of gravimetric wear when used with larger articulations (Zietz et al., 2013). A second *in vitro* study of the same XLPE liner against a 36mm articulation found that decreasing the liner thickness increased the volumetric wear rate (Johnson et al., 2014). The low amount of XLPE wear measured in these studies is difficult to quantify accurately *in vivo*.

The largest clinical study to investigate the effect of articulation size on XLPE wear was limited by its use of Hip Analysis Suite to measure wear, a method less sensitive than RSA (Bragdon et al., 2013). Furthermore, three different statistical methods were used to calculate wear rates, which resulted in contradictory findings. Specifically, this multicentre non-randomised study reported an increase in mean linear and volumetric wear rates of 36mm femoral heads compared to a combined sample of 28 and 32mm articulations with only one of three statistical methods used (linear: 0.076 vs 0.017 mm/yr respectively, volumetric: 75.5 vs 19.6 mm^3/yr). However the authors noted that the higher wear in patients with 36mm diameter femoral heads was still below the historical threshold of 0.1 mm/yr associated with osteolysis in THR involving conventional PE.

The scoping review of RSA studies of XLPE wear detailed in Chapter Three (Callary et al., 2015) identified only one RSA study that examined the effect of articulation size on wear. That small, non-randomized study found no significant difference between 36 and 28mm metal-on-XLPE articulations in median FHP at three years (0.21 vs 0.21 mm/yr) and no significant difference in the median proximal wear rate between one and three years (0.000 vs 0.026 mm/yr) (Bragdon et al., 2007).

4.1.4 Surgical Factors

4.1.4.1 Inclination Angle and Version

The position of the acetabular component is described as inclination angle (also known as abduction angle) in the coronal plane and version angle in the sagittal plane. Acetabular component positioning varies due to a number of factors including patient positioning on the operating table and surgical approach (Grammatopoulos et al., 2014). A finite element model has predicted that contact stress increases with an increased inclination angle and peak contact stresses are reduced with an increased anteversion angle (Patil et al., 2003). A study of 56 hips at five year follow-up demonstrated a 40% increase in the mean linear wear of conventional UHMWPE liners when the acetabular component was positioned with an inclination angle greater than 45 degrees (Patil et al., 2003). Similarly, a second clinical study of 139 hips at nine years follow-up found an association between increased UHMWPE wear rates in hips with an increased acetabular inclination but not the change in centre of rotation (Wan et al., 2008). Conversely, a hip simulator study of UHMWPE liners found an inverse relationship between volumetric wear rate and acetabular cup inclination angle, in that components with larger inclination angles demonstrated less wear (Korduba et al., 2014). To date, only one clinical study has investigated the influence of inclination angle on XLPE wear. A study of cemented XLPE components found no relationship between the inclination angle and FHP at two years follow-up (Kadar et al., 2012).

4.1.5 Effect of Factors on XLPE Wear as Measured by RSA

Despite the almost universal clinical acceptance of using XLPE liners, the scoping review in Chapter Three identified twelve small cohorts, constituting a total of only 261 patients, which have been examined in RSA wear studies of XLPE. These include 51 patients in two of the six cohorts examined in this thesis. The scoping review also identified that it was very difficult to interpret how implant, patient and surgical factors may influence the wear rate of XLPE due to the variation in both the methodology and manner of reporting RSA wear results. Clinical studies that have used methods other than RSA to investigate the effect of a number of different factors on the wear rate of XLPE have been limited because these methods are not sensitive enough to measure the low wear rates of XLPE (Shia et al., 2009). Hence, it would be advantageous to prospectively monitor the wear of XLPE from multiple patient cohorts, using the most sensitive method available, namely RSA, as established in Chapter Two, to investigate the effect of these factors. Importantly, the use of a consistent method of measuring the FHP, calculating the wear rate and reporting results would enable direct comparison between cohorts, which has not been able to be achieved because of the variations in the methods used in previous reports.

4.2 AIMS

The third aim of this thesis was to measure the wear rate of XLPE liners and investigate the influence of type of XLPE, articulation size, and patient age.

This was achieved by examining six patient cohorts, with the following specific aims:

- to measure the amount of bedding in and wear at two and six years follow-up of a 28mm XLPE liner manufactured with a lower range of gamma irradiation (Cohort A)
- to compare the amount of bedding-in and wear at three years follow-up of 28 and 36mm metal-on-XLPE articulations (Cohorts B and C)
- to measure the amount of bedding-in and wear at two and five years follow-up of a younger cohort of patients with a 28mm metal-on-XLPE articulation (Cohort D) and compare the results to an older cohort with the same articulation (Cohort B)
- to measure the amount of wear at two and five years follow-up of a second generation XLPE liner with a 32mm articulation (Cohort E).
- to compare the amount of wear at two and five years follow-up of 36/40mm articulations (Cohort F) and 32mm articulations (Cohort E) involving second generation XLPE liners.

Aggregate data from all six cohorts were analysed to investigate the influence of manufacturing method, articulation size and patient age on XLPE wear rates at five years follow-up.

4.3 METHODS

4.3.1 Cohort Details

Six patient cohorts were prospectively enrolled into clinical wear studies and RSA examinations were performed at regular intervals to calculate the wear rate of each hip between one and five years (Table 4.1). Each cohort differed with respect to either the type of XLPE component, articulation size used or the age of patients. The number of patients in each cohort ranged between 19 and 31. Ethics approval for each clinical study was obtained from the hospital in which patients underwent THR, namely the Royal Adelaide Hospital or Calvary Wakefield Hospital. Each patient gave written informed consent to have the required tantalum markers inserted intra-operatively and to undergo subsequent RSA radiographic examinations.

Table 4.1: Details of each cohort in clinical RSA wear studies

Cohort	XLPE Type	Head Size (mm)	Age Range (years)	Patients Recruited (n)	Publication	Section; Page	Follow-Up (years)
A	Marathon™	28	55-80	30	1 (Campbell et al., 2010a)	4.5.1; 66	2
					2 (Callary et al., 2013a)	4.5.8; 73	6
B	Longevity™	28	65-74	27	3 (Howie et al., 2016)	4.6.1; 83	2, 3 and 5*
C	Longevity™	36	65-74	29			
D	Longevity™	28	40-64	31	Unpublished at time of submission	4.7.1; 109	2*, 3* and 5*
E	X3™	32	47-76	21	4 (Campbell et al., 2010b)	4.8.1; 121	2
					5 (Callary et al., 2013b)	4.8.8; 128	5
F	X3™	36/40	55-76	19	6 (Callary et al., 2016)	4.9.1; 135	5

*wear results at this follow-up not in publication but included in thesis results

4.3.2 Methodology Inherent Across All Cohorts

4.3.2.1 Marker Beads

Six to twelve spherical tantalum markers (1.0mm diameter, RSA Biomedical™, Umeå, Sweden) were inserted into the outer rim of the XLPE liner at the time of surgery in all patients.

4.3.2.2 Patient Positioning

All RSA radiographic examinations were taken with each patient in a supine position as shown in Figure 4.1. The same RSA radiographic method was used for each examination across all cohorts. Two radiographic tubes (one room machine and one mobile machine) were angled at 40° to each other above a uniplanar calibration cage (Cage 43, RSA Biomedical™).

4.3.2.3 Software Analysis

All RSA radiographs were analysed using the UmRSA® software (version 6.0, RSA Biomedical™, Umea, Sweden) (Figure 4.2). All software analyses were undertaken by the candidate (SAC).

4.3.2.4 Condition Number and Rigid Body Error

Two quality assurance measures within the RSA software are condition number (CN) and the mean error of the rigid body fitting (MERBF). The CN is a fictive number that represents the three-dimensional spatial distribution of markers, with a lower CN representing a larger spread and more appropriate representation of the segment measured. The MERBF is commonly used to assess the stability of markers within one segment over time. The maximum CN and MERBF accepted for each reference segment were 150 and 0.35mm, respectively, as per suggested RSA guidelines (Valstar et al., 2005).

Figure 4.1: Supine RSA hip examinations were used in all cohorts with two radiographic tubes angled at 40 degrees to each other above a calibration cage.

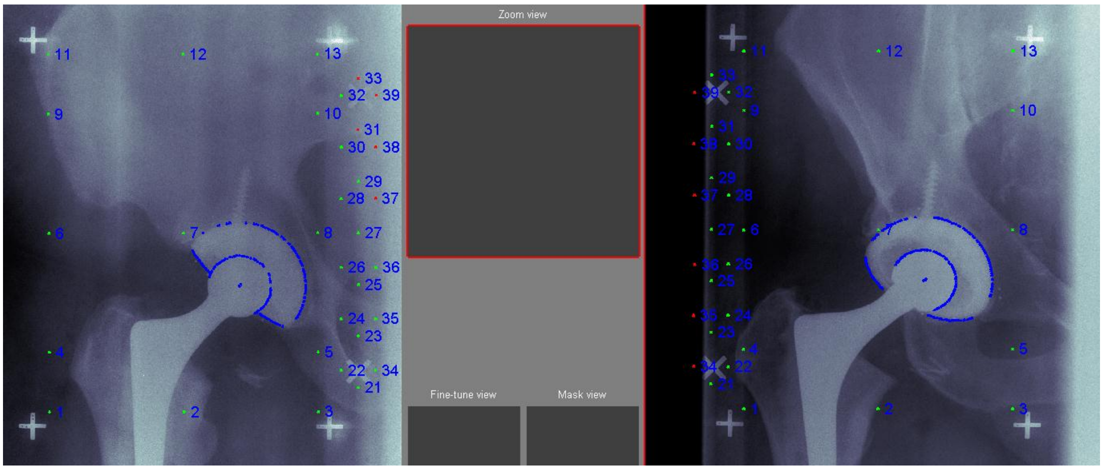

Figure 4.2: Resultant software analysis of one pair of RSA radiographs with the hip joint centred on both films.

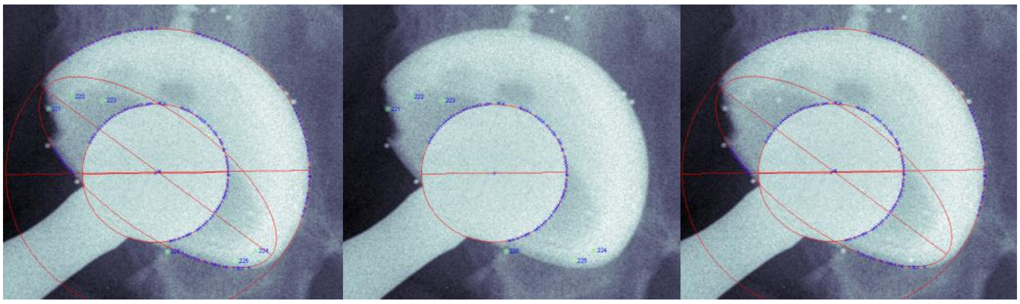

Figure 4.3: Different representation of the XLPE reference segment within the same THR A) Combined; B) Beaded; C) Unbeaded

4.3.2.5 Representation of the Acetabular Reference Segment

An edge-detecting ellipse algorithm in UmRSA software was used to outline the outer diameter and the opening of the metal backing of the cup (Borlin et al., 2006). In Cohorts A to E the ellipse algorithm was used in conjunction with between one and five liner beads visible in consecutive RSA radiographs to form a reference segment as seen in Figure 4.3A; this RSA method is referred to as “Combined” throughout this thesis. Results of Cohorts A to E were also analysed using only beads within the polyethylene liner as shown in Figure 4.3.B; this method is referred to as “Beaded” throughout this thesis. In Cohort F beads in the liner were not visible on RSA radiographs because of the large femoral heads used. Therefore only the ellipse of the acetabular component was used, as shown in Figure 4.3.C; this method is referred to as “Unbeaded”.

4.3.2.6 Femoral Head Penetration, Bedding-In and Wear

All RSA radiographic examinations measure the amount of movement of the femoral head within the acetabular component. As suggested by the scoping review in Chapter Three (Callary et al., 2015), three separate measurement parameters are calculated within RSA wear studies namely FHP, bedding-in and wear rate. Femoral head penetration refers to the total amount of movement between the initial examination (usually within the first postoperative week) and the latest follow-up. Bedding-in of the femoral head was assumed to be complete at one year and therefore the FHP recorded between the initial examination and one year follow-up is referred to as the amount of bedding-in. The wear rate for each individual is assumed to occur after one year and is calculated as the annual FHP occurring between one year examination and the latest follow-up. Patients who have multiple RSA measurements after one year have a wear rate calculated using a simple linear regression (slope) of all FHP values after one year. For example, a patient who had RSA examinations at four days and one, two, three and five years postoperatively had a wear rate calculated as the slope of the FHP measurements taken at two, three and five years.

4.3.2.7 Axes of Measurement

Medial-lateral, proximal-distal, and anterior-posterior measurements were made from translations in the x-, y-, and z-axes of the RSA calibration cage (Cage number 43; RSA Biomedical) (Figure 4.13). All raw RSA results were side adjusted to be a right hip where positive values in the x-axis represented medial FHP, positive values in the y-axis represent proximal FHP and positive values in the z-axis represent anterior FHP. To enable comparison to other *in vitro* and *in vivo* studies, two-dimensional (2D) FHP was calculated as the vectorial sum of medio-lateral (x-axis) and proximal-distal (y-axis) migrations. Three-dimensional (3D) FHP was calculated as the vectorial sum of medio-lateral, proximal-distal, and anterior-posterior (z-axis) migrations.

4.3.2.8 Precision

Two RSA examinations were undertaken on the same day fifteen minutes apart for patients in Cohorts A to D. The difference in FHP was assumed to be zero between these two examinations and the 95% confidence interval of measurements was used to represent the precision. These results are presented in the associated publications of individual cohorts.

4.3.2.9 Statistical Analysis

Details of statistical analysis of results relating to each individual cohort are presented in each publication.

4.4 RESULTS OF INDIVIDUAL COHORTS

The findings relating to individual cohorts A, B, C, E and F are presented in the form of the published manuscripts (Table 4.1). The results of Cohort D and subsequent comparison to Cohort B were not published prior to submission of this thesis.

4.5 COHORT A

The results of Cohort A at two and six years follow-up are reported in the following publications:

- Wear of a Highly Cross-Linked Polyethylene Liner: A Preliminary RSA Study. *European Journal of Orthopaedic Surgery Traumatology* 2010, 20(1): 23-27
- Wear of a 5 Megarad Cross-Linked Polyethylene Liner: A 6-year RSA Study. *Clinical Orthopaedics and Related Research* 2013, 471:2238-2244

Statement of Authorship

Title of Paper	Wear of a highly cross-linked polyethylene liner: A preliminary RSA study.
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Campbell D, Mercer G, Nilsson KG, Wells V, Field JR, Callary SA (2010). Wear of a highly cross-linked polyethylene liner: A preliminary RSA study. European Journal of Orthopaedic Surgery and Traumatology, 20(1): 23-27.

Principal Author

Name of Principal Author (Candidate)	Stuart Callary
Contribution to the Paper	Reviewed all literature, analysed all resultant RSA radiographs and collated results. Prepared all tables, assisted with initial draft and edited publication as requested during peer review process.
Overall percentage (%)	50%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.

Signature		Date	18 · 10 · 2016

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Contribution to the Paper	First author on the paper. Planned the study, prepared ethics application, performed surgeries including inserting RSA beads intraoperatively, reviewed patients in clinic and provided critical review of the manuscript.

Signature		Date	16 October 2016

Name of Co-Author	Graham Mercer
Contribution to the Paper	Planned the study performed surgeries including inserting RSA beads intraoperatively, reviewed patients in clinic and provided critical review of the manuscript.

Signature		Date	16 · 10 · 2016

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Contribution to the Paper	Assisted study design and the collection of data and provided critical review of the manuscript.		
Signature	[redacted]	Date	2016-10-23

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Contribution to the Paper	Assisted with organising patient reviews, the collection of data and provided critical review of the manuscript.		
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Contribution to the Paper	Assisted with the ethics submission, collection of data and provided critical review of the manuscript		
Signature	[redacted]	Date	Oct 16.2016

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ORIGINAL ARTICLE

Wear of a highly cross-linked polyethylene liner: a preliminary RSA study

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Abstract Wear induced peri-prosthetic osteolysis and aseptic loosening remain the major contributing factors to failure of total hip arthroplasty. To reduce wear particles from acetabular liners, the process of polyethylene cross-linking has been modified. In this study, we examine the wear of Marathon™ acetabular liners using Radiostereometric Analysis. Thirty patients were enrolled in a prospective cohort study. Femoral head penetration was calculated for 25 patients at 6 months, 1 and 2 years postoperatively. The mean proximal head penetration was 0.067 mm at 6 months, 0.113 mm at 1 year and 0.120 mm at 2 years. The mean three-dimensional femoral head penetration was 0.240 mm at 6 months, 0.230 mm at 1 year and 0.232 mm at 2 years. For both parameters, there was no measurable wear between 1 and 2 years, and the mean annual linear wear was less than 0.06 mm/year, which is less than the suggested osteolysis threshold for polyethylene. All patients demonstrated a dramatic improvement in clinical scores. These results were comparable with other studies that used alternative techniques with conventional radiography to evaluate wear for Marathon™. Long-term studies using the RSA method are recommended to further quantify the clinical performance of this polyethylene liner.

Keywords Hip · Wear · RSA · Polyethylene · Radiostereometric analysis · Cross-linked

Introduction

The proven biocompatibility and biomechanical properties of ultra high molecular weight polyethylene make it a desirable bearing surface for use in joint prostheses [1]. However, in this challenging biomechanical environment, deterioration of the polymer component still occurs, resulting in elaboration of wear particles. Wear-induced periprosthetic osteolysis, and consequently aseptic loosening remain the major contributing factors to failure of total hip arthroplasty [1–5], and are the most frequently cited indications for revision arthroplasty [2, 6–10].

For this reason, there is considerable interest in the development of new varieties of highly cross-linked polyethylene that are recognised as having a reduced propensity for wear [11, 12]. Unfortunately, the ability to translate their impressive performance seen in vitro, to correspondingly good clinical results, has proven challenging [13–15]. This highlights the need to evaluate new materials in clinical studies to confirm imputed superior wear-performance. Radiostereometric analysis (RSA) is a highly sensitive

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technique that is regarded as the gold standard of measuring prosthesis migration and wear in vivo [16].

Although the Marathon™ highly cross-linked polyethylene liner is in clinical use, there is a paucity of data available regarding its wear properties [17]. Therefore, the purpose of this study was to assess the clinical wear properties of the Marathon™ liner using RSA.

Materials and methods

Thirty patients from the orthopaedic waiting list allocated for primary total hip replacement, due to osteoarthritis, were prospectively recruited for the trial. This was based on the consultant surgeon determining that the Pinnacle™ acetabular component matched with a Marathon™ acetabular liner was an appropriate choice of implant for each patient. Ethics approval was obtained for this study from the Repatriation General Hospital Research and Ethics Committee. All patients provided informed consent for the insertion of tantalum markers during surgery and the subsequent RSA radiographs. Exclusion criteria were residence outside the metropolitan area, abnormal gross anatomy of the hip, age above 80 years and inflammatory arthritis or severe osteoporosis. At latest follow-up, one patient had died and one withdrew from the study early. Hence, 28 patients were included in the study (9 men, 19 women). The median age was 72 years (range 55–80 years). The median height was 161 cm (range 157–190 cm). The median weight was 77 kg (range 51–105 kg). The median cup size was 53 mm (range 48–62 mm). Inclination was 47.8° (range 35°–65°) and version was 19° (range 5°–34°).

All patients had a hemispherical, porous coated, metal backed shell (Pinnacle™, Depuy Orthopaedics Inc, Warsaw, Ind) implanted with a cross-linked polyethylene liner (Marathon™, Depuy Orthopaedics Inc, Warsaw, Ind). All patients received an uncemented femoral stem (Corrail™, Depuy Orthopaedics Inc, Warsaw, Ind) with a 28 mm cobalt chromium femoral head.

Six 1.0 mm tantalum markers (RSA Biomedical, Umeå, Sweden) were placed into the outer rim of the polyethylene liner at the time of surgery. Baseline RSA examinations were performed between 4 and 6 days after surgery and again at 6 months, 1 and 2 years postoperatively. Examinations were taken with each patient in a supine position. Bragdon et al. [18] and Von Schewelov et al. [19] have recently shown that weight-bearing radiographs are not required with any statistical difference between the wear measurements made from standing and supine RSA radiographs. Hence, patients in this study were examined in the supine position.

A ceiling mounted radiographic tube and a mobile radiographic tube were used simultaneously to take exposures of the hip above a calibration cage (no.43, RSA Biomedical, Umeå, Sweden). Twenty-five patients could be evaluated using RSA due to the reference postoperative radiographs not being taken for two patients and the radiographs of one patient not being adequate for analysis. Three patients did not have RSA radiographs taken at 6 months, but were included in the study. Femoral head penetration was calculated using UmRSA software (v6.0, RSA Biomedical, Umeå, Sweden). An edge-detecting ellipse algorithm in this software was used to outline the outer diameter and the opening of the metal backing of the cup [20]. The penetration of the femoral head was measured in relation to a reference segment consisting of the cup algorithms used in conjunction with the liner beads that were visible in consecutive radiographs.

Femoral head penetration into the polyethylene was calculated in three separate ways to enable comparison with other in vitro and in vivo studies. First, proximal head penetration was calculated from translations along the y-axis. Second, the amount of two-dimensional (2D) head penetration was calculated as the vectorial sum of medio-lateral (x-axis) and proximal–distal (y-axis) migrations. Third, the amount of three-dimensional (3D) head penetration was calculated as the vectorial sum of mediolateral, proximal–distal and anteroposterior (z-axis) migrations. These measurements of femoral head penetration use the immediate postoperative radiograph as a baseline and hence include the 'bedding-in' of the femoral head which occurs in the first 12 months. Hence, the penetration recorded after 1 year was identified as wear of the polyethylene liner and consequently, the proximal wear rate was calculated between 1 and 2 years.

Double radiographic examinations were taken at 1 year postoperatively for 22 patients to enable the precision of our clinical RSA measurements to be calculated and presented as the 95% confidence interval [21].

As a means of evaluating the outcomes of the surgery, Harris Hip Scores were recorded preoperatively and postoperatively at 1 and 2years.

Results

The mean proximal head penetration was 0.113 mm (range −0.012 to 0.389; SD 0.09) and 0.120 mm (range −0.100 to 0.376; SD 0.11) at 1 and 2 years, respectively (Fig. 1a). The majority of proximal head penetration occurred in the first 12 months postoperatively. Hence, the proximal wear rate calculated between 1 and 2 years was 0.007 mm/year. Measurement of 2D head penetration again demonstrated that most of the wear occurred in the first 12 months with a mean head penetration of 0.143 mm (range 0.010–0.448; SD 0.10) and 0.154 mm (range 0.015–0.415; SD 0.10) at 1

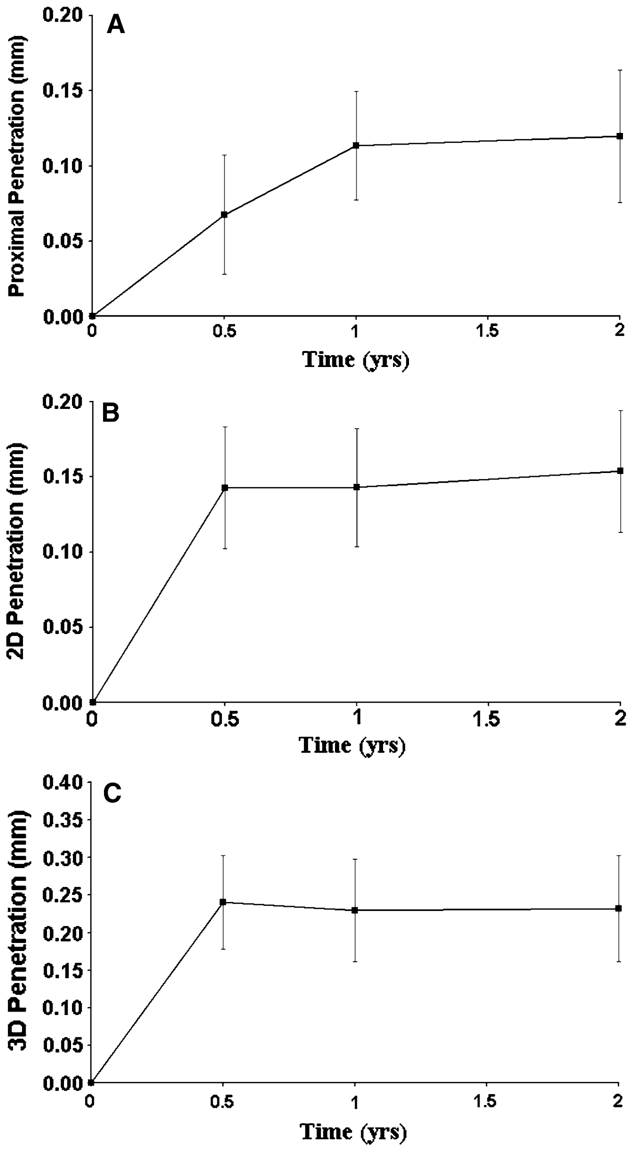

Fig. 1 The graphs show the mean proximal (**a**), 2D (**b**) and 3D (**c**) femoral head penetration over 2 years with 95% confidence intervals shown

and 2 years, respectively (Fig. 1b). The mean 3D head penetration was 0.230 mm (0.060–0.0928; SD 0.17) and 0.232 mm (0.017–0.841; SD 0.18) at 1 and 2 years, respectively.

The precision of these RSA measurements was 0.033 mm (mean 0.004, median −0.002); 0.019 mm (mean −0.010, median −0.008) and 0.072 mm (mean 0.011, median 0.032) in the *x*, *y* and *z* axes, respectively.

All patients demonstrated a dramatic improvement in clinical score using the Harris Hip Score. Preoperatively, patients had a mean total score of 35 ± 11 (median ± SD), at 1 year postoperatively the mean total score was 91 ± 13 (median ± SD) and at 2 years postoperatively, the mean total score was 92 ± 14 (median ± SD). There was a substantial improvement in functional outcome from preoperative to 1-year postoperative; however, the functional outcome remained unchanged between the first and second postoperative years.

Discussion

The aim of this study was to evaluate the results of wear of the Marathon™ highly cross-linked acetabular liner using RSA, and to compare these results with those previously published in the literature and to results seen in vitro. The RSA technique, used to measure wear in this study, is recognised as being a highly sensitive method of detecting motion of endoprostheses in vivo [22, 23]. Its high sensitivity makes it particularly useful for smaller scale studies such as the one presented here [21]. Recent improvements to the UmRSA software include edge-detecting ellipse algorithms that improve the sensitivity of the measurement method and enable previously unusable films to be analysed [20].

It is known from the literature that in vitro evaluation of polyethylene wear does not necessarily translate to the clinical performance of the same material [13–15]. For this reason, it is necessary to evaluate new highly cross-linked polyethylene liners in a clinical setting, over an appropriate period using a sensitive method.

Our study demonstrated 94% percent of the proximal head penetration measured, occurred within the first 12 months and there was negligible change in femoral head penetration between 1 and 2 years. The measurement of proximal head penetration in this study includes both the initial “bedding-in” of the liner into the metal shell and creep, along with the “true” wear (removal of polyethylene particles) of the polyethylene liner. It is accepted that the process of creep occurs early after implantation. A study by Estok et al. [24] showed that most of the creep occurs within the first 2.5 million cycles and it has been suggested that some permanent deformation of the liner can even occur in the first few postoperative weeks [1, 25–29]. To overcome the effects of creep, it has been recommended that measurements of proximal and 2D head penetration in the first 2 months of implantation be subtracted from the overall measurement of femoral head penetration to give a more accurate estimation of wear [30, 31]. However, 2 months may not be representative of the in vivo situation. The average walking activity of patients after total arthroplasty approaches 2 million cycles at 1 year [32]. Thus, according to the results of Estok et al. [24], the process of creep would take place for in excess of 12 months. Therefore, if the data from first 12 months of this study were excluded as being solely due to creep and only the second 12 months of the study contributing to “true” polyethylene wear, then the annual polyethylene wear rate would be below the detectable threshold for the RSA technique in this laboratory. This is similar to a study by Engh et al. [33] in which, a wear rate of 0.01 mm/year was measured and which was also below the published accuracy of the radiographic hip analysis software used.

The pattern of 3D femoral head penetration seen in this study, where there is a sharp increase in femoral head penetration in the first 6 months postoperatively, followed by a markedly lower magnitude of femoral head penetration in the following 18 months of the study concurs with that shown by Glyn-Jones et al. [34] in a similar study evaluating a different highly cross-linked polyethylene using the RSA technique.

If the amount of femoral head penetration were instead wholly attributed to wear, the mean annual linear wear rate, including creep, in this study would be less than 0.06 mm/year, which is again close to the published limit of accuracy and precision of the RSA technique [35, 36]. The annual linear wear rate in this study is consistent with the results of other studies evaluating the in vivo wear rate for similar, cross-linked polyethylenes [11, 13, 25, 30] in comparison with conventional polyethylene and in studies evaluating the wear of the Marathon™ acetabular liner. Bitsch et al. [17] and Hopper et al. [13] found the mean linear wear rate for Marathon™ to be in the vicinity of 0.03 mm/year and 0.08 mm/year, respectively, using measurements from plain radiographs**.** However, Heisel et al. [11], using a similar analysis technique, showed a mean linear wear rate of 0.02 mm/year. These differences highlight the value of using a highly sensitive method such as RSA when evaluating materials with a low propensity for wear, in comparison with conventional radiographic techniques.

In this study, the measurement of proximal head penetration and 2D wear yielded similar results at 1 and 2 years, indicating that most of the wear occurred proximally. The RSA measurements of wear in this study were found to be more precise than those previously reported, in particular for proximal wear (*y*-axis), 0.019 mm in our study compared to 0.098 mm [20]. This has also been shown in a similar study evaluating a different polyethylene using the RSA technique [34]. Linear measurements of wear (2D wear) may not be truly representative of the wear rate for this type of polyethylene. It has been suggested that such measurements may be less biologically important than measurement of volumetric wear and that 2D measurement of wear rate may underestimate the true wear rate [1, 28].

Taking into consideration the initial bedding-in and creep, the measured wear rate was well below the osteolysis threshold of 0.1 mm/year given by Dumbleton [1]. Other studies have shown that the incidence of osteolysis when cross-linked polyethylene liners are used is significantly less than for conventional polyethylene [12, 17, 37]. From this, it could be expected that that same would be true for the highly cross-linked polyethylene used in this study, and given the large body of existing data available in terms of proximal head penetration; we can satisfactorily compare our results to those in the literature.

A limitation of this study is that it was only performed over a 2 year period, making extrapolation to the long term clinical performance of the product difficult. However, it has been found that the average linear wear rate based on early clinical follow up is representative of the average long-term linear wear rate for a population [13]. Therefore, early clinical wear data as presented here may be useful in validating in vitro hip simulator studies. In order to quantify the exact wear rate of a new polyethylene, longer term studies may be needed as they approximate the sensitivities of the RSA method. Hypothetically, if the wear rate of the Marathon™ liner were as low as 0.01 mm/year, it would take a minimum of 5 years to reach the detectable threshold of the RSA technique.

The data from this study show that the Marathon™ acetabular liner does not exhibit measurable wear between 1 and 2 years postoperatively. The results are consistent with other studies evaluating wear of Marathon™ cross-linked liners using alternative techniques. Given that the amount of wear measured in this study falls below the detectable threshold for the RSA technique, a longer term follow-up is required to detect the presence of wear after the bedding-in process. However, the results are encouraging for the continued clinical performance of this cross-linked polyethylene liner.

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CLINICAL RESEARCH

Wear of a 5 Megarad Cross-linked Polyethylene Liner: A 6-year RSA Study

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Abstract

Background One cross-linked polyethylene (XLPE) liner is manufactured using a lower dose of radiation, 5 Mrad, which may result in less cross-linking. The reported in vivo wear rate of this XLPE liner in patients undergoing THA has varied, and has included some patients in each reported cohort who had greater than 0.1 mm/year of wear, which is an historical threshold for osteolysis. Previous studies have measured wear on plain radiographs, an approach that has limited sensitivity.

Questions/purposes We therefore measured the amount and direction of wear at 6 years using Radiostereometric analysis (RSA) in patients who had THAs that included a cross-linked polyethylene liner manufactured using 5 Mrad radiation.

Methods We prospectively reviewed wear in 30 patients who underwent primary THAs with the same design of cross-linked acetabular liner and a 28-mm articulation. Tantalum markers were inserted during surgery and all patients had RSA radiographic examinations at 1 week, 6 months, 1, 2, and 6 years postoperatively.

Results The mean proximal, two-dimensional (2-D) and three-dimensional (3-D) wear rates calculated between 1 year and 6 years were 0.014, 0.014, and 0.018 mm/per year, respectively. The direction of the head penetration recorded between 1 week and 6 years was in a proximal direction for all patients, proximolateral for 16 of 24 patients, and proximomedial for eight of 24 patients.

Conclusions The proximal, 2-D and 3-D wear of a XLPE liner produced using 5 Mrad of radiation was low but measurable by RSA after 6 years. No patients had proximal 2-D or 3-D wear rates exceeding 0.1 mm/year. Further followup is needed to evaluate the effect of XLPE wear particles on the development of long-term osteolysis.

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Each author certifies that his institution has approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
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Introduction

Conventional UHMWPE used in THA is prone to wear-particle formation [6, 8]. The presence of UHMWPE wear particles elicits an inflammatory reaction that is associated with periprosthetic bone resorption and implant failure [8, 9, 14, 15, 18, 25, 28]. The rate at which wear particles are generated, along with their size and volume are important factors in determining the likely occurrence of osteolysis [18, 23]. Dumbleton et al. in a review of the literature suggested osteolysis is infrequent with a wear rate less than 0.1 mm/year and almost absent at a rate less than 0.05 mm/year [8]. To decrease the wear rates observed with conventional UHMWPE, manufacturers now cross-link polyethylene using different amounts of radiation, then remelt or anneal the material to remove free radicals released during the irradiation process. Bragdon et al. in an in vitro hip simulator study of cross-linked polyethylene (XLPE) reported much lower wear than conventional UHMWPE [3].

Radiographic measurements are made to determine the amount of in vivo femoral head penetration in the metal-backed acetabular component with time. Penetration in the first postoperative year is assumed to be part of the creep and bedding-in phase. Penetration after 1 year is assumed to be wear of the polyethylene liner. With the small amounts of wear typically seen with XLPE liners, sensitive radiographic techniques are required to measure the in vivo wear rates. Radiostereometric analysis (RSA) offers improved accuracy and precision compared with other computer-assisted edge-detection techniques such as Devane's PolyWare (Draftware Inc, Vevay, IN, USA) and Martell's Hip Analysis Suite (University of Chicago, Chicago, IL, USA) [22]. Hui et al. [16] reported the precision for two-dimensional (2-D) wear measurements using PolyWare and the Hip Analysis Suite to be 0.414 mm and 0.242 mm, respectively. Ebramzadeh et al. showed that the PolyWare method has a tendency to overestimate the amount of wear by 0.18 mm [10]. Although RSA is an extremely precise method for wear analysis [4, 19], its use has been limited by its expense, its requirement for prospective assessment, and the expertise required for analysis [23].

In 2003 we commenced a prospective cohort study in which we used RSA to measure the wear of one type of cross-linked polyethylene liner (Marathon™, DePuy Orthopaedics Inc, Warsaw, IN, USA) that had been cross-linked with 5 Mrad (50 kGy) of gamma-radiation and annealed at greater than 150°C to eliminate free radicals. At 2 years we found the wear rate for this material was less than 0.01 mm and below the detectable level with RSA [5]. The precision (95% CI) of the RSA method for this cohort was 0.033, 0.019, and 0.072 mm for medial, proximal, and anterior wear respectively [5]. Recently, the amount of wear for the same liner has been measured in five prospective studies over five years using the computer-based methods, Polyware Auto [24], Martell's Hip Analysis Suite [1, 11, 12], and AutoCAD® (Autodesk®, San Rafael, CA, USA) [20]. These five studies reported varying mean 2-D wear rates of 0.01 [12], 0.031 [1], 0.04 [11], 0.05 [24], and a 2-D penetration rate of 0.06 mm/year [20]. Given the excellent precision of RSA, and the variability of these findings, we sought to measure the amount and direction of wear of the Marathon™ cross-linked polyethylene liner in a similar cohort at 6 years.

Patients and Methods

We prospectively enrolled 30 consecutive patients who underwent primary THA for osteoarthritis between September 2003 and July 2004. Inclusion was based on the decision of the consulting surgeon that a cementless hip arthroplasty was clinically appropriate. The components used for this study cohort (Pinnacle™ acetabular component [DePuy Orthopaedics Inc] matched with a Marathon™ [DePuy Orthopaedics Inc] cross-linked liner) were the routine implant used for cementless hip arthroplasties in our institution. Inclusion criteria for the study patients were radiographically verified primary hip osteoarthritis and between the ages of 55 to 80 years. Exclusion criteria were residing outside the metropolitan area, abnormal gross anatomy of the hip, and inflammatory arthritis or severe osteoporosis. Before the latest followup, one patient died, one withdrew from the study early, and one was unable to attend the 6-year radiographic examination owing to illness but this patient had not undergone revision surgery. Therefore, 27 of the 30 patients were included in the study (nine men and 18 women). The median age of the patients was 72 years (range, 55–80 years), median height was 161 cm (range, 157–190 cm), and median weight was 79 kg (range, 63–105 kg). Ethics approval was obtained for this study from the Repatriation General Hospital Research and Ethics Committee. All patients provided informed consent for insertion of tantalum markers during surgery and the subsequent RSA radiographs.

Two experienced surgeons (DC and GM) performed the surgical procedures using the posterolateral approach. All patients received uncemented femoral stems (Corail™, DePuy Orthopaedics Inc) with 28-mm Co-Cr femoral heads. The median cup size was 52 mm (range, 48–62 mm). Median inclination was 47° (range, 35°–65°), and the median version was 17° (range, 5°–32°). Six 1.0-mm tantalum markers (RSA Biomedical™, Umeå, Sweden) were placed into the outer rim of the polyethylene liner at the time of surgery.

All patients were allowed to bear weight as tolerated after surgery.

RSA examinations were performed at 1 week, 6 months, 1 year, 2 years, and 6 years postoperatively. Examinations were taken with each patient in a supine position. A ceiling-mounted, radiographic tube and a mobile, radiographic tube were used simultaneously to take exposures of the hip above a calibration cage (No. 43, RSA Biomedical™). The radiographic exposures were taken using 100 kV and 4 to 6 mAS. Of the 27 patients who underwent RSA examinations at 6 years, 24 could be evaluated. The reference postoperative radiographs were not taken for two patients, and the radiographs of one patient were not adequate for analysis. Femoral head penetration was calculated using UmRSA® software (v6.0, RSA Biomedical™). An edge-detecting ellipse algorithm in this software was used to outline the outer diameter and the opening of the metal backing of the cup [2]. The ellipse algorithm was used in conjunction with between one and five liner beads visible in consecutive radiographs to form a reference segment. The maximum condition number and rigid body error accepted for each reference segment were 70 and 0.3 mm respectively.

Femoral head penetration into the polyethylene was calculated in three separate ways to enable comparison to other in vitro and in vivo studies. First, proximal head penetration was calculated from translations along the y-axis. Then, the amount of 2-D femoral head penetration was calculated as the vectorial sum of mediolateral (x-axis) and proximodistal (y-axis) translations. Finally, the amount of three-dimensional (3-D) femoral head penetration was calculated as the vectorial sum of mediolateral, proximodistal, and anteroposterior (z-axis) translations. These measurements of femoral head penetration used the postoperative radiograph at 1 week as baselines, and therefore include bedding in of the femoral head, which occurs during the first 12 months. The penetration recorded after 1 year was assumed to be wear of the polyethylene liner. Therefore, for each individual the proximal, 2-D, and 3-D wear rates were calculated using simple linear regression of the head penetration at 1, 2, and 6 years. Each individual's wear rate then was averaged to calculate the mean proximal, 2-D and 3-D wear rates.

Results

The mean proximal head penetration at 6 years was 0.188 mm (range, 0.003–0.506 mm; SD, 0.121) (Table 1). The majority of proximal head penetration occurred during the first 12 months postoperatively. The mean proximal wear rate calculated between 1 and 6 years was 0.014 mm/year. The mean 2-D femoral head penetration was 0.218 mm (range, 0.032–0.520 mm; SD, 0.127). The mean 2-D wear rate between 1 and 6 years was 0.014 mm/year. The mean 3-D femoral head penetration was 0.320 mm (0.052–0.601 mm; SD 0.140). The mean 3-D wear rate between 1 and 6 years was 0.018 mm/year. The direction of the head penetration recorded between 1 week and 6 years was in a proximal direction for all patients; proximolateral for 16 of 24 patients, and proximomedial for eight of 24 patients (Fig. 1). No patient in this cohort had a proximal, 2-D, or 3-D wear rate exceeding 0.1 mm/year, which is an historical threshold for osteolysis [8], and only three of 24 patients had 3-D wear rates greater than 0.05 mm/year.

Table 1. Summary data

Variable	Medial	Proximal	Anterior	2-D	3-D
Head penetration between 1 week and 6 years (mm)					
Median	−0.040	0.177	−0.098	0.210	0.337
Mean	−0.036	0.188	−0.088	0.218	0.320
SD	0.114	0.121	0.229	0.127	0.140
Range	−0.255–0.270	0.003–0.506	−0.571–0.417	0.032–0.520	0.052–0.601
Bedding-in/creep between 1 week and 1 year (mm)					
Median	0.010	0.111	−0.081	0.151	0.163
Mean	0.026	0.113	−0.096	0.143	0.0230
SD	0.094	0.092	0.210	0.100	0.174
Range	−0.155–0.223	−0.012–0.389	−0.812–0.147	0.010–0.448	0.060–0.928
Wear rate between 1 and 6 years (mm/year)					
Median	−0.009	0.010	0.002	0.009	0.018
Mean	−0.012	0.014	0.004	0.014	0.018
SD	0.022	0.020	0.051	0.020	0.037
Range	−0.058–0.031	−0.019–0.061	−0.089–0.121	−0.025–0.063	−0.109–0.075

2-D = two-dimensional; 3-D = three-dimensional.

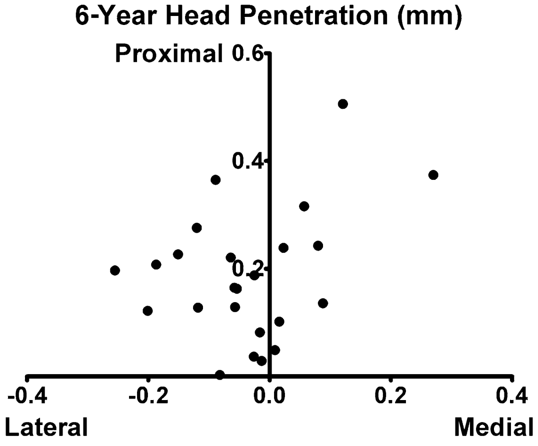

Fig. 1 This graph shows the head penetration (mm) recorded between 1 week and 6 years in the proximal and mediolateral directions for each individual.

Discussion

There are numerous different XLPE liners, each produced with various manufacturing methods which may influence their clinical performance. The reported in vivo wear rate of a XLPE liner irradiated with 5 Mrad varies from 0.01 to 0.05 mm/year. Some patients in each reported cohort had wear rates greater than 0.1 mm/year which historically is associated with osteolysis. These studies all used measurements made from plain radiographs. RSA is an accurate and precise technique to measure femoral head penetration. Therefore, in 2003 we initiated a study [5] to measure the wear of Marathon^{TM} XLPE liners with RSA. The mean rates calculated between 1 and 2 years in that study [5] suggested that the amount of wear would exceed the precision and be at a detectable level at 6 years.

We acknowledge limitations of the current study. First, we provided only descriptive data for one liner in a small consecutive cohort and did not have a control group receiving conventional UHMWPE or another type of XLPE. A control group in a similar cohort of patients would have allowed further comparisons to previous studies and investigation of other patient factors that may have influenced the reported wear rate. Second, there are various obstacles in comparing clinical wear studies, including different measurement methods and the calculations of wear rates. Other factors may influence the wear rate reported including differing implants, implant positioning, differing patient populations, and uncontrolled activity levels. Unfortunately, it is not possible to adequately analyze these data for influencing factors owing to the small sample size. Third, we did not evaluate the presence of osteolysis. Although we confirmed the low wear rate observed at 2 years, we do not know the long-term effects on osteolysis. Although the wear rate was less than the osteolysis threshold suggested by Dumbleton et al. [8], Illgen et al. [17] suggested that the benefit of a decrease in wear rate for XLPE may be offset by an increase in the inflammatory profile of these wear particles compared with those from conventional polyethylene. Leung et al. [21] reported three of 36 patients with Marathon^{TM} liners had osteolytic lesions observed on CT scans at 5 years. Therefore, long-term studies investigating the presence of osteolysis are needed to confirm the clinical benefits of reduced wear with XLPE liners.

Five recent studies [1, 11, 12, 20, 24] measured femoral head penetration of the Marathon^{TM} polyethylene liner, with at least 5 years of followup using computer-based analyses of plain radiographs (Table 2). The 2-D wear rate measured in our study, 0.014 mm/year, was at the lower end of these varying reports and with a smaller range of results. This is likely attributable to the superior accuracy and precision of the RSA method. The 2-D wear rate observed in our study was more than three times less than that reported by Mutimer et al. [24]. Possible explanations for the larger wear rate reported is that the patient cohorts may have been different, and the wear was calculated after 6 months which may have been insufficient to account for all of the creep and bedding-in. Estok et al. [13] reported the majority of creep occurs within the first 2.5 million cycles, which, based on the average walking activity of patients after THA, is likely to be reached at approximately 1 year. This is supported in our RSA study; the majority of head penetration occurred during the first year.

The proximal and 3-D head penetration between 1 week and 6 years (including creep and bedding-in) measured in our study (0.32 mm) was similar to those in other reports [7, 26, 27, 29] of XLPE liners using RSA at greater than 5 years (Table 3). The majority of the head penetration was in the proximolateral direction (Fig. 1), similar to that reported by Thomas et al. [29]. Small differences may exist in the in vivo wear rates for different XLPE liners owing to different polyethylene stock and manufacturing methods being used. Our mean 3-D wear rate of 0.018 mm/year for the Marathon^{TM} is higher than 0.005 mm/year for the Longevity^{TM} [29]. The reported 3-D wear rate of the Crossfire^{TM} liner was 0.033 mm/year at 6 years [26], but this decreased to 0.002 mm/year at 10 years followup [27]. This may be attributable to no additional head penetration, however, only nine and then eight patients were included in each report.

The proximal 2-D and 3-D wear of Marathon^{TM} XLPE liners was low but measurable by RSA after 6 years. The majority of the head penetration was in the proximolateral direction. No patients had proximal 2-D or 3-D wear rates exceeding 0.1 mm/year. Additional followup is needed to evaluate the effect of XLPE wear particles on the development of long-term osteolysis.

Table 2. Reports of in vivo wear rates of the Marathon^{TM} polyethylene liner at greater than 5 years followup

Study/year	Analysis method	Femoral head size; material	Mean followup (years) (range)	Number of patients with wear measured/initial cohort	Mean age at surgery (years) (range)	2-D head penetration (mm) mean ± SD (range)	2-D head penetration rate (mm/year) mean ± SD (range)	2-D creep/bedding-in (mm) mean ± SD (range)	2-D wear rate (mm/year) mean ± SD (range)
Engh et al. 2006 [12]	Martell's Hip Analysis Suite	28 mm; cobalt-chromium	5.5 (4.1–7.0)	86/116	62.5 (26–87)	0.24 ± 0.42 (−1.18 to 1.02)	NR	0.22 ± 0.31 (−0.54 to 0.94)	0.01 ± 0.07 (−0.18 to 0.17)
Engh et al. 2012 [11]	Martell's Hip Analysis Suite	As above	10.6 (9.0–12.5)	79/116	As above	0.60 ± 0.49 (−0.74 to 2.05)	0.06 ± 0.05	As above	0.04 ± 0.06 (−0.09 to 0.19)
Bitsch et al. 2008* [1]	Martell's Hip Analysis Suite	28 mm (n = 27); 32 mm (n = 7); cobalt-chromium (n = 31); ceramic (n = 3)	5.8 (5.0–7.7)	32/34	60 (26–83)	NR	NR	0.139 ± 0.102 (0.006–0.364)	0.031 ± 0.047 (0.004–0.196)
Mutimer et al.[†] 2010 [24]	PolyWare Auto	28 mm; cobalt-chromium	5.5 (4.1–7.0)	55/61	61 (46–75)	NR	NR	0.30	0.05 (95% CI, 0.03–0.07)
Kim et al. 2009[‡] [20]	AutoCAD	28 mm; alumina	5.6 (5–7)	100/105	45 (25–49)	NR	0.06 ± 0.03 (0 to 0.08)	NR	NR
Current study	RSA	28 mm; cobalt-chromium	5.8 (5.3–6.3)	24/30	72 (55–80)	0.218 ± 0.128 (0.032– 0.520)	0.025 ± 0.020 (−0.009 to 0.072)	0.143 ± 0.100 (0.010– 0.448)	0.014 ± 0.020 (−0.025 to 0.063)

2-D = two-dimensional; RSA = radiostereometric analysis; NR = not reported; * this study included eight revision hips, all other studies were primaries; [†]this study assumed creep to finish at 6 months and wear was calculated after 6 months, all other studies assumed creep to finish at 12 months; [‡]this study used 6 weeks as baseline examination; did not separate creep from wear.

Table 3. Reports of in vivo wear rates of the XLPE polyethylene liners using RSA at greater than 5 years followup

Study	XLPE liner	Femoral head size; material	Mean followup (years) (range)	Number of patients with wear measured/initial cohort	Mean age at surgery (years) (range)	Proximal head penetration (mm) mean ± SD (range)	Proximal wear rate (mm/year) mean ± SD (range)	3-D head penetration (mm) mean ± SD (range)	3-D wear rate (mm/year) mean ± SD (range)
Digas et al. 2007* [7]	Durasul® (Zimmer)	28 mm; cobalt-chromium	5	28/30	55 (35–70)	0.15 (−0.10 to 0.86)	0.001†	0.23 (0.02– 0.91)	NR
Digas et al. 2007* [7]	Longevity™ (Zimmer)	28 mm; cobalt-chromium	5	19/32	48 (29–70)	0.08 (−0.02 to 0.24)	NR‡	0.20 (0.10–0.60)	NR
Rohrl et al. 2007§ [26]	Crossfire™ (Stryker)	28 mm metal	6	9/10	61 (49–79)	0.08 (0.02–0.13)	0.006	0.23 (0.1–0.35)	0.033
Röhrl et al.§ 2012 [27]	As above	As above	10	8/10	As above	0.07 (−0.015 to 0.153)	0.002 (−0.003 to 0.006)	0.2 (0.026–0.36)	0.002 (−0.047 to 0.008)
Thomas et al. 2011 [29]	Longevity™ (Zimmer)	28 mm; cobalt-chromium	7 (7.0–7.8)	22/27	68 (52–76)	NR	NR	0.33 ± 0.10	0.005 ± 0.015
Current study	Marathon™ (Depuy)	28 mm; cobalt-chromium	5.8 (5.3–6.3)	24/30	72 (55–80)	0.188 ± 0.121 (0.003–0.506)	0.014 ± 0.020 (−0.089 to 0.121)	0.32 ± 0.14 (0.052–0.601)	0.018 ± 0.037 (−0.109 to 0.075)

XLPE = cross-linked polyethylene; RSA = radiostereometric analysis; 3-D = three-dimensional; NR = not reported; * results from supine examinations; †wear rate calculated between 2 years and 5 years; ‡it was stated "no further penetration was detected after 1 year"; §creep was assumed to finish at 2 months, therefore wear rate was calculated at greater than 2 months.

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4.6 COHORTS B AND C

The results of a randomised controlled trial comparing Cohorts B and C at three years follow-up are reported in the following publication:

- The Wear Rate of Highly Cross-Linked Polyethylene in Total Hip Replacement Is Not Increased by Large Articulations: A Randomised Controlled Trial. *Journal of Bone and Joint Surgery - American* 2016, Accepted for publication on 6th June 2016.

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Name of Principal Author (Candidate)	Stuart Callary
Contribution to the Paper	Reviewed all literature, analysed all RSA radiographs and collated results. Prepared all tables, wrote initial draft and edited publication as requested during peer review. Acted as corresponding author.
Overall percentage (%)	50%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.

Signature		Date	18 · 10 · 2016

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Donald Howie
Contribution to the Paper	First author on the paper. Planned the study, performed surgeries including inserting RSA beads intraoperatively, reviewed patients in clinic and provided critical review of the manuscript.

Signature		Date	19/10/16

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The wear rate of highly cross-linked polyethylene is not increased by large articulations of total hip arthroplasties: a randomized controlled trial

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ABSTRACT

Background:

Larger articulations reduce the risk of dislocation following primary total hip arthroplasty (THA), leading to increased use of these articulations. The wear rate of highly cross-linked polyethylene (XLPE) used in standard diameter articulations is low but remains unclear in larger articulations. The aim of this randomized controlled trial was to compare the mean wear rates between one and three years of 36-mm and 28-mm metal-on-XLPE articulations.

Methods:

Fifty-six middle-aged and elderly patients undergoing primary THA were randomized intra-operatively to receive either a 36-mm or 28-mm metal-on-XLPE articulation. Factors that may affect wear were controlled by study design. Wear was measured using radiostereometric analysis.

Results:

Mean annual proximal wear rates between one and three years were 0.00 and 0.01 mm/year for the 36 and 28-mm articulation cohorts, respectively. No patients had a proximal wear rate above 0.1 mm/yr. Mean wear was very low in all directions and wear rate of 36-mm articulations was not statistically significantly greater than that of 28-mm articulations in proximal, medial, 2D and 3D directions.

Conclusions:

The wear rate of a larger 36-mm metal-on-XLPE articulation between one and three years following primary THA was low and no greater than that of a 28-mm articulation. However, before a 36-mm metal-on-XLPE articulation is widely recommended, particularly in young active patients, long-term wear rates and association between wear and periprosthetic osteolysis should be determined.

Level of evidence:

Randomized controlled trial, Level I

INTRODUCTION

Tissue response to polyethylene wear particles leads to periprosthetic osteolysis[1-9] and subsequent component loosening, the most common causes of long-term failure of primary total hip arthroplasty (THA)[10]. *In vitro* and *in vivo* studies have shown significant improvement in wear resistance of highly cross-linked polyethylene (XLPE) components compared to those made from conventional polyethylene[11-14]. This reduction in wear has encouraged use of large diameter articulations in primary THA to reduce risk of dislocation[15], the most common cause of early failure of THA[10].

Acetabular liners used in large articulations are relatively thin, which may alter the wear of polyethylene. A number of studies have examined *in vivo* wear rates of XLPE in different sized articulations, but interpretation of these studies is complicated by differences in precision and accuracy of instruments used to measure wear, as well as methods of analysis[16,17].

Radiostereometric analysis (RSA) is recognized as the gold standard for *in vivo* wear measurement[18], particularly in the context of relatively low wear of XLPE[19]. A recent review of RSA studies of XLPE wear[19] identified only one small, non-randomized study that examined the effect of articulation size on wear[20]. This study found no significant difference between 36 and 28-mm metal-on-XLPE articulations in median femoral head penetration (FHP) at three years, and no significant increase in median proximal wear between one and three years. To date, there have been no published reports of randomized controlled trials (RCT) examining effect of articulation size on wear of XLPE, measured using RSA.

The aim of this study was to compare XLPE wear rates between one and three years of patients randomized intra-operatively to receive either a 36 or 28-mm articulation. Our primary hypothesis was that the mean proximal wear rate of 36-mm metal-on-XLPE articulations is no greater than that of 28-mm articulations.

MATERIALS AND METHODS

Results of this trial are reported in accordance with CONSORT (Consolidated Standards of Reporting Trials) 2010 guidelines[21]. The study was undertaken as a stratified, parallel-group RCT at the Royal Adelaide Hospital, a teaching and tertiary referral hospital. Consultants, or fellows or residents under their supervision, performed all procedures. The trial involved patients undergoing primary THA who were aged between 65 and 74 years, had a primary or secondary diagnosis of osteoarthritis and whose walking was restricted only by their hip(s). Patients were intra-operatively randomized to receive either a 36 or 28-mm articulation. Ethics approval was received from the institutional review board of the hospital. The trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000860763).

Every patient who was to undergo primary THA by one of the collaborating surgeons was screened for inclusion in the RCT. The reasons for, and numbers of, pre-operative exclusions are shown in Table 1.

Written informed consent was obtained from every eligible patient willing to participate in the trial. The first 34 patients enrolled in the trial were also part of our RCT examining the effect of articulation size on dislocation[15] and consented to participate in both trials. Prior to randomization, patients were stratified by surgeon and gender. Within each of the two strata per surgeon, allocation of randomization sequences, with an allocation ratio of 1:1, was undertaken in block sizes of two or four. The eight possible allocation sequences were listed numerically and each sequence was chosen with random-number generation in Excel, without repetition. Sealed envelopes containing either a “36” or “28” sticker were prepared in accordance with each consecutive allocation of a 36 or 28-mm articulation, over the two strata per surgeon. Each envelope was then assigned a number with use of RANUNI, an SAS software random-number function programmed to generate 64 random numbers without replacement. The study coordinator was notified of the next envelope number in the appropriate stratum, and that envelope was taken to the operating room. Envelopes allocated to patients who were excluded intra-operatively were returned unopened, to be reused when appropriate.

The study epidemiologist (OTH) was responsible for every aspect of stratification and randomization. Participating surgeons and the study co-ordinator responsible for enrolling patients were not aware of stratification and randomization protocols.

Reasons for, and numbers of, intra-operative exclusions are shown in Table 2. The randomization envelope was opened in the operating room after it had been determined the patient was to be included and after the acetabular component had been inserted and fixed with at least one screw but prior to insertion of the stem. The patient received either a 36 or 28-mm articulation, according to the number in the envelope.

All arthroplasties were undertaken using a cemented femoral stem with a 12/14 taper (CPT; Zimmer, Warsaw, IN), a cobalt-chrome femoral head and an uncemented acetabular component, which comprised a cluster three-holed acetabular shell (Trilogy; Zimmer) fixed with one or two screws and a 36 or 28-mm-inner-diameter XLPE liner (Longevity; Zimmer). Throughout the trial, all patients requiring an acetabular component with an outer diameter (OD) less than 50-mm were excluded intra-operatively prior to randomization and all patients randomized to a 28-mm articulation received a 10° elevated liner. Changes to intra-operative exclusion criteria were necessary during the trial because a number of cases of elevated liner fracture were reported in the literature[22,23]. Specifically, all patients requiring an acetabular component with an OD of 50 to 56-mm were excluded from July 2007 to July 2008. From August 2008 these patients received neutral liners if randomized to a 36-mm articulation. Patients requiring an acetabular component with an OD of 58-mm or greater were excluded from August 2008 to January 2010 because the manufacturer temporarily withdrew 36-mm 10° elevated liners.

All arthroplasties were through a posterior approach and repair of the capsule and external rotators was undertaken routinely. The operative technique for insertion of the acetabular component through a posterior approach included reliance mainly on the alignment guide and confirmation by the surgeon's judgment that the component was reasonably positioned. Patients, surgeons, and research staff were not blinded to the articulation size received.

Twelve tantalum beads (1.0mm diameter, RSA Biomedical, Umea, Sweden) were inserted into the peripheral rim of the polyethylene liner intra-operatively. RSA radiographs were taken 4 to 6 days following THA and at 3, 12, 24 and 36 months after surgery, with the patient supine. A uniplanar RSA set-up was used. Two radiographic tubes, a room-mounted unit (Philips Bucky Diagnost; Philips Healthcare, Andover, MA) and a mobile radiographic unit (Philips Practix 8000; Philips Healthcare) were positioned 1.6m above a calibration cage (Cage no.43; RSA Biomedical, Umea, Sweden) with a 40° angle between the tubes. The calibration cage contained two 35 cm × 43 cm high-resolution digital radiographic cassettes. The radiographic tubes were exposed simultaneously at 120 Kv and 16 mAs. Cassettes were digitized with an AGFA Centricity CR SP1001 processor (AGFA Healthcare, Mortsel, Belgium). Radiographs were analyzed using RSA software (UmRSA version 6.0 and UmRSA DICOM link; RSA Biomedical, Umea, Sweden) by one of the authors (SAC). Analysis of RSA radiographs utilizing both tantalum markers in the XLPE liner and outer ellipse of the metal-backed shell to represent the acetabular component achieves the best precision for measurement of wear[20,24,25]. Therefore results presented in this paper use this method. Following guidelines for reporting RSA studies[26], maximum acceptable condition number was 150 and maximum acceptable mean error of rigid body fitting was 0.3mm.

FHP was measured along x- (medial), y- (proximal) and z- (anterior) axes. Two-dimensional (2D) FHP was calculated as the vectorial sum of medial and proximal translations and three-dimensional (3D) FHP was calculated as the vectorial sum of medial, proximal and anterior translations. The process of bedding-in and creep was assumed to occur within the first 12 months following THA. Therefore total FHP from the first post-operative radiograph (4-6 days after THA) to 3 and 12 months was reported as bedding-in/creep. Further FHP after one year was assumed to be wear. Annual mean wear rates were calculated for each individual using the slope of FHP at one, two and three years in each axis. The 2D wear coordinates in the AP plane, measured by RSA between one and three years, were rotated so that the x-axis aligned with the opening of the acetabular component by correcting for the inclination angle for each individual (measured on plain radiographs). Direction of 2D wear (beta angle) was determined for each individual. Volumetric wear rate (mm^3/yr) for each individual was calculated using Martell’s method[27] which adjusts the wear rate according to wear direction and femoral head size.

Statistical analysis

Wear rates from one to three years following THA were calculated. The aim of this study was to determine whether wear of the 36-mm articulation was no worse than, that is no greater than, wear of the 28-mm articulation. Therefore a one-sided test of non-inferiority was considered the most appropriate statistical test. The rationale for selecting 0.03 as the non-inferiority margin was that (1) the annual mean proximal wear rate of 28-mm metal-on-XLPE articulations has been reported as 0.02 mm/yr[28] and (2) for 36-mm articulations, an additional wear rate of 0.03 mm/yr would result in a wear rate of 0.05 mm/yr, below which osteolysis has been found to be almost absent with conventional polyethylene[29]. Therefore wear of the 36-mm articulation was determined to be not inferior (ie not greater) than that of the 28-mm articulation if the 90% (ie 100-2α%, where α=0.05) lower confidence limit of the difference between means did not exceed the lower bound of -0.03, resulting in a p-value less than 0.05.

Because of the higher than anticipated loss of patients prior to three-year RSA, a post hoc power analysis was undertaken. With sample sizes of 19 and 24 for the 36 and 28-mm articulation cohorts, respectively, and a difference between means of 0.01 with a SD of 0.03, the study had 99% power to detect non-inferiority of the 36-mm articulation relative to the 28-mm articulation with a threshold of -0.03 and an α=0.05.

Source of funding

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RESULTS

Patients were recruited between December 2002 and July 2011. The numbers of patients who were assessed for eligibility, excluded pre-operatively or intra-operatively, randomized and included in analyses are shown in Figure 1. Patients randomized to a 36-mm articulation were similar to those randomized to a 28-mm articulation (Table 3). There were two breaches of protocol, both involving inclusion of patients who should have been excluded; one 75 year old patient should have been excluded pre-operatively because he was older than 74, and the other patient received a neutral liner instead of a 10° elevated liner at the time when elevated liners were used in all patients.

The two patients who underwent revision THA prior to three year follow-up and were thus excluded, had been randomised to a 28-mm articulation at primary THA and received a 32-mm articulation at revision. One patient underwent a two-stage revision for infection at 21 and 26 months after THA, with all components being revised. The other patient underwent head and liner exchange at 36 months because of dislocation and instability. Two other patients required re-operation but were included in the analysis: one underwent open reduction and internal fixation at 5 months for a peri-prosthetic femoral fracture, and the other required three wound debridements for infection two to six months after THA. Median scores of a modified version of the Harris Hip Score[30] were similar for each cohort pre-operatively and at each follow-up (Table 4).

To determine precision, 49 patients underwent two RSA examinations on the same day, with the patient and radiographic tubes being repositioned between each examination. Precision was calculated by multiplying the standard deviation (SD) by the appropriate critical value (t), based on a t-distribution with n-1 degrees of freedom. The precision interval (mean ± (SD x critical value)) is the range of values in which any additional observation is expected to occur. Precision of proximal measurements in our study was 0.107mm (-0.109 to 0.104), similar to the proximal precision of 0.115mm (-0.128 to 0.102) reported recently using the same shell plus liner method of calculation[24]. The 95% confidence interval of our proximal measurements was -0.018 to 0.013mm (Table 5).

Scatterplots in Figure 2 show FHP of the 36 and 28-mm articulations from the first post-operative radiograph to radiographs at three months and one, two and three years. These emphasize the low amount of proximal FHP and the data variability in both cohorts. One outlier, with a 36-mm articulation, had a higher amount of proximal penetration (0.42mm), which did not progress after 3 months. The majority of bedding-in occurred within the first three months. The mean bedding-in was similar for both cohorts at one year in any axis (Table 6).

Table 7 shows that the mean annual wear rate from one to three years in all directions was very low and that wear of 36-mm articulations was no higher than that of 28-mm articulations in the medial (p=0.02), proximal (p=0.00), 2D (p=0.01) and 3D directions (p=0.02). Mean annual wear rate in the anterior direction was statistically significantly higher (p=0.39), albeit still relatively low, for 36-mm articulations; measurements in this axis had the poorest precision. No patients in either cohort had a proximal wear rate above 0.1mm/year (Figure 3).

The median volumetric wear rate of 28-mm articulations was 7mm^3/yr (range 0 to 45mm^3/yr) and that of 36-mm articulations was 14mm^3/yr (range 0 to 69mm^3/yr). No patients exceeded a volumetric wear rate of 80mm^3/yr, the threshold that was associated with osteolysis with the use of conventional polyethylene[31].

DISCUSSION

The purpose of the present RCT was to determine whether, during the first three years following primary THA, XLPE wear rates of 36-mm articulations were no greater than those of 28-mm articulations. Our previous RCT showed that incidence of dislocation during the first year following THA was significantly lower with 36-mm than with 28-mm metal-on-XLPE articulations[15].

The current RCT demonstrates that mean wear rates from one to three years were low in all directions measured. Importantly, the proximal, medial, 2D and 3D wear rates of 36-mm articulations were no higher than that of 28-mm articulations. The mean proximal wear rates of 0.00 and 0.01 mm/yr for 36 and 28-mm articulations, respectively, are similar to those reported in other RSA wear studies of XLPE[19], including the non-randomized comparison of 36 and 28-mm articulations which reported median proximal wear rates of 0.00 and 0.03 mm/yr, respectively, at three years[20].

Distributions of individual proximal wear rates were similar in both the 36 and 28-mm articulation cohorts. Importantly, no patients in either cohort had a proximal wear rate above 0.1 mm/yr, which is the threshold associated with development of osteolysis for conventional polyethylene[29]. Given that a threshold has not yet been established for

XLPE, presentation of scatterplots of individual proximal wear rates, as in this paper, is considered appropriate to facilitate retrospective identification of wear rates in patients who may subsequently develop osteolysis[19].

The median proximal FHP of 0.03 and 0.05 mm at three years for our 36 and 28-mm articulations respectively, is similar to the median of 0.04 mm at 3 years using the same XLPE[32]. The majority of this FHP occurred within the first year and is assumed to be bedding-in of the XLPE liner. The mean proximal bedding-in within the first year of our 36 and 28-mm articulations, 0.04 mm and 0.05 mm respectively, is lower than that of some other types of XLPE, as measured by RSA and reported to be as high as 0.11 mm[19,33].

A major strength of our study is that it is the first RCT to examine the effect of articulation size on wear of XLPE. Specifically, patients were randomized to either a 36-mm or 28-mm articulation and variables that may affect wear, including age and activity, were controlled for through study design. The age range of 65-74 years chosen as the inclusion criterion for the study was supported by data from the Australian National Joint Replacement Registry, which shows that the age range of 65-74 years represents the most common 10-year age range of all patients undergoing primary THA[10]. However, it is acknowledged that the restricted age range may limit the generalizability of the study's findings. A further strength is the utilization of RSA, the most sensitive technique available to measure polyethylene wear. A limitation of our study is that 13 of the 56 patients originally randomized were not available for analysis at three years after THA and that ten of these patients had received a 36-mm articulation. However, a post hoc power analysis confirmed the adequacy of the sample sizes used in the analyses.

Primarily because of the benefits of a reduced risk of dislocation, larger articulations incorporating XLPE are now used more commonly in primary arthroplasties[10]. The present study is the first RCT to show that the early wear of larger 36-mm metal-on XLPE articulations was no greater than that of 28-mm articulations following primary THA. However, the use of such articulations is not without potential risks, given the reduction in mechanical properties through the process of cross-linking and the risk of oxidation of XLPE with ageing, which may degrade the material and decrease wear resistance[34]. Furthermore a larger articulation may be associated with increased wear at the head-taper junction. Therefore before a 36-mm metal-on-XLPE articulation is widely recommended, particularly in younger patients or those at lower risk of dislocation, longer term wear rates and the association between wear and periprosthetic osteolysis need to be determined.

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TABLE 1 Numbers of Patients Excluded Pre-operatively According to Exclusion Criteria

Exclusion criterion	No. excluded*
Too young (<65 years old)	251
Too old (≥75 years old)	156
Previous fracture, dislocation or surgery involving index hip	10
Diagnosis other than osteoarthritis	16
Charnley class C	28
Planned prosthesis not Trilogy / CPT 12/14 with 28 or 36 mm head	12
Planned approach not posterior	0
Simultaneous bilateral total hip arthroplasty	0
Contralateral hip already in trial	12
Previous infection in hip	3
Intention to return to sports involving running or contact sports	0
Abnormal acetabulum	6
Abnormal abductor mechanism	0
Likely post-operative leg length inequality of >5 cm	0
Neuromuscular disease affecting hip	3
Primary or metastatic tumor involving index hip	0
Unable to provide informed consent (insufficient ability to communicate in English language/cognitive disorder/psychiatric illness)	14
Unable to complete follow-up (life expectancy <2 years/unable to complete English-language questionnaires/unable to return easily)	22
Total	533

*Patients were excluded in a hierarchical manner, with only the first listed relevant exclusion criterion being recorded.

TABLE 2 Numbers of Patients Excluded Intra-operatively According to Exclusion Criteria

Exclusion criterion	No. of Patients Excluded*
Surgical approach not posterior	0
Infection involving joint	0
Abnormal acetabulum	5
Abnormal abductor mechanism	1
Not CPT stem	0
Acetabular component OD <50 mm	1
Acetabular component OD <58 mm (July 2007 - July 2008)	5
Acetabular component OD ≥58 mm (August 2008 – January 2010)	4
28-mm head not appropriate	2
Total	18

*Patients were excluded in a hierarchical manner, with only the first listed relevant exclusion criterion being recorded.

TABLE 3 Characteristics of Patients at Time of Primary Total Hip Arthroplasty, by Allocation to Articulation Size

	Articulation Size		**Total**
	36 mm **n=29**	**28 mm** **n=27**	**N=56**
Female (%)	48.3	51.9	50.0
Age			
mean (SD)	70.0 (2.9)	70.4 (2.8)	70.2 (2.9)
range	65 - 75	65 - 74	65 - 75
BMI			
mean (SD)	29.4 (5.5)	29.0 (5.1)	29.2 (5.3)
range	19.6 - 44.0	25.2 - 32.7	19.6 - 44.0
Inclination			
mean (SD)	43 (7.5)	42 (6.1)	42 (6.8)
range	30 - 55	27 - 54	27 - 55
Anteversion			
mean (SD)	17 (8.5)	18 (6.3)	18 (7.5)
range	4 - 35	9 - 32	4 - 35
Cup OD (%):			
50-54 mm	44.8	40.7	42.9
56 mm	10.3	25.9	17.9
58 mm	20.7	22.2	21.4
$\geq$60 mm	24.1	11.1	17.8

TABLE 4: Modified version of the Harris Hip Score, by Allocation to Articulation Size

	Articulation Size			
	36 mm		**28 mm**	
HHS	n	Median (IQR)	n	Median (IQR)
Pre-op	29	34 (30-38)	26	35 (31-39)
3 month	26	86 (75-91)	26	80 (70-89)
1 year	26	91 (75-96)	27	86 (79-94)
2 year	22	90 (76-96)	23	88 (78-95)
3 year	16	90 (73-96)	18	86 (83-96)

TABLE 5: Precision of RSA Results from Double Examinations of 49 Patients

	Direction of Femoral Head Penetration (mm)				
	Medial	**Proximal**	**Anterior**	**2D**	**3D**
median	-0.006	-0.004	-0.039	0.057	0.105
mean	-0.001	-0.002	-0.043	0.063	0.139
95% CI	-0.015 to 0.014	-0.018 to 0.013	-0.087 to 0.002	0.052 to 0.073	0.108 to 0.170
SD	0.050	0.053	0.156	0.037	0.108
2.011xSD	0.101	0.107	0.313	0.074	0.218
mean ± 2.011xSD	-0.102 to 0.100	-0.109 to 0.104	-0.356 to 0.270	-0.012 to 0.137	-0.079 to 0.357

TABLE 6: Bedding-In (mm) at Three and Twelve Months after THA, according to Allocation to Articulation Size

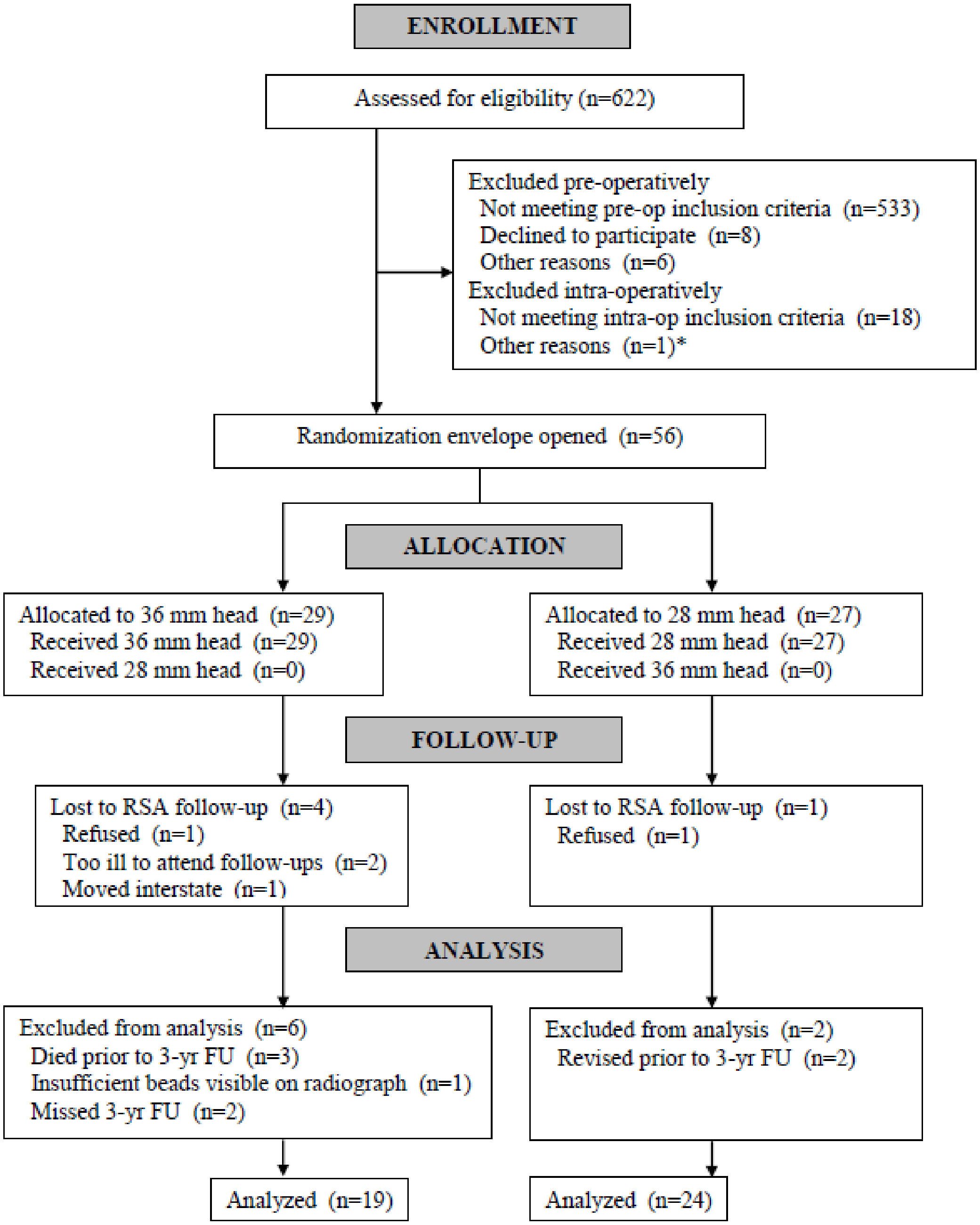
	Three months after THA				12 months after THA			
	36 mm articulation cohort (n=26)		28 mm articulation cohort (n=27)		36 mm articulation cohort (n=23)		28 mm articulation cohort (n=27)	
	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
Medial	0.01 (.09)	-0.03 to 0.04	0.00 (.07)	-0.03 to 0.03	0.02 (.13)	-0.03 to 0.07	0.03 (.13)	-0.02 to 0.09
Proximal	0.06 (.06)	0.03 to 0.08	0.06 (.07)	0.03 to 0.09	0.04 (.10)	-0.01 to 0.08	0.05 (.09)	0.01 to 0.09
Anterior	-0.03 (.13)	-0.08 to 0.02	-0.05 (.23)	-0.14 to 0.04	0.06 (.20)	-0.02 to 0.14	-0.01 (.18)	-0.09 to 0.07
2D	0.10 (.07)	0.08 to 0.13	0.10 (.05)	0.08 to 0.12	0.11 (.13)	0.05 to 0.16	0.12 (.12)	0.06 to 0.17
3D	0.16 (.10)	0.12 to 0.19	0.21 (.15)	0.15 to 0.27	0.19 (.18)	0.12 to 0.26	0.20 (.15)	0.13 to 0.26

TABLE 7: Polyethylene Wear Rate (mm/year) from One to Three Years after THA, according to Allocation to Articulation Size

	36 mm articulation cohort (n=19)		28 mm articulation cohort (n=24)		Difference bet. means	90% lower CI limit of diff	p-value
	Mean (SD)	95% CI	Mean (SD)	95% CI			
Medial	0.00 (.04)	-0.01 to 0.02	0.00 (.04)	-0.02 to 0.01	-0.01*	-0.02	0.02
Proximal	0.00 (.04)	-0.03 to 0.02	0.01 (.03)	-0.01to 0.02	0.01	-0.01	0.00
Anterior	0.02 (.08)	-0.02 to 0.06	0.00 (.12)	-0.05 to 0.05	-0.02	-0.08	0.39
2D	0.01 (.03)	0.00 to 0.03	0.01 (.04)	0.00 to 0.03	0.00	-0.02	0.01
3D	0.01 (.06)	-0.02 to 0.04	0.04 (.09)	0.00 to 0.08	0.03	-0.02	0.02

* because numbers have been rounded to 2 decimal places, difference between means appears discrepant

Figure 1: Consort Flow Diagram



*One patient was withdrawn intra-operatively: the patient suffered arrhythmia intra-operatively requiring surgery to be completed as quickly as possible. Inclusion in the trial was therefore considered inappropriate.

Figure 2: The median proximal head penetration (mm) for each individual in the 28 and 36-mm articulation cohorts. Error bars represent interquartile range.

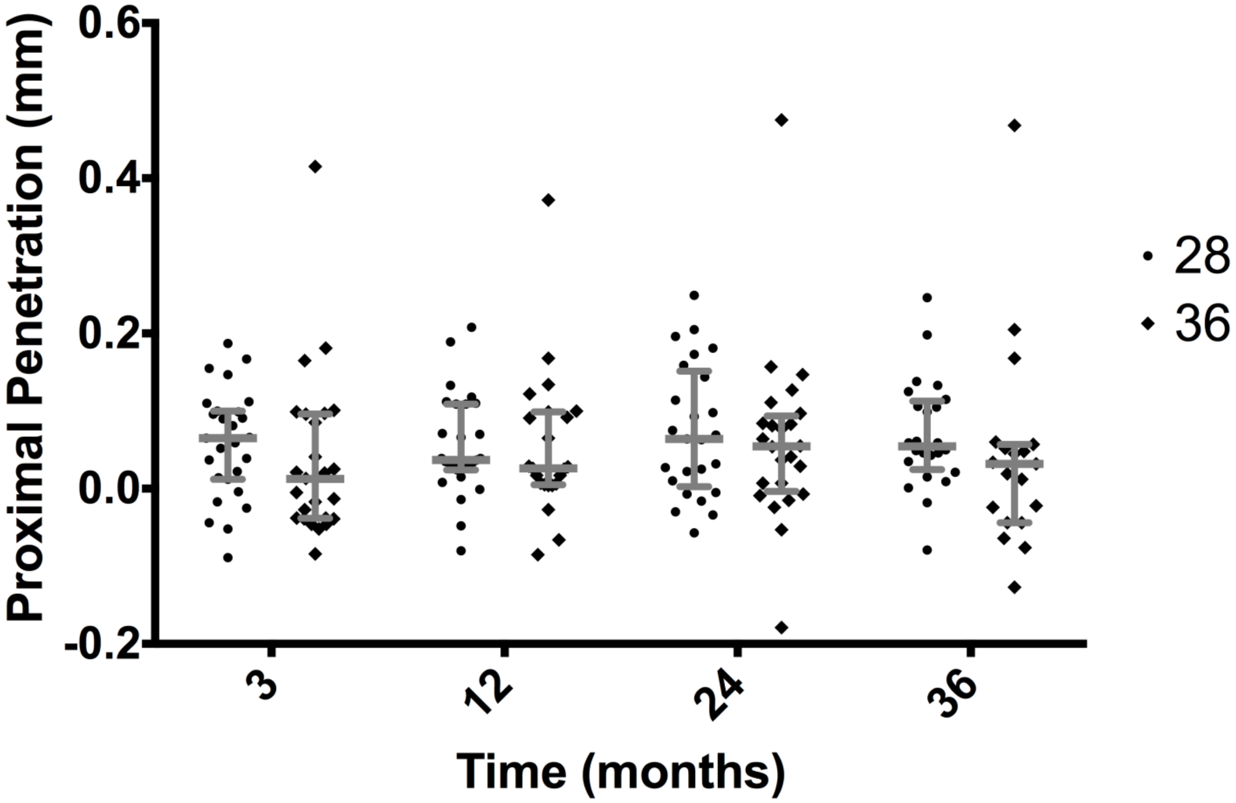
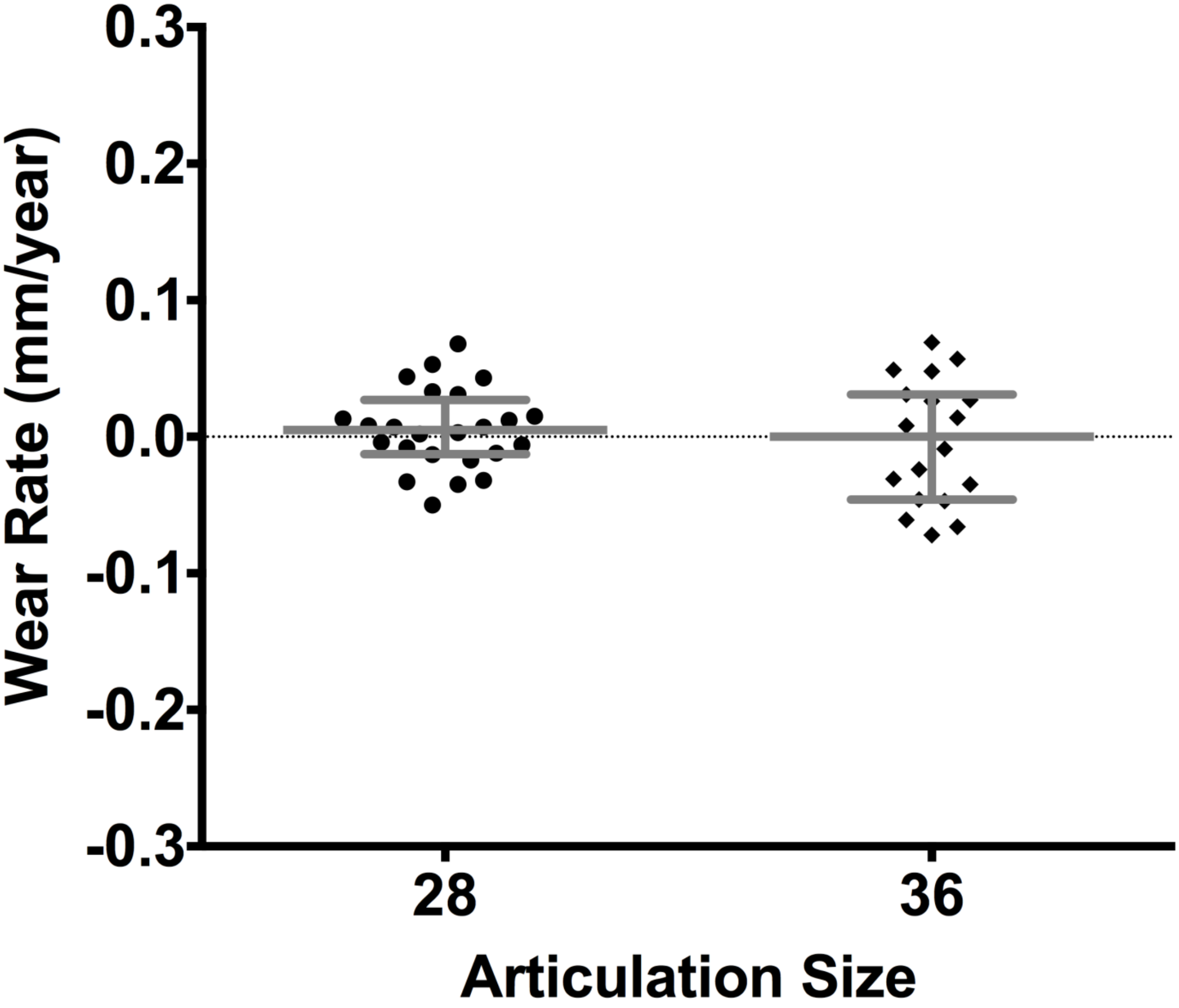


Figure 3: The median proximal wear rate (mm/year) between one and three years for each individual in the 28 and 36-mm articulation cohorts. Error bars represent interquartile range.



4.7 COHORT D

A randomised controlled trial (RCT) was undertaken at the Royal Adelaide Hospital to compare the migration of a highly porous tantalum metal acetabular component press-fit without screws to that of a titanium fibre acetabular component fixed with at least one screw. Migration was measured with RSA. One arm of this RCT received the same prostheses as those used in Cohort B (Section 4.6) but included patients ranging in age between 40 and 64 years instead of 65 to 74 years. The patients in this arm of the RCT constitute Cohort D in this thesis.

4.7.1 Aim

RSA radiographs which were originally taken to measure migration were able to be re-analysed to determine the bedding-in and wear of the XLPE liner. The aim of this section of Chapter 4 of this thesis was to report the bedding-in and wear of the younger patients comprising Cohort D. A comparison of these results with those of older but otherwise comparable patients included in Cohort B enabled an examination of the effect of age on XLPE bedding-in and wear.

4.7.2 Methods

This RCT is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000882729). Ethical approval was received from the Human Research Ethics Committee of the Royal Adelaide Hospital (#031114c). All patients who were undergoing primary THR by collaborating surgeons were screened for inclusion in the trial. Written informed consent was obtained from every patient eligible and willing to participate in the trial. At the time of primary THR, patients were all aged between 40 and 64 years. They all had a diagnosis of osteoarthritis and walking was restricted only by their hips. All arthroplasties were performed via a posterior approach by consultants, or residents or fellows under consultant supervision. The capsule and external rotators were routinely repaired. The insertion of the uncemented acetabular component relied mainly on the alignment guide and the surgeon’s judgement that it was adequately positioned.

Patients were randomised intra-operatively to receive either a cementless solid-backed porous tantalum metal-coated acetabular component (Trabecular Metal; Zimmer, Warsaw, IN) or cementless cluster-holed titanium fibre metal-coated acetabular component fixed with one screw (Trilogy; Zimmer). Cohort D in this thesis includes all patients who received a titanium fibre metal-coated acetabular component fixed with one screw as part of this RCT. It should be noted that patients who received the tantalum acetabular component were not included as part of this thesis because RSA wear measurements could not be made with the same sensitivity within this component, which is more radiopaque and occludes the majority of the femoral head and all RSA beads within the polyethylene liner.

All patients in Cohort D received the same prosthetic components as Cohort B, namely a cementless cluster-holed titanium fibre metal-coated acetabular component fixed with one screw (Trilogy; Zimmer), a cemented polished tapered femoral stem (CPT 12/14; Zimmer), a cobalt chrome alloy 28mm femoral head, and a 10° elevated XLPE liner (Longevity; Zimmer).

Nine tantalum beads (1.0mm diameter, RSABiomedical, Umea, Sweden) were inserted intra-operatively into the peripheral rim of the polyethylene liner. RSA radiographs were taken 4 to 6 days following THR and at 6 weeks and 3, 12, 24, 36 and 60 months after surgery, with the patient supine. The same uniplanar RSA radiographic set-up was used as described for Cohorts B and C (Section 4.6.4).

All RSA radiographs were analysed using the UmRSA® software (version 6.0, RSA Biomedical™, Umea, Sweden) (Figure 4.2). All RSA software analyses were undertaken by the candidate (SAC). Combined representation of the acetabular component (Section 4.3.2.5) was used to calculate FHP, bedding-in and the wear rates at two, three and five years follow-up (Section 4.3.2.6).

A one-sided test of non-inferiority was considered the most appropriate statistical test to determine if the wear rate of the same XLPE liner in younger patients (Cohort D) was no greater than the rate in older patients (Cohort B). The mean proximal wear rate between one and two years for Cohort B was 0.02 mm/yr (Howie et al., 2016). Hence, a non-inferiority margin of 0.03 mm was chosen because an additional wear rate of 0.03 mm/yr would result in a clinically relevant wear rate of 0.05 mm/yr, below which osteolysis is very rarely seen (Dumbleton et al., 2002). If the lower limit of the 90% confidence interval of the mean difference of wear between cohorts exceeded -0.03 (for example was -0.02), non-inferiority was supported ($p<0.05$) and the mean wear rate of the younger Cohort D was deemed not be significantly greater than that of the older Cohort B.

A post hoc power analysis was performed for available wear results at two, three and five years. At three years assuming a mean difference of 0.001 with a SD of 0.035 and current cohort sizes (18 and 24), there was 94% power to detect non-inferiority of the young relative to the old cohort with a threshold of 0.03 and an $\alpha=0.05$. At five years assuming a mean difference of 0.005 with a SD of 0.023 and current cohort sizes (11 and 21) there was 99.7% power to detect non-inferiority of the old young relative to the old with a threshold of 0.03 and an $\alpha=0.05$. At two years the study was underpowered (72%) and would have required six more patients in each cohort to achieve 80% power.

4.7.3 Results

66 patients were recruited into the RCT between March 2007 and October 2013. The characteristics of the 31 patients randomised to receive the titanium fibre metal-coated acetabular component at the time of surgery, namely Cohort D, are compared to those of patients in Cohort B in Table 4.12. The patients' ages and BMIs were similar across Cohorts D and B.

At the time of submission of this thesis 24 of the 31 patients were at least two years post THR. Of these 24 patients, one withdrew from the trial before six weeks follow-up, one had poor RSA radiographs, one had a femoral peri-prosthetic fracture prior to two year follow-up, one did not attend the one and two year follow-up and two did not attend their two year follow-up and were therefore excluded, resulting in 18 hips being included in the analyses of wear between one and two years.

At the same time 22 of the 31 patients were at least three years post THR. Of these patients one had withdrawn, one had poor radiographs, one did not attend the one and two year follow-up and one patient did not attend their three year follow-up. This resulted in 18 hips being included in the analyses of wear between one and three years.

At the time of submission 16 of the 31 patients were at least five years post THR. Of these patients one had withdrawn, one had poor radiographs and three patients did not attend their five year follow-up, resulting in 11 hips being included in the analyses of wear between one and five years. The patient who did not attend the one and two year follow-up had three and five year RSA examinations and was therefore included.

There was a trend for younger patients, namely Cohort D, to have a higher median proximal bedding-in within the first postoperative year (0.072mm) compared to older patients, namely Cohort B (0.037mm) (Table 4.13, Figure 4.9). However the proximal FHP at five years of Cohort D was not significantly higher than that of Cohort B ($p = 0.04$) (Table 4.13). The median proximal wear rate of Cohort D recorded at three and five years (0.001 and 0.004 mm/yr) was less than that at two years (0.017 mm/yr) and had less variability (Table 4.13, Figures 4.10, 4.11, 4.12). The mean proximal, 2D and 3D wear rates of the younger Cohort D were not significantly greater than those of the older Cohort B between one and three years ($p=0.004$, $p=0.0002$ and $p=0.002$ respectively) (Table 4.13, Figure 4.11). Similarly, the mean proximal, 2D and 3D wear rates of Cohort D were not significantly greater than those of Cohort B between one and five years ($p=0.0002$, $p<0.0001$ and $p=0.001$ for each axis respectively) (Table 4.13, Figure 4.12).

Table 4.12: Patient and implant characteristics at time of primary total hip replacement by cohort

	COHORT	
	B **n=27**	**D** **n=31**
Female (%)	52	58
Age (years)		
mean (SD)	70 (2.8)	54 (6.2)
median	71	56
range	65 - 74	43 - 64
BMI (kg/m^2)		
mean (SD)	29.0 (5.1)	32.3 (7.1)
median	28.0	30.6
range	21.3 - 39.1	20.2 - 48.9
Inclination (degrees)		
mean (SD)	42 (6.1)	41 (5.6)
median	41	45
range	27 - 54	34 - 53
Cup OD Interval (%):		
50-54mm	40.7	48.4
56mm	25.9	19.4
58mm	22.2	12.9
≥60mm	11.1	19.4

Table 4.13: Femoral head penetration, bedding-in and wear rate results by cohort and years since THR

		Proximal (+ve) Distal (-ve)	**Two-dimensional**	**Three-dimensional**
Femoral Head Penetration between 1 week and 5 years (mm)				
COHORT B	Median	0.050	0.100	0.185
	Mean	0.078	0.126	0.209
	SD	0.094	0.077	0.131
	Range	-0.084 to 0.329	0.040 to 0.333	0.058 to 0.558
COHORT D	Median	0.058	0.102	0.170
	Mean	0.053	0.116	0.205
	SD	0.058	0.063	0.128
	Range	-0.085 to 0.132	0.058 to 0.282	0.087 to 0.476
Difference between means		0.025	0.010	0.005
Lower limit of 90% CI*		-0.028	-0.036	-0.077
Non inferiority supported		yes	no	no
p-value		0.04	0.07	0.24
Bedding-in/creep between 1 week and 1 year (mm)				
COHORT B	Median	0.037	0.100	0.120
	Mean	0.056	0.105	0.156
	SD	0.065	0.068	0.097
	Range	-0.080 to 0.208	0.020 to 0.267	0.047 to 0.399
COHORT D	Median	0.072	0.110	0.177
	Mean	0.063	0.115	0.179
	SD	0.080	0.064	0.075
	Range	-0.126 to 0.200	0.015 to 0.283	0.076 to 0.386
Difference between means		-0.007	-0.009	-0.024
Lower limit of 90% CI*		-0.043	-0.042	-0.067
Non inferiority supported		no	no	no
p-value		0.044	0.15	0.40
Wear rate between 1 and 2 years (mm/year)				
COHORT B	Median	0.011	0.003	-0.008
	Mean	0.016	0.005	0.015
	SD	0.066	0.061	0.087
	Range	-0.143 to 0.167	-0.153 to 0.135	-0.149 to 0.187
COHORT D	Median	0.017	0.002	0.015
	Mean	0.025	0.005	0.028
	SD	0.068	0.054	0.108
	Range	-0.100 to 0.218	-0.096 to 0.101	-0.129 to 0.282
Difference between means		-0.009	0.000	-0.013
Lower limit of 90% CI*		-0.044	-0.030	-0.064
Non inferiority supported		no	no	no
p-value		0.16	0.05	0.29

Table 4.13: (continued)

		Proximal (+ve) Distal (-ve)	Two-dimensional	Three-dimensional
Wear rate between 1 year to 3 years (mm/year)				
COHORT B	Median	0.005	0.008	0.013
	Mean	0.005	0.010	0.039
	SD	0.029	0.035	0.092
	Range	-0.050 to 0.068	-0.064 to 0.067	-0.105 to 0.362
COHORT D	Median	0.001	0.001	-0.012
	Mean	0.005	0.003	-0.006
	SD	0.042	0.024	0.052
	Range	-0.080 to 0.112	-0.046 to 0.043	-0.108 to 0.096
Difference between means		0.001	0.008	0.045
Lower limit of 90% CI*		-0.018	-0.008	0.004
Non inferiority supported		yes	yes	yes
p-value		0.004	0.0002	0.002
Wear rate between 1 year to 5 years (mm/year)				
COHORT B	Median	0.003	0.003	0.005
	Mean	0.003	0.008	0.018
	SD	0.022	0.020	0.038
	Range	-0.045 to 0.048	-0.024 to 0.049	-0.048 to 0.105
COHORT D	Median	0.004	0.001	0.002
	Mean	-0.001	-0.001	0.008
	SD	0.025	0.012	0.020
	Range	-0.049 to 0.034	-0.023 to 0.017	-0.014 to 0.048
Difference between means		0.005	0.009	0.010
Lower limit of 90% CI*		-0.010	-0.002	-0.011
Non inferiority supported		yes	yes	yes
p-value		0.0002	<0.0001	0.001

*Lower limit of 90% confidence interval of mean difference

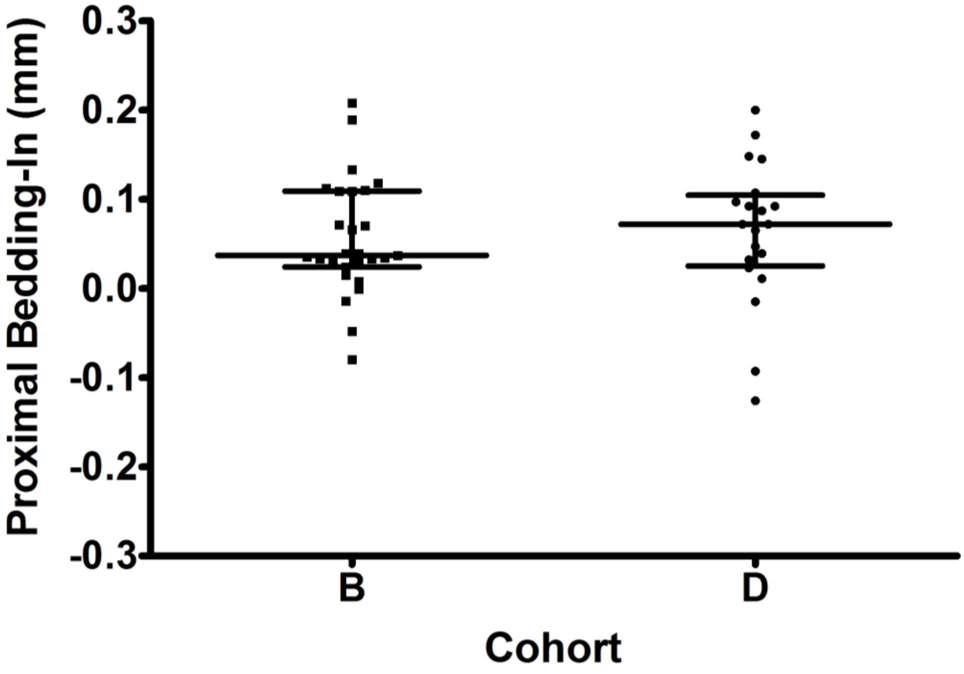


Figure 4.9: Proximal bedding-in within the first year (median and interquartile range) by cohort

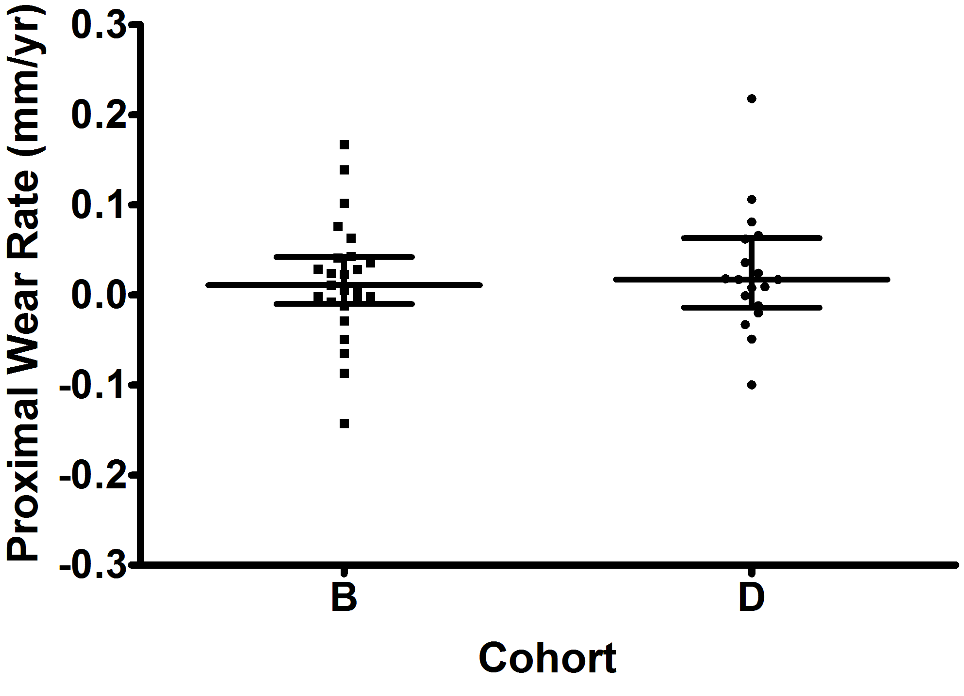


Figure 4.10: Proximal wear rate between one and two years (median and interquartile range) by cohort

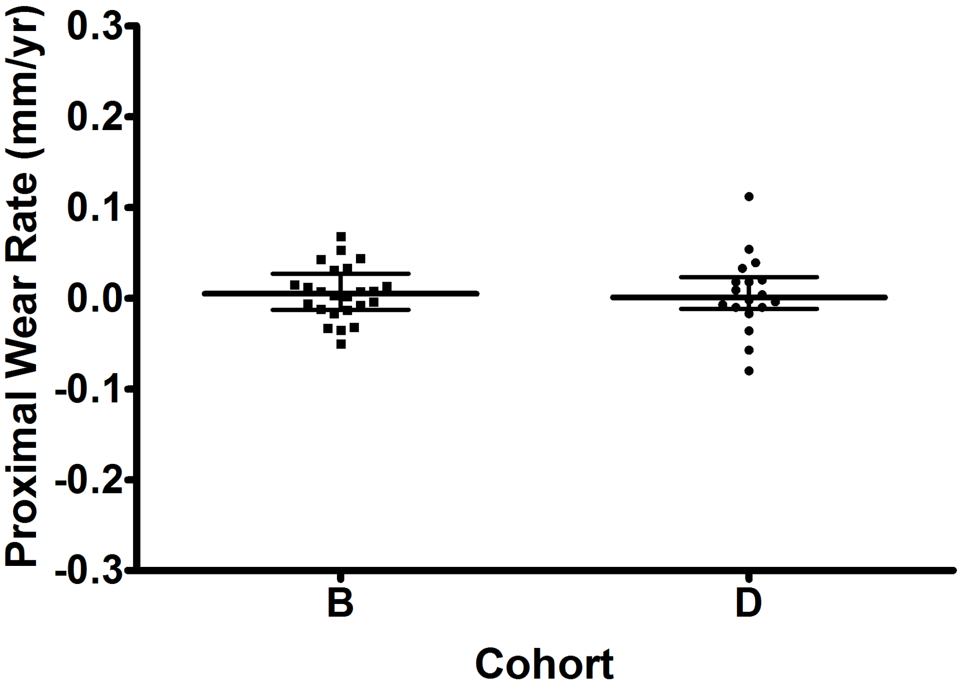


Figure 4.11: Proximal wear rate between one and three years (median and interquartile range) by cohort

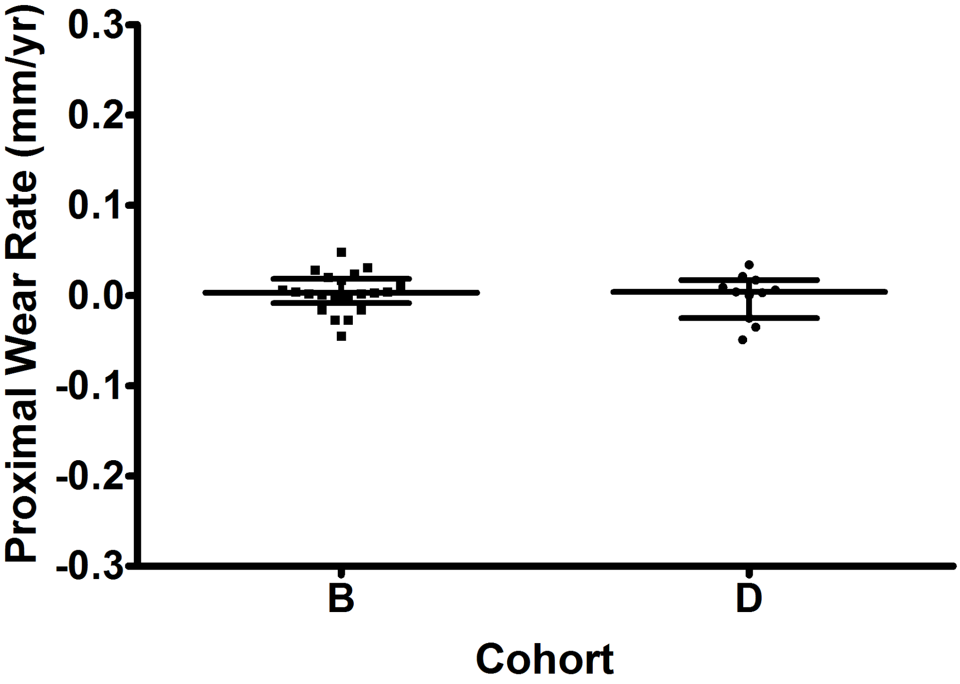


Figure 4.12: Proximal wear rate between one and five years (median and interquartile range) by cohort

4.7.4 Discussion

While there has been minimal change over time in the proportion of patients aged younger than 55 years relative to all primary THRs undertaken in Australia (11.7% in 2003 to 13.1% in 2015), the actual number of these younger patients are increasing given the increase in total numbers of THR undertaken (17,073 in 2003 to 33,502 in 2015) (AOANJRR, 2016). This translates to approximately 2400 more patients under the age of 55 undergoing THR in 2015 than in 2003 (AOANJRR, 2016). With the low wear rates reported for XLPE, surgeons may be more likely to perform THR in the younger patient who may be more active, have higher demands of the THR and a longer life expectancy. Comparison of XLPE wear rates between cohorts of different ages would be of interest to the orthopaedic community. No clinical study has previously compared the wear rate of XLPE liners between younger and older patients using RSA.

As identified in the scoping review in Chapter Three of this thesis, RSA wear studies of XLPE often include patients of various ages (Callary et al., 2015). For example, one RSA study included patients with an age range of 29 to 70 years (Digas et al., 2004) and another 36 to 77 years (Bragdon et al., 2007). One RSA study of younger patients (mean age at time of THR was 58 years, SD 8) with the same XLPE liner reported a mean proximal wear rate between one and two years of 0.02 mm/year (Ayers et al., 2009) and a mean proximal wear rate of 0.004 mm/yr at five years (Ayers et al., 2015). This is very similar to the mean proximal wear rates of 0.025 and -0.001 mm/yr at two and five years respectively of the younger patients in the current study, even though patients in Cohort D were slightly younger at the time of THR (mean 54 years, SD 6).

One limitation of the current study was the small number of patients in Cohort D included in the five year analysis. This was because, at the time of thesis submission, almost half of the patients originally enrolled in the RCT had not yet reached the time point of five years since THR. However, a posthoc power analysis revealed the study had 99.7% power to detect non-inferiority of the younger patients relative to the older patients. This is due to the very small range of wear results reported at five years follow-up. In contrast, all patients enrolled in the RCT had completed two year follow-up at the time of thesis submission and the study did not achieve sufficient power for two year wear results due to the larger variation in wear rates in both cohorts. There is a tendency for the not to increase over time in XLPE liners and hence the mean and range of wear rates decreases over time (Callary et al., 2015). A second limitation is the age range of patients included in the study. It would have been of interest to include younger THR patients but this was not possible because it was deemed important to maintain consistency in preoperative diagnosis to compare results to Cohort B. Younger patients (less than 40 years of age) are unlikely to be osteoarthritic and more likely to undergo THR for other diagnoses. The age of patients in the control Cohort B was supported by data from the AOANJRR, which shows that the most common 10-year age range of primary THR patients is 65 to 74 years (mean 67.7 years) (AOANJRR, 2016). A third limitation of this study is that patient activity was not monitored. While younger patients are thought to be more active this may not always be the case. Increased activity for example, may have been responsible for the trend of Cohort D having an increased median proximal bedding-in within the first year compared Cohort B. However we are unable to determine if the younger patients were actually more active within the first year.

4.7.5 Conclusion

The very low proximal, 2D and 3D wear rates reported for younger patients in Cohort D were not significantly greater than those of older patients in Cohort B at three and five years follow-up. There was a trend for median proximal bedding-in within the first year to be higher in younger patients compared to an older cohort. However, there was no difference in the proximal FHP at five years between Cohorts D and B. FHP measurements at longer term follow-up are required to determine wear rates and the prevalence of peri-prosthetic osteolysis in the mid- to long-term, before the use of XLPE in THRs undertaken in younger patients should be widely encouraged, given their higher activity and longer life expectancy.

4.8 COHORT E

The results of Cohort E were published at two and five year's follow-up in the following publications:

- Second-generation Highly Cross-Linked X3™ Polyethylene Wear: A Preliminary Radiostereometric Analysis Study. *Clinical Orthopaedics and Related Research* 2010, 468:2704-2709
- Low Wear of a Second-Generation Highly Crosslinked Polyethylene Liner: A 5 Year Radiostereometric Analysis Study. *Clinical Orthopaedics and Related Research* 2013, 471:3596-3600

Statement of Authorship

Title of Paper	Second-generation Highly Cross-Linked X3™ Polyethylene Wear: A Preliminary Radiostereometric Analysis Study
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Campbell DG, Field JR, Callary SA (2010). Second-generation highly cross-linked X3 polyethylene wear: a preliminary radiostereometric analysis study. Clinical Orthopaedics and Related Research. 468(10): 2704-2709.

Principal Author

Name of Principal Author (Candidate)	Stuart Callary		
Contribution to the Paper	Reviewed all literature, analysed all resultant RSA radiographs and collated results. Prepared all tables, wrote initial draft and edited publication as requested during peer review.		
Overall percentage (%)	65%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper		
Signature		Date	18 · 10 · 2016

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	David Campbell		
Contribution to the Paper	First author on the paper. Planned the study, prepared ethics application, performed surgeries including inserting RSA beads intraoperatively, reviewed patients in clinic and provided critical review of the manuscript.		
Signature		Date	16 October 2016

Name of Co-Author	John Field		
Contribution to the Paper	Assisted with the collection of data and provided critical review of the manuscript.		
Signature		Date	Oct 16 · 2016

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BASIC RESEARCH

Second-generation Highly Cross-linked X3^{TM} Polyethylene Wear

A Preliminary Radiostereometric Analysis Study

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Abstract
Background First-generation highly cross-linked polyethylene liners have reduced the incidence of wear particle-induced osteolysis. However, failed acetabular liners have shown evidence of surface cracking, mechanical failure, and oxidative damage. This has led to the development of second-generation highly cross-linked polyethylene, which has improved wear and mechanical properties and resistance to oxidation in vitro. Owing to its recent introduction, there are no publications describing its clinical performance.
Questions/purposes We assessed early clinical wear of a second-generation highly cross-linked polyethylene liner and compared its clinical performance with the published results of hip simulator tests and with first-generation highly cross-linked polyethylene annealed liners.
Patients and Methods Twenty-one patients were enrolled in a prospective cohort study. Clinical outcome and femoral head penetration were measured for 19 patients at 6 months and 1 and 2 years postoperatively.
Results The median proximal head penetration was 0.009 mm and 0.024 mm at 1 and 2 years, respectively. The median two-dimensional (2-D) head penetration was 0.083 mm and 0.060 mm at 1 and 2 years, respectively. The median proximal wear rate between 1 and 2 years was 0.015 mm/year.
Conclusions The wear rate calculated was similar to the in vitro wear rate reported for this material; however, it was less than the detection threshold for this technique. Although longer followup is required for wear to reach a clinically quantifiable level, this low level of wear is encouraging for the future clinical performance of this material.
Level of Evidence Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Component loosening is the most common reason for early to midterm revision of hip prostheses [2, 27]. A major contributor to the loosening observed at revision arthroplasty is osteolysis related to wear of UHMWPE [10, 17, 18, 23, 26, 40, 45, 46]. To overcome the problems of wear associated with conventional UHMWPE, highly cross-linked polyethylene (HXLPE) was introduced [11]. The first-generation HXLPEs in clinical use have exhibited markedly less wear than conventional UHMWPE [12, 14, 28, 30, 31]; however, there have been some reports of surface cracking, mechanical failure, and oxidative damage in failed acetabular liners [5, 22, 25].

The reduced mechanical properties of first-generation HXLPE can be attributed to the process of cross-link

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This work was performed at Wakefield Orthopaedic Clinic.

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formation, which is achieved by irradiation and heating of the polyethylene [16, 37]. Materials that are heated above their melting temperature (remelted) have reduced fatigue strength [41, 42] owing to alteration of the material's crystalline structure [38]. Heating to just below the melting point (annealing) maintains the mechanical properties of the material; however, the ability to eliminate free radicals using this technique is reduced as a consequence of their limited mobility in the polymer, which increases the propensity for late oxidative damage to the material [42, 43]. To improve the efficiency of free radical elimination, a new process of sequential irradiation and annealing has been introduced in a new second-generation material X3^{TM} (Stryker Orthopaedics, Mahwah, NJ). A hip simulator study has shown, in addition to excellent mechanical properties, acetabular liners made from this material have superior wear properties in comparison to conventional UHMWPE and clinically successful first-generation HXLPE [16].

Unfortunately, the ability to translate positive findings from hip simulator studies to equally good results clinically has proven challenging [29, 32, 39]. This highlights the importance of confirming the safety and wear performance of new materials in clinical studies using a sensitive evaluation technique. There is currently no published data describing the clinical performance of the second-generation highly cross-linked polyethylene X3^{TM} acetabular liner. Therefore, we assessed the early clinical wear properties of the X3^{TM} liner using radiostereometric analysis (RSA) to compare its clinical performance with the results of hip simulator tests and with those of first-generation annealed acetabular liners. We hypothesize the X3^{TM} liner will have a clinical wear rate similar to that reported from hip simulator tests and less than that reported for first-generation annealed acetabular liners.

Patients and Methods

We recruited a prospective consecutive series of 21 patients with osteoarthritis of their hip for the trial. Inclusion criteria were the consultant surgeon selecting cementless components with the Trident® acetabular system (Stryker Orthopaedics) matched with an X3^{TM} acetabular liner (Stryker Orthopaedics) as the preferred choice of implant and surgery scheduled at the Calvary Wakefield Hospital, which is equipped for RSA. Ethics approval was obtained for this study from the Wakefield Hospital ethics committee. All patients provided informed consent for the insertion of tantalum markers during surgery and the subsequent RSA radiographs. Exclusion criteria were residence outside the metropolitan area, abnormal gross anatomy of the hip, age older than 80 years, and inflammatory arthritis or severe osteoporosis. Two patients were excluded from the study owing to incomplete RSA evaluation at 12 months. Therefore, 19 patients were included in the study (10 men, nine women). Their median age was 63 years (range, 47–76 years); median male weight was 84 kg (range, 72–100 kg) and median female weight was 71 kg (range, 60–78 kg). Sixteen patients were Charnley grade A and three were Charnley grade B. The mean cup size was 54.6 mm (range, 48–62 mm). The mean inclination was 45.6° (range, 39°–58°).

All patients had a hemispheric, porous-coated, metal-backed shell (Trident® acetabular system) implanted with a HXLPE liner (X3^{TM}). The cross-link formation process of the liner involved three cycles of sequential irradiation and annealing. Each cycle consisted of gamma irradiation at a dose of 3 Mrad followed by annealing at 130°C for 8 hours [16]. The total cumulative radiation dose was 9 Mrad. Terminal sterilization was achieved through a gas plasma process. All patients received a cementless femoral stem (Accolade®; Stryker Orthopaedics) with a 32-mm cobalt-chromium femoral head.

Six tantalum markers (1.0-mm diameter; RSA Biomedical, Umeå, Sweden) were placed in the outer rim of the polyethylene liner at the time of surgery. Baseline RSA examinations were performed within 7 days of surgery and again at 6 months and 1 and 2 years postoperatively. Examinations were taken with each patient in a supine position. Bragdon et al. [8] and von Schewelov et al. [50] reported no statistical difference between the wear measurements made from standing and supine RSA radiographs; therefore, patients in our study were examined in the supine position.

A ceiling-mounted radiographic tube and a mobile radiographic tube were used simultaneously to take exposures of the hip with a calibration cage (Number 43; RSA Biomedical). Wear was measured by penetration of the femoral head inside the polyethylene liner with UmRSA® software (v6.0; RSA Biomedical). The program identifies the center of the outer ellipse of the femoral head and acetabular cup with an edge detection algorithm used in conjunction with tantalum markers placed in the outer rim of the polyethylene liner. This combined measurement technique using edge detection in conjunction with marker beads was proven to have the highest precision clinically in a study by Borlin et al. [4] with a conservative detectable limit for measuring wear of 80 μm.

Femoral head penetration into the polyethylene was calculated in three separate ways to enable comparison to other in vitro and in vivo studies. First, proximal head penetration was calculated from translations along the y axis (Fig. 1). Second, the amount of 2-D head penetration was calculated as the vectorial sum of medial-lateral (x axis) and proximal-distal (y axis) migrations. Third, the

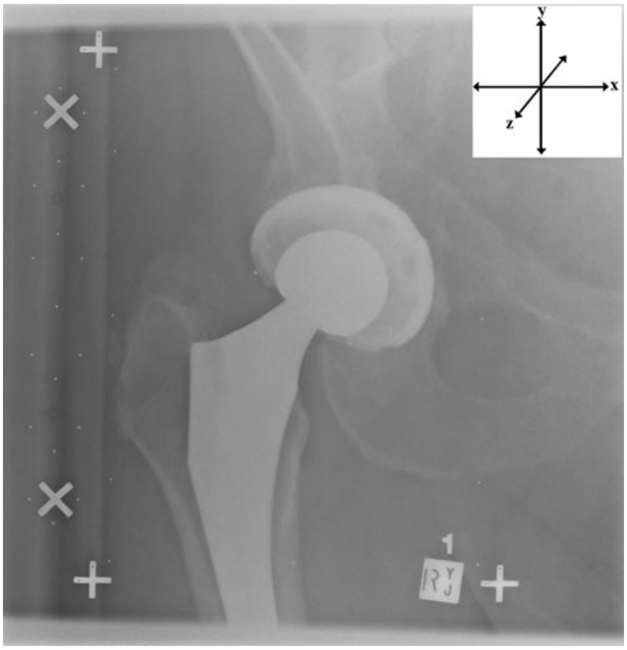

Fig. 1 A postoperative RSA radiograph of a right hip is shown, with an inset illustrating the three axes used to measure head penetration. Positive x-axis translations represent medial head penetration; positive y-axis translations represent proximal head penetration; and positive z-axis translations represent anterior head penetration.

amount of 3-D head penetration was calculated as the vectorial sum of medial-lateral, proximal-distal, and anterior-posterior (z axis) migrations. These measurements of femoral head penetration used the immediate postoperative radiograph as a baseline and therefore included "bedding-in" of the femoral head. The penetration recorded after 1 year was identified as true wear of the polyethylene liner, and consequently, the proximal wear rate was calculated between 1 and 2 years. Median wear rate was calculated as the difference in head penetration between 1 and 2 years for each individual.

To document that this series of patients achieved a typical outcome with usual physical activity after TKA, clinical outcome was measured using Oxford Hip and SF-12 scores recorded preoperatively and postoperatively.

Sample size was based on a power calculation made using the Altman normogram [1, 52]. Previous RSA studies [22, 41] showed wear of conventional polyethylene of 0.1 to 0.085 mm and a standard deviation less than 0.07. RSA studies on cross-linked polyethylenes support in vitro observations that wear would be less than the detection threshold of 0.80 mm. A power calculation indicated a total of less than 20 subjects was required to detect a target difference of less than 50% wear compared with published results of noncross-linked polyethylene ($\alpha = 0.05$, $\beta = 0.9$). A post hoc power calculation [33, 52] with 2-year results showed a β value greater than 90% for vertical, 2-D, and 3-D wear. Changes in clinical outcomes scores assessed preoperatively and at 1 year followup were compared using the Wilcoxon's matched pairs signed-ranks test. Significance was set at $p = 0.05$.

Results

There were no mechanical failures or reoperations in any of the patients. All patients showed improvement in preoperative and 1-year postoperative clinical scores ($p < 0.5$, Wilcoxon's matched pairs signed-ranks test). Oxford Hip Score improved from a preoperative median of 36 (range, 26–54) to a postoperative median of 18 (range, 12–30). The median preoperative SF-12 scores for pain and motivation were 30 (range, 21–43) and 42 (range, 31–61), respectively. Postoperatively, the median SF-12 scores for pain and motivation were 39 (range, 25–56) and 52 (range, 34–65), respectively. SF-12 scores were comparable to those of age-matched population normals [3]: in subjects aged 55 to 64 years, the mean physical component is 46.7 (range, 45.4–48.0) and the mean mental component is 53.4 (range, 52.4–54.5).

Femoral head penetration was observed during the initial 6 months, which plateaued with minimal wear at 1 and 2 years of followup. The median proximal head penetrations were 0.009 mm (range, −0.094–0.119 mm; SD, 0.063 mm) and 0.024 mm (range, −0.070–0.160 mm; SD, 0.061 mm) at 1 and 2 years, respectively (Fig. 2A). The median proximal wear rate calculated between 1 and 2 years was 0.015 mm/year. The median 2-D head penetration showed most of the migration occurred during the first 12 months. The median 2-D head penetrations were 0.083 mm (range, 0.017–0.152 mm; SD, 0.040 mm) at 1 year and 0.060 mm (range, 0.014–0.165 mm; SD, 0.040 mm) at 2 years (Fig. 2B). The median 2-D wear rate between 1 and 2 years was 0.009 mm/year. The median 3-D head penetrations were 0.159 mm (range, 0.017–0.317 mm; SD, 0.080 mm) and 0.156 mm (range, 0.067–0.256 mm; SD, 0.059 mm) at 1 and 2 years, respectively (Fig. 2C). The median 3-D wear rate between 1 and 2 years was −0.043 mm/year.

Discussion

As a consequence of its recent introduction to clinical use, there currently are no publications describing the clinical wear properties of the X3^{TM} acetabular cup insert. One hip simulator study reports the in vitro wear of this insert [16], and therefore our purpose was to compare these in vitro wear results with those after clinical use during a 2-year period. Furthermore, as this is the first report of the clinical

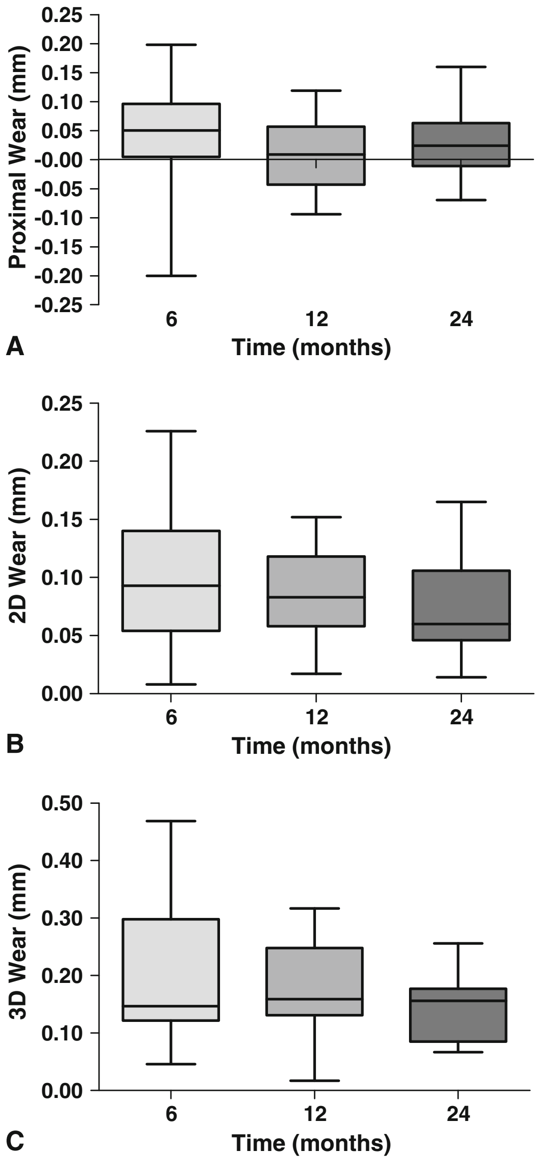

Fig. 2A–C Box-and-whisker plots show (**A**) proximal, (**B**) 2-D, and (**C**) 3-D head penetration measured at 6, 12, and 24 months. Horizontal bar = median; box = upper and lower quartiles; error bars = range.

wear characteristics of a second-generation HXLPE acetabular liner, we were interested in comparing the results from this study with literature reports of first-generation annealed highly cross-linked UHMWPE liners. We hypothesized the findings of this study would be consistent with the in vitro wear results and show clinical wear comparable or less than wear for first-generation HXLPE liners.

The high sensitivity of the RSA measurement technique, in conjunction with the ability to extrapolate results of short-term average linear wear rate to the average long-term linear wear rate for a population, makes this a useful tool for screening newly introduced prostheses [13, 29, 49]. Despite this, the RSA technique has limitations in accuracy and precision [4, 7, 51] that make it challenging to measure very small amounts of wear that are less than the detection threshold. In an optimal experimental setup, the accuracy of RSA is reported to range from 0.022 mm to 0.086 mm depending on the vector direction [7]. Our study is further limited in that no measurement of precision was made for this data set. The precision of our results should be similar to those validated previously for the combined liner and marker technique [4].

Dowd et al. [15] reported a linear increase in true wear with time is characteristic of polyethylene acetabular liners. However, we measured an uncharacteristic pattern of proximal femoral head penetration in that numerous patients had negative wear, particularly within the first year of the study. This finding has been reported previously [6, 20, 34–36] and is a result of femoral head penetration measurements lying within the accuracy limit of the technique and therefore being outside the limit of detection. The migration calculated between 1 and 2 years represents the actual rate of wear, but the numerical value of this should be interpreted with caution as it also lies within the detection threshold of the RSA technique.

The calculation of annual wear in this study was based only on wear that occurred between 1 and 2 years. Although the amount of head penetration was recorded at three times, the measurements were relative to the immediate postoperative radiographs and consequently included the initial creep and bedding-in of the liner. Studies have shown the majority of bedding-in occurs within 2.5 million cycles [21], which usually is complete after approximately 1 year [47]. This being the case, only wear measured between the first and second years was considered true wear. This is supported by the findings of Glyn-Jones et al. [24] in an RSA study of the creep and wear characteristics of HXLPE. They concluded femoral head penetration within the first 6 months was dominated by creep whereas penetration after 1 year was virtually all attributable to wear.

In the only published hip simulator study comparing the X3^{TM} liner with conventional UHMWPE and a first-generation annealed HXLPE liner (Crossfire$^{®}$; Stryker Orthopaedics), the X3^{TM} liners had a markedly lower wear rate than the conventional and first-generation HXLPE liners [16]. Based on their findings, Dumbleton et al. [16] predicted the clinical wear rate of the X3^{TM} liners should be 14 μm/year. The wear rate of 15 μm/year of median proximal wear measured in our study between 1 and 2 years is consistent with the predicted wear rate of 14 μm/year but should be considered a serendipitous result as this amount of wear is within the limits of accuracy for RSA and is not valid at this time. If we assume a conservative detectable limit for measuring wear of 80 μm, which is consistent with the precision measurements reported by Borlin et al. [4] for this technique (68 μm, 98 μm, 138 μm in the x, y, z axes, respectively), it would take more than 5 years before there is evidence of measurable wear. Similar findings have been reported for first-generation HXLPE liners, which highlights the need to evaluate HXLPE over a period of at least 5 years [9, 35]. The annual 2-D wear rate calculated in our study was considerably less than for proximal wear; however, linear measurements of 2-D wear are thought to underestimate the true wear rate [17, 48] and therefore may not truly represent the wear rate for this type of polyethylene.

First-generation annealed Crossfire® liners are reported to have an annual wear rate of 36 μm/year based on a 5-year evaluation of plain radiographs [12]. The annual wear rate for the X3™ liner found in our study (15 μm/year) is 58% less than this, which is consistent with the hip simulator results of Dumbleton et al. [16], who found the X3™ material had 62% less wear than Crossfire® liners. Rohrl et al. [44] reported a mean wear of 23 μm between 2 and 24 months for Crossfire® inserts. This is similar to the mean proximal head penetration we found (28 μm) for the X3™ liner; however, an accurate comparison requires a longer study to quantify the potential differences in wear between these materials.

A low rate of polyethylene wear is advantageous as it reduces the likelihood of wear particle-induced osteolysis and the subsequent need for revision arthroplasty owing to aseptic loosening. Dumbleton et al. [17] have assigned an osteolysis threshold for wear of 0.1 mm/year, below which osteolysis occurs infrequently, and a rate of 0.05 mm/year, which is considered safe, as the occurrence of osteolysis is almost eliminated. The annual wear rate calculated in our study was well below this threshold. We can expect the need for revision arthroplasty attributable to wear particle-induced osteolysis to be unlikely at least in the short term. The functional biologic activity of this material is likely to be lower than conventional polyethylene owing to a combination of similar specific biologic activity and lower wear rate [16, 19].

Our study showed that wear of X3™ acetabular liners after 2 years is less than a clinically quantifiable level, making accurate comparison with first-generation Crossfire® liners challenging. A longer period of evaluation is required until wear reaches a level that is clinically detectable. However, it is clear X3™ liners have wear properties superior to those of conventional polyethylene. Our measurements between 1 and 2 years followup suggest wear is nearly undetectable, which is encouraging for the future clinical performance of this material.

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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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CLINICAL RESEARCH

Low Wear of a Second-generation Highly Crosslinked Polyethylene Liner: A 5-year Radiostereometric Analysis Study

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Abstract

Background A sequentially irradiated and annealed, second-generation highly crosslinked polyethylene (XLPE) liner was introduced clinically in 2005 to reduce in vivo oxidation. This liner design has also been shown to reduce wear in vitro when compared with conventional and first-generation crosslinked liners. To date, there is only one study reporting an in vivo wear rate of this liner at 5 years' followup. However, that study used measurements made from plain radiographs, which have limited sensitivity, particularly when monitoring very low amounts of wear.

Questions/purposes What is the amount and direction of wear at 5 years using radiostereometric analysis (RSA) in patients who had THAs that included second-generation XLPE?

Methods We prospectively reviewed 21 patients who underwent primary cementless THA with the same design of XLPE acetabular liner and 32-mm articulation. Tantalum markers were inserted during surgery and all patients had RSA radiographs at 1 week, 6 months, and 1, 2, and 5 years postoperatively. Femoral head penetration within the acetabular component was measured with UmRSA® software. One patient died and two had incomplete radiographs leaving 18 radiographic series for analysis.

Results The mean amounts of proximal, two-dimensional, and three-dimensional head penetration between 1 week and 5 years were 0.018, 0.071, and 0.149 mm, respectively. The mean proximal, two-dimensional, and three-dimensional wear rates calculated between 1 year and 5 years were all less than 0.001 mm/year with no patient recording a wear rate of more than 0.040 mm/year.

Conclusions The head penetration of a second-generation XLPE liner remained low at 5 years and the wear rate calculated after the first year was low in all directions. This low level of wear remains encouraging for the future clinical performance of this material.

Level of Evidence Level IV, therapeutic study. See Instructions for Authors for a complete description of levels of evidence.

The institution of one or more of the authors (DGC) has received, during the study period, funding from Stryker Australia (St Leonards, NSW, Australia).

Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
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Introduction

First-generation highly crosslinked ultrahigh-molecular-weight polyethylene (XLPE) liners used as part of THA have been shown to reduce wear and osteolysis when compared with conventional UHMWPE liners [14]. However, first-generation XLPE may be susceptible to fatigue cracking and annealed XLPE may be susceptible to in vivo oxidation [8]. To improve the efficiency of free radical elimination, a new process of sequential irradiation and annealing was introduced in a second-generation XLPE liner (X3^{TM}; Stryker Orthopaedics, Mahwah, NJ, USA). A hip simulator study has shown acetabular liners made from this material have superior wear properties in comparison with both conventional UHMWPE and clinically successful first-generation XLPE [8].

In 2005, we started a prospective study in which we used radiostereometric analysis (RSA) to measure the wear of this second-generation XLPE liner. At 2 years, we found that the mean proximal wear rate was 0.015 mm/year [5]. There is currently only one other published study describing the clinical performance of the second-generation XLPE liner [6]. That study, however, used Martell's Hip Analysis Suite software [15]. Measurements made from plain radiographs have limited precision [11] and may overestimate the wear rate when compared with more sensitive methods such as RSA [3, 10].

We asked the question, what is the amount and direction of wear at 5 years using RSA in patients who had THAs that included a second-generation XLPE?

Patients and Methods

We prospectively enrolled 21 patients who underwent primary THA for osteoarthritis between September 2005 and July 2006. Inclusion was based on the decision of the surgeon (DGC) that a cementless THA was clinically appropriate; during that period, cementless components were used in patients with Type A and B femurs resulting in a bias toward younger and more male patients. The components used for this study cohort (Trident® acetabular component [Stryker Orthopaedics] matched with an X3^{TM} liner) were the routine implant used for cementless THAs in our institution. Inclusion criteria for the study were patients with radiographically verified primary hip osteoarthritis who were between the ages of 45 and 80 years. Exclusion criteria were patients with residence outside the Adelaide metropolitan area, abnormal gross anatomy of the hip, and inflammatory arthritis or severe osteoporosis. All of the patients having cementless THA and meeting these criteria were invited to participate in this study; of these, all 21 did so.

Of the 21 patients, none were lost to followup before the 5-year minimum followup period was completed, one patient died, and two patients had no RSA radiographic examinations at 1 year. Therefore, 18 patients were included in the study (10 men, eight women). The median age was 63 years (range, 47–73 years); median male body mass index (BMI) was 28 kg/m^2 (range, 27–31 kg/m^2), and median female BMI was 26 kg/m^2 (range, 22–29 kg/m^2). Sixteen were Charnley Grade A and two Charnley Grade B. The median cup size was 54 mm (range, 48–62 mm). The median inclination was 44° (range, 39°–58°). All patients had a cementless femoral stem (Accolade®; Stryker Orthopaedics) with a 32-mm cobalt-chromium femoral head. There were no mechanical failures or reoperations in any of the patients at latest followup.

The XLPE liner was manufactured using a cycle of 3 Mrad of gamma irradiation followed by annealing at 130° C for 8 hours, repeated three times [8].

All patients provided informed consent for the insertion of tantalum markers during surgery and the subsequent RSA radiographs. All patients had RSA examinations at 1 week, 6 months, and 1, 2, and 5 years. The minimum followup was 4.8 years (mean, 5.3 years; range, 4.8–6.2 years). Ethics approval was obtained for this study from the Calvary Wakefield Hospital Research and Ethics Committee.

The detailed methods of the RSA technique and statistics of sample size can be found in an earlier publication [5]. Wear was measured by penetration of the femoral head inside the acetabular component with UmRSA® software (Version 6.0; RSA Biomedical, Umea, Sweden). The ellipse algorithm of the metal-backed shell was used in conjunction with between one and four liner beads to form a reference segment. The maximum condition number and rigid body error accepted for each reference segment was 50 (median, 32; range, 22–48) and 0.35 mm (median, 0.14 mm; range, 0.06–0.33 mm), respectively [17]. Although the authors did not use double examinations in the current study, the precision of RSA measurements in a similar study using the same setup was 0.033 mm, 0.019 mm, and 0.072 mm in the x, y, and z axes, respectively [4].

Bedding-in and creep was assumed to be finished at 1 year. We therefore recorded three separate measurement parameters: femoral head penetration (mm) calculated between 1 week and 5 years; bedding-in (mm) calculated between 1 week and 1 year; and the wear rate (mm/year) between 1 and 5 years calculated as the simple linear regression (slope) of the head penetration values recorded for each individual at 1, 2, and 5 years. Medial, proximal, and anterior measurements were made from translations in the x, y, and z axes of the RSA calibration cage (Cage number 43; RSA Biomedical). To enable comparison to other in vitro and in vivo studies, the two-dimensional (2-D) head penetration was calculated as the vectorial sum of mediolateral (x axis) and proximal-distal (y axis) migrations. The three-dimensional (3-D) head

Table 1. Summary data

Variable	Medial (positive), lateral (negative)	Proximal (positive), distal (negative)	Anterior (positive), posterior (negative)	Two-dimensional	Three-dimensional
Head penetration between 1 week and 5 years (mm)					
Median	0.012	0.013	0.089	0.057	0.130
Mean	0.005	0.018	0.075	0.071	0.149
SD	0.063	0.061	0.123	0.052	0.076
Range	−0.167 to 0.095	−0.108 to 0.128	−0.199 to 0.291	0.014–0.167	0.040–0.321
Bedding-in/creep between 1 week and 1 year (mm)					
Median	0.016	0.010	0.025	0.085	0.161
Mean	0.008	0.007	0.045	0.082	0.187
SD	0.070	0.063	0.182	0.043	0.083
Range	−0.119 to 0.120	−0.094 to 0.119	−0.293 to 0.309	0.017–0.152	0.017–0.317
Wear rate between 1 and 5 years (mm/year)					
Median	−0.002	0.004	0.001	−0.004	−0.005
Mean	−0.002	0.001	0.007	−0.002	−0.007
SD	0.020	0.018	0.038	0.016	0.024
Range	−0.062 to 0.027	−0.033 to 0.033	−0.061 to 0.081	−0.028 to 0.032	−0.061 to 0.040

penetration was calculated as the vectorial sum of mediolateral, proximal-distal, and AP (z axis) migrations.

Results

The mean amounts of medial, proximal, anterior, 2-D, and 3-D head penetration between 1 week and 5 years were 0.005, 0.018, 0.075, 0.071, and 0.149 mm, respectively (Table 1). The majority of this head penetration occurred within the first 12 months and the amount of head penetration was less than 0.2 mm in the proximal and medial directions at 5 years (Fig. 1). The mean medial, proximal, anterior, 2-D, and 3-D wear rates between 1 and 5 years were −0.002, 0.001, 0.007, −0.002, and −0.007 mm/year, respectively (Table 1). No patient in this cohort had a medial, proximal, 2-D, or 3-D wear rate of more than 0.040 mm/year.

Discussion

The dramatic reduction of wear observed with in vitro studies examining crosslinked polyethylene acetabular components [8] is a formidable challenge for in vivo wear measurement. Wear studies using measurements made from plain radiographs have limited sensitivity, particularly when monitoring very low amounts of wear [11]. For example, the amount of wear measured using Martell's Hip Analysis Suite software [15] may overestimate wear in comparison to more sensitive techniques such as RSA [3]. In an optimal experimental setup, the accuracy of RSA to measure femoral head penetration is reported to be 33 μm, 22 μm, and 86 μm in the x, y, and z axes, respectively [2], which is consistent with the precision measurements reported by Borlin et al [1] for the beaded plus ellipse technique (68 μm, 98 μm, and 138 μm in the x, y, and z axes, respectively). This sensitivity implies the wear of conventional polyethylene can readily be measured and clinically important wear thresholds such as wear greater than 0.05 mm/year should be measurable after 1 to 2 years. However, in vitro testing of this second-generation highly crosslinked polyethylene liner predicted a wear rate as low as 0.014 mm/year and our early report at 2 years found a wear rate of 0.015 mm/year. Hence, it would theoretically take approximately 5 years before there is evidence of measurable wear. Subsequently, we elected to measure the wear of this second-generation highly crosslinked polyethylene liner with RSA at 5 years followup.

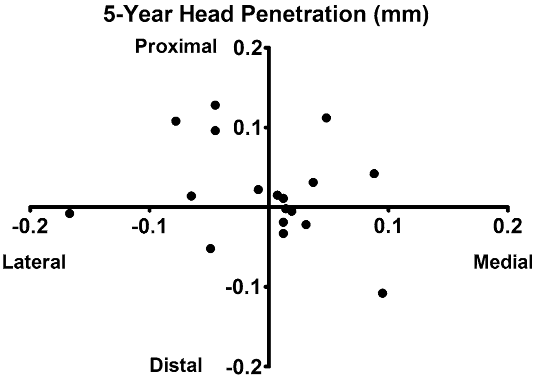

Fig. 1 Graph showing the femoral head penetration for each individual between 1 week and 5 years in the proximal-distal and mediolateral directions.

We acknowledge the limitations of our study. First, we only provide descriptive data of a small cohort and did not have a control group for comparison. Second, clinical wear studies often include different measurement and wear rate calculation methods, which make comparison between groups difficult. RSA studies may calculate wear differently than other in vivo radiological methods such as Martell's [15] and readers should be aware of the limitations and measurement bias when comparing studies. Differences may even exist when the same software is used as a result of improvements made in later versions [13]. Studies may also report wear parameters (femoral head penetration, bedding-in, wear rate) differently, which we have attempted to present as clearly as possible for future comparative studies. Third, we did not assess the presence of osteolysis in this patient cohort and ultimately osteolysis is the clinically relevant parameter of interest; wear is an imperfect surrogate. Fourth, although RSA is considered the most accurate technique to measure wear in vivo, the amount of femoral head penetration actually occurring in XLPE liners is very low and may actually be less than the sensitivity of RSA at 5 years. The low mean proximal wear rate of 0.001 mm/year (range, −0.062 to 0.027 mm/year) reported in our study is similar to that reported in other RSA studies of first-generation XLPE liners with greater than 5 years' followup (eg, 0.001 [7], 0.002 [16], 0.005 [12], and 0.014 mm/year [4]). As a result of wear being measured as the slope of the penetration measurements made after 1 year for each individual and the penetration being so small, some negative wear rates are reported in all clinical wear studies. To calculate the wear of very low wearing implants, further time is required until the total amount of wear produces a measurable positive wear slope.

In a study of 51 hips using the same second-generation XLPE liner, D'Antonio et al [6] reported the mean 2-D head penetration between 6 weeks and 5 years was 0.072 mm (SD, 0.286 mm), which was similar to our result of 0.071 mm (SD, 0.052) between 1 week and 5 years. However, D'Antonio et al [6] reported a mean 2-D wear rate of 0.015 mm/year, which is higher than our mean 2-D wear rate of −0.002 mm/year (range, −0.028 to 0.032 mm/year). The negative mean wear rate is a result of the small amount of wear being measured over the 4-year period. Unfortunately, no range or SD of the wear rate was included in the previous publication [5] for further comparison. The range is important when reporting the number of individual outliers above certain wear rates. A wear rate of 0.05 mm/year or more has been cited by some to have an association with osteolysis [9]. No patients in our study were found to have a 2-D wear rate of more than 0.04 mm/year. A less sensitive measurement technique may have erroneously reported some patients above this wear rate.

We found that the femoral head penetration within a second-generation XLPE liner remained very low at 5 years, and the wear rate calculated after 1 year is very low in all directions. No patients had a proximal, 2-D, or 3-D wear rate exceeding 0.04 mm/year. However, longer-term and larger studies need to be performed to determine whether this results in decreases in osteolysis. The low observed level of wear remains encouraging for the future clinical performance of this material.

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4.9 COHORT F

The results of Cohort F were published at five years follow-up in the following publication:

- The rate of wear of second-generation highly crosslinked polyethylene liners five years post-operatively does not increase if large femoral heads are used. *Bone and Joint Journal* 2016, Accepted for publication on 12th August 2016

Statement of Authorship

Title of Paper	Large articulations do not increase wear rates of second-generation highly cross-linked polyethylene liners at five years.
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Publication Details	Callary SA, Field JR, Campbell DG (2016). Second-generation highly cross-linked polyethylene liners with large articulations do not increase wear rates at five years. Bone and Joint Journal. Accepted for publication on 12th August 2016. Scheduled for publication in December 2016.

Principal Author

Name of Principal Author (Candidate)	Stuart Callary
Contribution to the Paper	First author on the paper. Reviewed all literature, analysed all resultant RSA radiographs and collated results. Prepared all tables, wrote initial draft and edited publication as requested during peer review. Acted as corresponding author.
Overall percentage (%)	70%
Certification	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 18 · 10 · 2016

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	John Field
Contribution to the Paper	Assisted with the collection of data, statistical analysis and provided critical review of the manuscript.
Signature	Date Oct 16. 2016

Name of Co-Author	David Campbell
Contribution to the Paper	Planned the study, prepared ethics application, performed surgeries including inserting RSA beads intraoperatively, reviewed patients in clinic and provided critical review of the manuscript.
Signature	Date 16 October 2016

The rate of wear of second-generation highly crosslinked polyethylene liners five years post-operatively does not increase if large femoral heads are used

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

This work was performed at Wakefield Orthopaedic Clinic, Adelaide, South Australia, Australia.

ABSTRACT

Aims

The increased in vivo resistance to wear of highly crosslinked polyethylene (HXLPE) in total hip arthroplasty (THA) has led to an increased use of larger articulations which have been shown to reduce the incidence of early dislocation. To date, there are few reports of the wear of larger articulations using second generation HXLPE liners. Our prospective cohort study measured the bedding-in and early wear of large (36 mm and 40 mm diameter) articulations involving a second generation X3 HXLPE liner and compared our findings with previous clinical and in vitro studies of the same material.

Patients and Methods

The proximal penetration of the femoral head five years post-operatively was measured for 15 patients using radiostereometric analysis (RSA).

Results

The median proximal bedding-in within the first post-operative year was 0.022 mm (interquartile range (IQR) -0.050 to 0.091). The median proximal rate of wear between one and five years was -0.004 mm/year (IQR -0.021 to 0.022). The rates of proximal, medial, 2D or 3D wear between one and five years post-operatively of the X3 HXLPE liner did not increase with larger articulations compared with our previous study of 32 mm articulations.

Conclusion

Although reassuring, the use of larger articulations requires continued monitoring to determine whether the low wear observed in the short-term continues to the mid- to long-term.

INTRODUCTION

Dislocation remains a common cause for revision surgery following total hip arthroplasty (THA). The Australian National Joint Replacement Registry reports dislocation as the second most common indication for revision of primary THA after aseptic loosening.[1] The use of larger articulations has long been known to increase the stability of the joint by increasing the distance required for the femoral head to disengage from the acetabular component.[2,3] A large multi-centre randomized controlled trial found that the incidence of dislocation one year after primary THA was significantly lower in patients who received a 36 mm articulation (0.8%) than in patients receiving a 28 mm articulation (4.4%, $p = 0.024$).[4] Cohort studies have also found a decreased risk of revision THA for dislocation or instability when larger articulations were used.[5-8] However, when used in conjunction with conventional ultra-high molecular weight polyethylene (UHMWPE) larger articulations had increased clinical wear rates.[9-11] The introduction of highly cross-linked polyethylene (HXLPE) acetabular components in the late 1990s as a result of laboratory studies[12] has subsequently resulted in decreased clinical wear rates.[13-15] Consequently the use of larger articulations in primary THA has increased over the last ten years.[1]

Second generation HXLPE liners are manufactured using a different sequence of treatments in an attempt to further reduce the production of free radicals.[16] One type of second generation HXLPE liner (X3, Stryker Orthopaedics, Mahwah, New Jersey) manufactured with sequential irradiation and annealing showed significantly reduced gravimetric wear *in vitro* when used in a standard-sized articulation compared to conventional polyethylene.[17] However, in the same study, the use of larger articulations against an X3 liner significantly increased the amount of gravimetric wear ($p = 0.013$).[17] A second *in vitro* study of the same X3 liner against a 36 mm femoral head found that decreasing the liner thickness increased the volumetric wear rate.[18] The low amount of wear measured in these studies is difficult to quantify accurately *in vivo*. Radiostereometric analysis (RSA) is acknowledged as the most accurate and precise method to measure polyethylene wear rates *in vivo*.[19-21] We have previously used RSA to show that the wear rate of a second generation HXLPE liner is very low when used in conjunction with a 32 mm metal femoral head at two[22] and five years.[23] Hence, the aim of the current study was to measure the bedding-in and early wear rates of the second generation HXLPE liner with 36 or 40 mm articulations.

PATIENTS AND METHODS

This prospective cohort study involved 19 consecutive patients who underwent primary THA with a 36 mm or 40 mm articulation between May 2007 and January 2009 by a single surgeon (DGC). The need to use an acetabular component with an outer diameter less than 52 mm was an intra-operative exclusion criterion due to this resulting in a liner thickness below 5.8 mm with a 36 mm articulation. This cohort was compared to a previous consecutive cohort of 21 patients who underwent THA between September 2005 and July 2006 involving a 32 mm articulation incorporating the same HXLPE liner. All THA’s in both cohorts were undertaken by the same surgeon (DGC) at Wakefield Hospital. For both cohorts, patients were eligible for inclusion if they had a diagnosis of osteoarthritis; were aged between 45 and 80 years; were deemed suitable for an uncemented THA; and resided within the Adelaide metropolitan area.[22,23] Ethical approval had been obtained from the Institutional Ethics Committee and the trial is registered with Australian New Zealand Clinical Trials Registry (#ACTRN12616000952448).

All patients in both cohorts received a second generation HXLPE liner (X3™, Stryker Orthopaedics, Mahwah, NJ). The HXLPE liner was manufactured using a cycle of 30 kGy of gamma irradiation followed by annealing at 130° C for 8 hours, repeated three times for a cumulative dose of 90 kGy. All patients had flat liners within a hemispherical shell (Trident™, Stryker Orthopaedics). All patients received the same femoral stem with a cobalt chrome femoral head (Accolade™, Stryker Orthopaedics). Whether a 36 or 40 mm liner was used in the current cohort was determined by the outer diameter of the acetabular component (Trident, Stryker Orthopaedics, Mahwah, NJ). Specifically, seven patients requiring an acetabular component with an outer diameter of 52 or 54 mm received a 36 mm articulation with a resultant minimum HXLPE liner thickness of 5.9 mm; ten patients requiring an acetabular component with an outer diameter of 56 or 58 mm received a 40 mm articulation with a resultant minimum HXLPE liner thickness of 5.8 mm; and two patients requiring an acetabular component with an outer diameter of 60 or 62 mm received a 40 mm articulation with a resultant minimum HXLPE liner thickness of 7.4 mm. No patients required an acetabular component with an outer diameter greater than 62 mm.

Supine RSA examinations were undertaken within the first post-operative week and at six months, one, two and five years post-operatively. A ceiling-mounted radiographic tube and a mobile radiographic tube were used simultaneously to take exposures of the hip with a calibration cage (Number 43; RSA Biomedical, Umeå, Sweden). Penetration of the femoral head into the acetabular component was measured using UmRSA software (v6.0; RSA Biomedical, Umeå, Sweden). The outer ellipse and opening of the acetabular component were used to represent the acetabular segment for both cohorts in the RSA software. The maximum condition number and rigid body error accepted for each reference segment were 50 and 0.35 mm respectively.

Proximal head penetration was calculated in the medial, proximal and anterior axes. Two-dimensional (2D) head penetration was calculated as the vectorial sum of medial and proximal migrations and three-dimensional (3D) head penetration was calculated as the vectorial sum of medial, proximal and anterior migrations. The immediate post-operative radiographs provided a baseline for calculation of ‘bedding-in’ migration of the femoral head at one year. The slope of the penetration recorded for each individual between one and five years was assumed to represent wear of the liner.

Two patients did not have post-operative RSA examinations within the first week and two additional patients did not have RSA examinations at five years. Therefore, 15 hips (four 36 mm and eleven 40 mm articulations) were included in the study (12 men, 3 women) (Table 1). Median age of these 15 patients was 64 years (range, 55–76 years) and median body mass index was 28 (range, 22-35). The median cup size was 56 mm (range, 52 to 62). The median inclination of the acetabular component was 47° (range, 40 to 50). Clinical outcome was measured using the Oxford Hip Score, which was recorded pre-operatively and at one and two years post-operatively.

Statistical analysis

The data analysis was performed using SAS software (Version 9.4 of the SAS System for Windows, SAS Institute Inc., Cary, NC, USA). A one-sided test of non-inferiority was considered the most appropriate statistical test to determine if the wear of the larger articulations was no greater than 32 mm articulations. We reported the median proximal wear rate between one and two years for the 32 mm cohort to be 0.02 mm/yr.[22] Hence, a non-inferiority margin of 0.03 mm was chosen as an additional wear rate of 0.03 mm/yr would result in a clinically relevant wear rate of 0.05 mm/yr below which osteolysis is very rarely seen.[24] Hence, the wear of the larger articulation cohort was not significantly greater than the 32 mm cohort if the non-inferiority was supported ($p<0.05$). Non-inferiority was supported if the 90% lower confidence limit of the pooled difference between means did not exceed the lower bound of -0.03. A post hoc power analysis was undertaken. Using the sample sizes of 15 and 18 for the large and 32 mm articulation cohorts respectively, and a difference between means of 0.01 with a SD of 0.02 indicated that the study had 99% power to detect non-inferiority of the larger articulations relative to the 32 mm articulations with a threshold of -0.03 and an $\alpha=0.05$.

RESULTS

No patients required revision or re-operation at two year follow-up. Median Oxford Hip Scores improved from 24 (range, 7-36) pre-operatively to 47 (range, 25-48) at one year and 45 (range, 27-48) at two years. There were no differences in Oxford Hip Scores between the current cohort and the control cohort with 32 mm articulations (Table 2).

The median proximal femoral head penetration of the larger articulations between one week and five years was -0.016 mm (range -0.186 to 0.164) (Table 3). The median proximal femoral head penetration at one year of the larger articulations, interpreted as bedding-in, was 0.022 mm (range -0.157 to 0.138). The median proximal wear rates recorded at five years were less than that at two years for each cohort and had less variability (Figure 1 and 2). The median proximal wear rate between one and five years was -0.004 mm/yr (-0.052 to 0.032) which was not statistically significantly greater than the median proximal wear rate of the 32 mm articulation cohort, 0.003 mm/yr (-0.049 to 0.020) ($p=0.00$) (Figure 2, Table 3). The medial, 2D and 3D wear rate of the large articulations between one and five years were also not significantly greater than the 32 mm cohort ($p<0.05$, Table 3).

DISCUSSION

The introduction of HXLPE in THA has significantly reduced polyethylene wear.[14] This reduction in wear has encouraged the use of larger articulations, which have been shown to reduce the rates of early dislocation.[4,6] Implant Registry data have reported widespread acceptance of HXLPE, improved clinical results and increased use of femoral heads 36 mm or larger in primary THA.[1] However, the effect of larger articulations with relatively thin HXLPE liners on *in vivo* wear is unknown. Metal-backed acetabular components have been designed to be used in conjunction with a number of different combinations of liner thickness and femoral head size to allow surgeons to select an implant appropriate for the individual patient. Historically the minimum thickness recommended for UHMWPE was 8 mm.[25] Catastrophic failures have been observed in UHMWPE liners with a minimum thickness of less than 5mm,[26] and some designs of HXLPE are vulnerable to rim cracking when positioned incorrectly.[27] *In vitro* studies of the X3 HXLPE liner have reported larger gravimetric wear with increasing head sizes[17] and increased wear rates with thinner liners.[18]

A recent systematic search of RSA wear studies of HXLPE[28] revealed that there is only one published RSA study that measures the wear rate of a 36mm or larger articulation.[29] At three years, the median proximal wear rate of the Longevity HXLPE liner used with 36 mm articulations was 0.000 mm/yr, compared to 0.026 mm/yr for the 28 mm articulations.[29] Our *in vivo* results showed no statistically significant increase in the X3 liner wear between one and five years with larger articulations. Importantly the median proximal wear rates reported for both the larger and 32mm cohorts were very low below 0.005 mm/year. These wear rates are very similar to those reported in the only other RSA study of X3 liners by Gascoyne et al[30] who found a proximal wear rate of 0.001 mm/year using mostly with 32 mm femoral heads. There are only two *in vivo* wear studies of X3 liners used with larger 36 mm articulations.[31,32] Sayeed et al reported a mean 2D wear rate of 0.0004 mm/yr at two years for 26 primary THA prostheses with a 3.9 mm polyethylene thickness[31], while Selvarajah et al reported a much higher 2D wear rate between one and five years of 0.109 mm/year for 36 mm articulations.[32] A wear rate of 0.109 mm/year would mean that a high percentage of these hips were at risk of developing osteolysis.[24,32] This report is very concerning for surgeons using X3 liners with large articulations. Larger articulations were also found to increase the wear rates of an electron beam-irradiated and melted HXLPE in a large cohort study.[33] However, both of these Selvarajah[32] and Bragdon[33] studies were limited by the use of measurements made from plain radiographs and highlight the importance of using a more sensitive radiographic technique such as RSA used in our study.

The wear rate decreased for both cohorts at further five year follow-up compared to two years. This decrease is consistent with three other RSA studies that have measured the wear of HXLPE at longer follow-up.[28] No individual in our larger or 32 mm cohorts had a proximal or 2D wear rate above 0.045 mm/year at five years. This is below the historical threshold of 0.05 mm/yr wear rate associated with osteolysis in patients with older UHMWPE liners.[24] The wear rate threshold of HXLPE liners is currently unknown and will require long term clinical studies. The very low wear reported in our study in encouraging for future clinical use of larger articulations but it should be noted that the same linear wear rate of larger articulations will result in a larger volume of wear.[34] There are also some recent concerns regarding the potential for increased corrosion and metal release at the head-neck taper junction of larger articulations.[34] However, head size has yet to be shown to effect the incidence of resultant adverse local tissue reactions in metal on poly articulations.[34]

The main limitation of our study is that it is a comparison of two prospective cohorts recruited at different points in time. Specifically, wear rates of the relatively new X3 HXLPE liner was investigated initially in THAs with a standard 32 mm articulation. After early wear was established to be low in this cohort, THAs with larger articulations were undertaken by the same surgeon in a similar cohort of patients, enabling determination of wear rate of larger articulations. A second limitation is the small number of patients included in each cohort, which is common to most RSA studies. However, a post hoc power analysis confirmed the adequacy of the sample sizes used in the comparison at five years. The same post hoc power analysis at two years revealed inadequate power (44%) due to the increased variability of the wear rates in both cohorts. A third limitation is the use of the ellipse as the acetabular reference segment in our RSA results presented for both cohorts. The RSA results of the 32 mm articulation control group previously reported[22,23] used a combination of the tantalum markers placed in the outer rim of the liner and the ellipse of the metal shell as the acetabular reference segment. Although the acetabular reference segment used did not influence the accuracy of RSA wear measurements in a phantom study,[21] the combined method has been shown to have the greatest precision clinically.[35,36] The combined method could not be utilized in the current study because beads implanted in the periphery of the liner, irrespective of whether they received a 32, 36 or 40 mm articulation, were commonly occluded by the larger femoral heads.

In conclusion, larger articulations did not significantly increase the mean rate of proximal, medial, 2D or 3D wear between one and five years of the X3 HXLPE liner when compared to our previous study of 32mm articulations. This bodes well for the continued use of larger articulations, particularly in those patients, such as the elderly, in whom a decreased risk of dislocation is a priority. However, the use of larger articulations requires continued monitoring to determine whether the early low rates of wear observed continue in the long term.

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Conflict of interest and funding

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Table 1: Patient and implant details for the 32 mm and the larger 36/40 mm cohorts. Mann-Whitney comparison of age, BMI and inclination.

Cohort		**32mm**	**36/40mm**	**p value**
Sex	**m:f**	10:8	12:3	
Head Size (mm)	**32**	18	0	
	36	0	4	
	40	0	11	
Side	**L:R**	14:4	4:11	
Cup Outer Diameter (mm)	**48**	1	0	
	50	1	0	
	52	4	1	
	54	4	3	
	56	6	7	
	58	1	2	
	60	1	1	
	62	0	1	
Liner Thickness (mm)	**5.8/5.9**	2	13	
	7.4/7.9	8	2	
	9.9	7	0	
	11.4	1	0	
Median Age (years, range)		63 (47-73)	64 (55-76)	0.43
Median BMI (kg/m2, range)		28 (22-35)	27 (22-31)	0.35
Inclination (degrees, range)		47 (40-50)	44 (39-58)	0.85

Table 2: Oxford Hip Scores for the 32 mm and the larger 36/40 mm cohorts

	Oxford Hip Scores		
32mm Cohort	**Preop**	**1yr**	**2yr**
Mean	20	42	45
Median	22	44	47
Min	6	30	35
Max	48	48	48
36/40mm Cohort	**Preop**	**1yr**	**2yr**
Mean	23	44	43
Median	24	47	45
Min	7	25	27
Max	36	48	48
p-value of Mann-Whitney comparison	0.38	0.15	0.57

Table 3: Femoral head penetration, bedding-in and wear for each cohort in each axis

		Medial (+ve) Lateral (-ve)	Proximal (+ve) Distal (-ve)	Anterior (+ve) Posterior (-ve)	Two-dimensional	Three-dimensional
Femoral Head Penetration between 1 week and 5 years (mm)						
32 mm Articulation	Median	-0.027	-0.004	0.207	0.099	0.275
	Mean	-0.038	-0.029	0.090	0.108	0.262
	SD	0.078	0.106	0.260	0.086	0.155
	Range	-0.193 to 0.141	-0.266 to 0.104	-0.752 to 0.317	0.014 to 0.324	0.029 to 0.765
36/40 mm Articulation	Median	-0.026	-0.016	0.030	0.120	0.160
	Mean	-0.007	-0.009	0.051	0.110	0.179
	SD	0.063	0.108	0.155	0.051	0.091
	Range	-0.097 to 0.132	-0.186 to 0.164	-0.160 to 0.356	0.037 to 0.190	0.054 to 0.381
Difference between means		-0.030	-0.020	0.039	-0.002	0.083
90% lower CI limit of diff		-0.073	-0.083	-0.093	-0.046	0.005
Non inferiority supported		no	no	no	no	yes
p-value		0.504	0.394	0.191	0.142	0.010
Bedding-in/creep between 1 week and 1 year (mm)						
32 mm Articulation	Median	-0.053	-0.017	0.040	0.140	0.222
	Mean	-0.022	-0.001	0.087	0.118	0.247
	SD	0.098	0.086	0.224	0.055	0.106
	Range	-0.205 to 0.142	-0.151 to 0.186	-0.293 to 0.406	0.039 to 0.224	0.068 to 0.455
36/40 mm Articulation	Median	0.020	0.022	-0.009	0.130	0.212
	Mean	-0.003	0.010	-0.037	0.117	0.236
	SD	0.096	0.095	0.245	0.059	0.139
	Range	-0.160 to 0.198	-0.157 to 0.138	-0.534 to 0.404	0.034 to 0.199	0.045 to 0.553
Difference between means		-0.019	-0.010	0.124	0.001	0.012
90% lower CI limit of diff		-0.079	-0.065	-0.018	-0.034	-0.062
Non inferiority supported		no	no	yes	no	no
p-value		0.382	0.276	0.038	0.070	0.172

Wear rate between 1 and 2 years (mm/year)						
32 mm Articulation	Median	-0.041	-0.020	0.052	-0.046	-0.025
	Mean	-0.028	-0.008	-0.022	-0.020	-0.021
	SD	0.110	0.083	0.239	0.090	0.184
	Range	-0.205 to 0.161	-0.182 to 0.133	-0.459 to 0.248	-0.171 to 0.129	-0.387 to 0.466
36/40 mm Articulation	Median	0.034	0.012	0.139	-0.015	-0.066
	Mean	0.036	0.019	0.060	0.002	-0.010
	SD	0.087	0.094	0.255	0.096	0.173
	Range	-0.118 to 0.159	-0.146 to 0.157	-0.399 to 0.421	-0.113 to 0.206	-0.284 to 0.313
Difference between means		-0.065	-0.026	-0.082	-0.021	-0.011
90% lower CI limit of diff		-0.125	-0.079	-0.228	-0.076	-0.118
Non inferiority supported		no	no	no	no	no
p-value		0.832	0.454	0.723	0.395	0.383
Wear rate between 1 year to 5 years (mm/year)						
32 mm Articulation	Median	-0.004	0.003	-0.009	-0.007	0.001
	Mean	-0.001	-0.006	0.001	-0.005	0.004
	SD	0.020	0.022	0.049	0.022	0.030
	Range	-0.037 to 0.031	-0.049 to 0.020	-0.088 to 0.101	-0.045 to 0.045	-0.037 to 0.090
36/40 mm Articulation	Median	0.001	-0.004	0.013	0.006	-0.004
	Mean	0.005	-0.003	0.005	-0.003	-0.012
	SD	0.029	0.027	0.073	0.030	0.066
	Range	-0.034 to 0.092	-0.052 to 0.032	-0.186 to 0.111	-0.093 to 0.026	-0.207 to 0.109
Difference between means		-0.006	-0.003	-0.004	-0.002	0.016
90% lower CI limit of diff		-0.021	-0.017	-0.040	-0.017	-0.014
Non inferiority supported		yes	yes	no	yes	yes
p-value		0.005	0.002	0.111	0.002	0.007

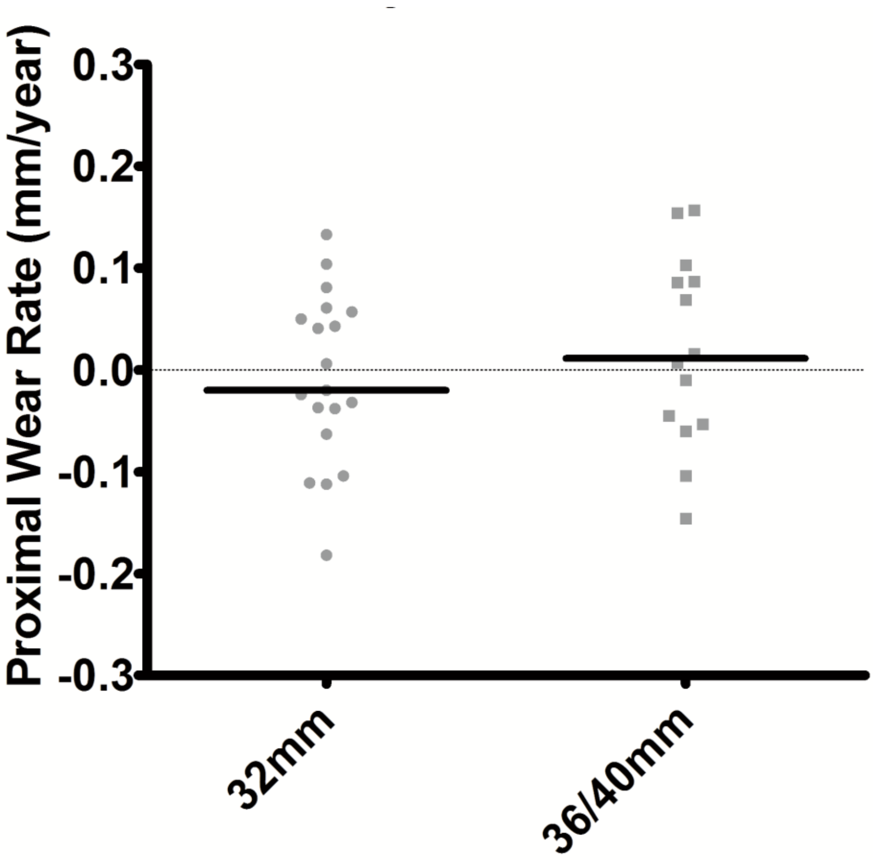

Figure 1: Proximal wear rate between 1 and 2 years for each cohort

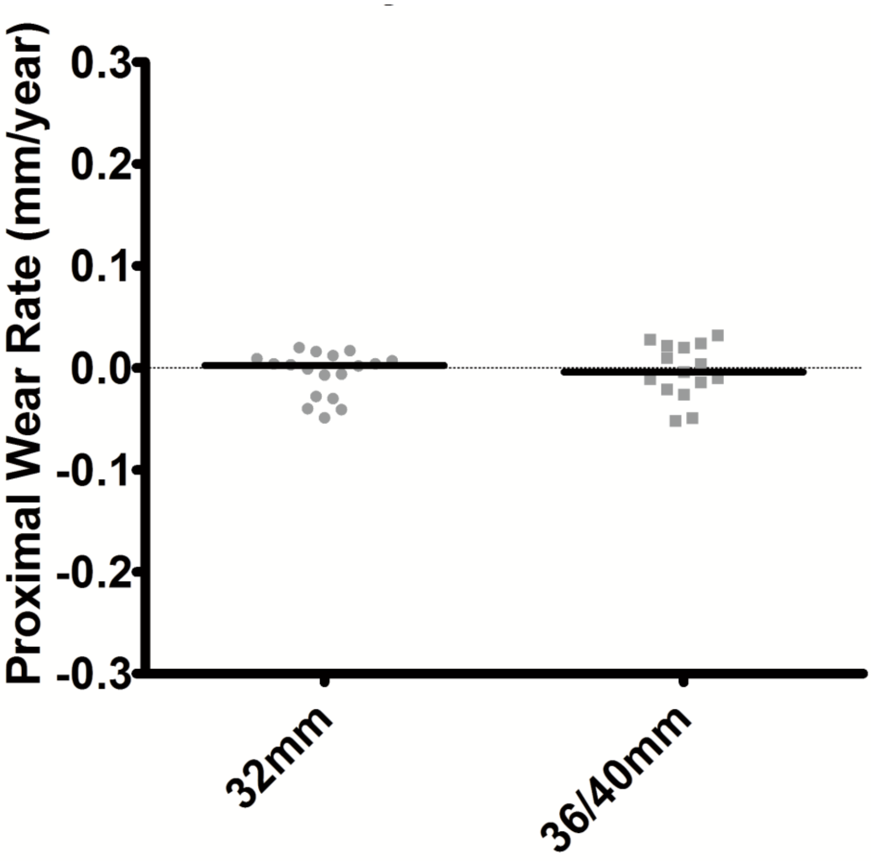

Figure 2: Proximal wear rate between 1 and 5 years for each cohort

4.10 ANALYSIS OF THE AGGREGATE SAMPLE OF COHORTS A to F

Implant, RSA and patient details for each of the six cohorts included in these analyses are shown in Table 4.18. The number of patients from each cohort included in the analyses of FHP, bedding-in and wear at each time point are shown in Table 4.19. It should be noted that in the following tables and figures, the wear rate of Cohort A is between one and six years and not between one and five years, as for Cohorts B to F. The reasons for exclusions have been provided in the relevant earlier sections of this Chapter when describing the results of the individual cohorts.

Table 4.18: Implant, RSA and patient characteristics by cohort

Cohort	XLPE Type	Head Size (mm)	RSA Analysis	Median Age (years, range)	Median BMI (kg/m^2, range)	Median Acetabular Component Outer Diamter (mm, range)	Median Inclination (degrees, range)
A	Marathon	28	Combined	72 (56-80)	28 (16-37)	52 (48-62)	47 (35-65)
B	Longevity	28	Combined	71 (65-74)	28 (21-39)	56 (50-64)	41 (27-54)
C	Longevity	36	Combined	71 (65-74)	29 (20-44)	56 (50-64)	42 (30-55)
D	Longevity	28	Combined	56 (43-64)	31 (20-49)	56 (50-64)	45 (34-53)
E	X3	32	Combined	63 (46-75)	28 (22-31)	54 (48-62)	44 (39-58)
F	X3	36/40	Unbeaded	64 (55-76)	28 (22-35)	56 (50-62)	46 (40-50)

Table 4.19: Numbers of patients included in bedding-in and wear rate analyses, by cohort and time point

Cohort	Bedding-In	Wear Rate			
	0 to 1yr	1 to 2yrs	1 to 3 yrs	1 to 5 yrs	1 to 6yrs
A	25	25	-	-	24
B	27	25	24	21	-
C	23	23	19	16	-
D	20	18	18	11	-
E	19	19	-	18	-
F	13	14	-	15	-

4.10.1 Statistical Analysis

A multiple regression analysis was performed of medial, proximal, anterior, 2D and 3D FHP, bedding-in and wear rates of patients in all six cohorts combined. Stratified means and medians were used to summarise associations between bedding-in and wear rate and categorical predictors (XLPE type and sex). Statistical significance was assessed using the Kruskal-Wallis or Wilcoxon test as appropriate depending on the normality of data distribution. A p value <0.05 was interpreted to represent a significant difference between two or more groups within a categorical predictor.

Articulation size was not included as a categorical predictor because not every type of XLPE component examined was used with varying articulation sizes. Therefore the effect on wear would not be able to be definitively distinguished as being due to articulation size or type of XLPE. Moreover, the influence of articulation size on XLPE wear had already been directly compared within the same XLPE liners in two publications in this thesis (Callary et al., 2016; Howie et al., 2016), the latter publication reporting the results of an RCT with the specific aim of determining the effect of articulation size on XLPE wear.

Associations between medial, proximal, anterior, 2D and 3D bedding-in and wear rate and continuous predictors (acetabular component outer diameter, acetabular component inclination, BMI and patient age at the time of THR) were assessed using Spearman's correlation coefficient. Because data were not normally distributed, Spearman's correlations were utilized rather than Pearson's correlations. Acetabular component outer diameter was considered a continuous predictor rather than categorical due to the low number of hips with 48, 62 and 64mm components.

4.10.2 Femoral Head Penetration

The associations between XLPE type (Marathon/Longevity/X3) and proximal, medial, anterior, 2D and 3D FHP at two and five years were examined. Median proximal FHP over time is shown for each cohort in Table 4.20 and Figure 4.18.

Type of XLPE was significantly associated with proximal FHP at two ($p<0.0001$) and five years ($p=0.0006$). Marathon XLPE (Cohort A) had the highest mean proximal FHP at two and five years follow-up (0.120 and 0.188 mm, respectively) compared to Longevity (0.070 and 0.068 mm, respectively), comprising Cohorts B to D, and X3 (0.024 and 0.005 mm, respectively), comprising Cohorts E and F (Figures 4.19 and 4.20). Type of XLPE was also significantly associated with 2D and 3D FHP at five years ($p<0.0001$ and $p=0.0221$, respectively), with Marathon XLPE having the highest mean 2D and 3D FHP.

Sex was not significantly associated with medial, anterior, 2D or 3D FHP at two or five years.

No continuous predictors (acetabular component outer diameter, acetabular inclination, BMI or age) showed a strong correlation with any FHP at two and five years.

Table 4.20: Proximal FHP (mm) at two and five years by cohort

Femoral Head Penetration at 2 years (mm)						
	A	B	C	D	E	F
Median	0.140	0.064	0.055	0.072	0.024	0.006
Mean	0.120	0.074	0.060	0.079	0.028	0.018
SD	0.113	0.085	0.114	0.065	0.061	0.063
Range	-0.100 to 0.376	-0.336 to 0.249	-0.336 to 0.144	-0.020 to 0.236	-0.071 to 0.160	-0.056 to 0.120
Femoral Head Penetration at 5* years (mm)						
	A	B	C	D	E	F
Median	0.177	0.050	0.047	0.058	0.013	-0.016
Mean	0.188	0.078	0.065	0.053	0.014	-0.009
SD	0.121	0.094	0.099	0.058	0.070	0.108
Range	0.003 to 0.506	-0.084 to 0.329	-0.069 to 0.379	-0.085 to 0.132	-0.138 to 0.128	-0.186 to 0.164

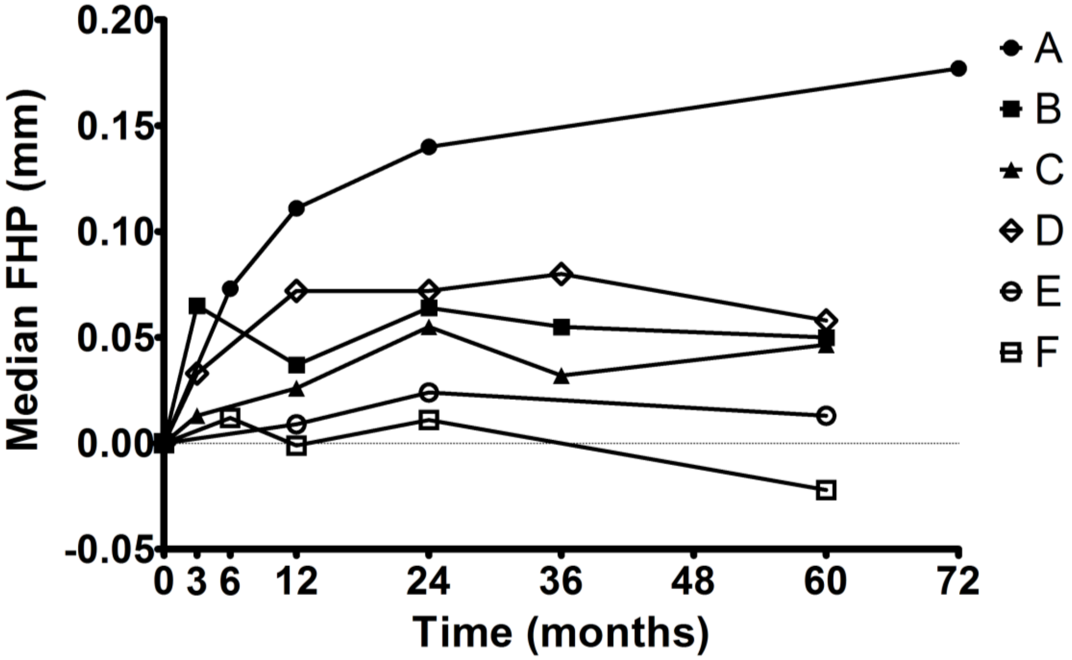

Figure 4.18: The median proximal femoral head penetration over time by cohort

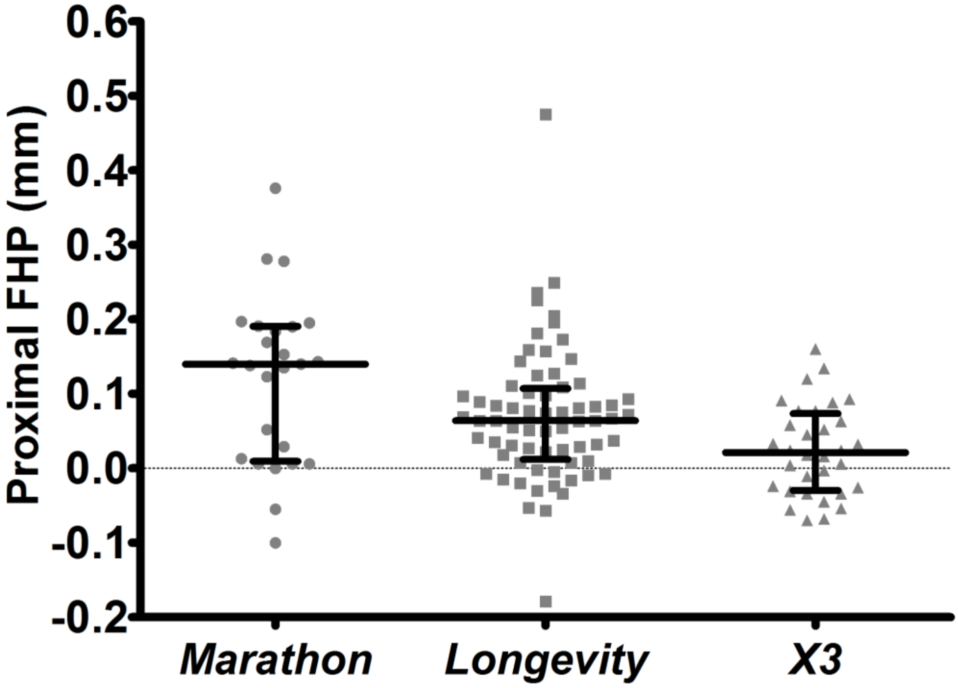

Figure 4.19: The proximal FHP at two years (median, interquartile range) by XLPE type

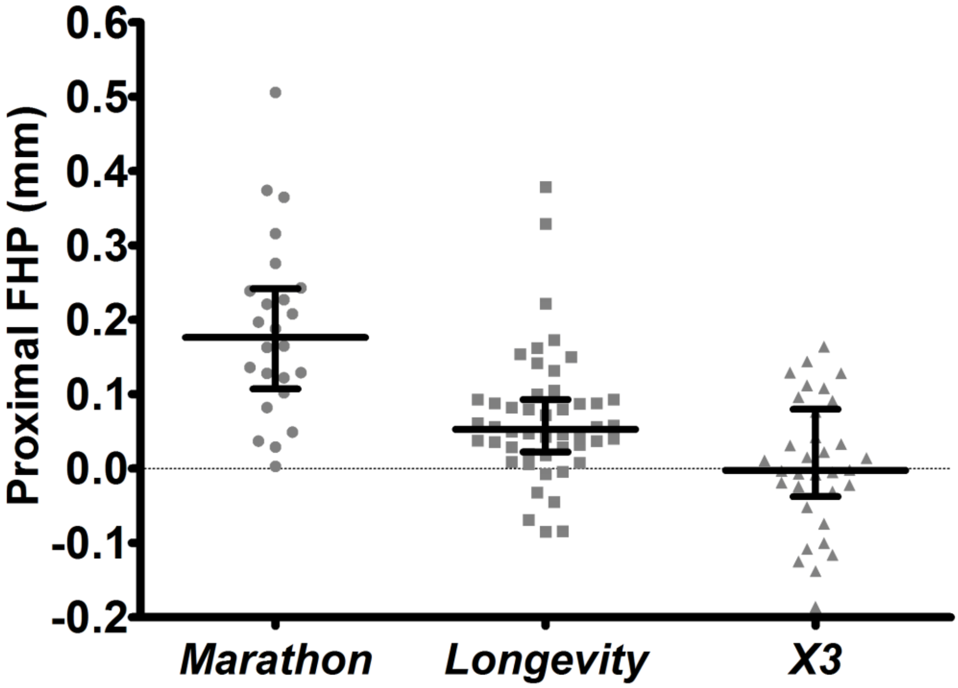

Figure 4.20: The proximal FHP at five years (median, interquartile range) by XLPE type

4.10.3 Bedding-In

The associations between XLPE type (Marathon, Longevity and X3) and medial, proximal, anterior, 2D and 3D bedding-in were examined. Only proximal bedding-in was found to be significantly associated with XLPE type ($p<0.0001$), with Marathon XLPE (Cohort A) having the highest mean proximal bedding-in (0.11 mm) compared to Longevity (Cohorts B, C, D combined: 0.06 mm) and X3 XLPE (Cohort E, F combined: 0.01 mm), as seen in Figure 4.21. Proximal bedding-in within the first year for each cohort is presented in Table 4.21 and Figure 4.22. XLPE type was not associated with medial, anterior, 2D or 3D bedding-in. Sex was not associated with medial, proximal, anterior 2D or 3D bedding-in.

No continuous predictors (acetabular component outer diameter, acetabular component inclination, BMI or age) showed a strong correlation with any axis of bedding-in.

Table 4.21: Proximal bedding-in (mm) by cohort

Bedding-in between 1 week and 1 year (mm)						
	A	B	C	D	E	F
Median	0.111	0.037	0.026	0.072	0.009	0.022
Mean	0.113	0.056	0.054	0.063	0.005	0.010
SD	0.092	0.065	0.093	0.080	0.061	0.094
Range	-0.012 to 0.389	-0.080 to 0.208	-0.085 to 0.372	-0.126 to 0.200	-0.094 to 0.119	-0.157 to 0.138

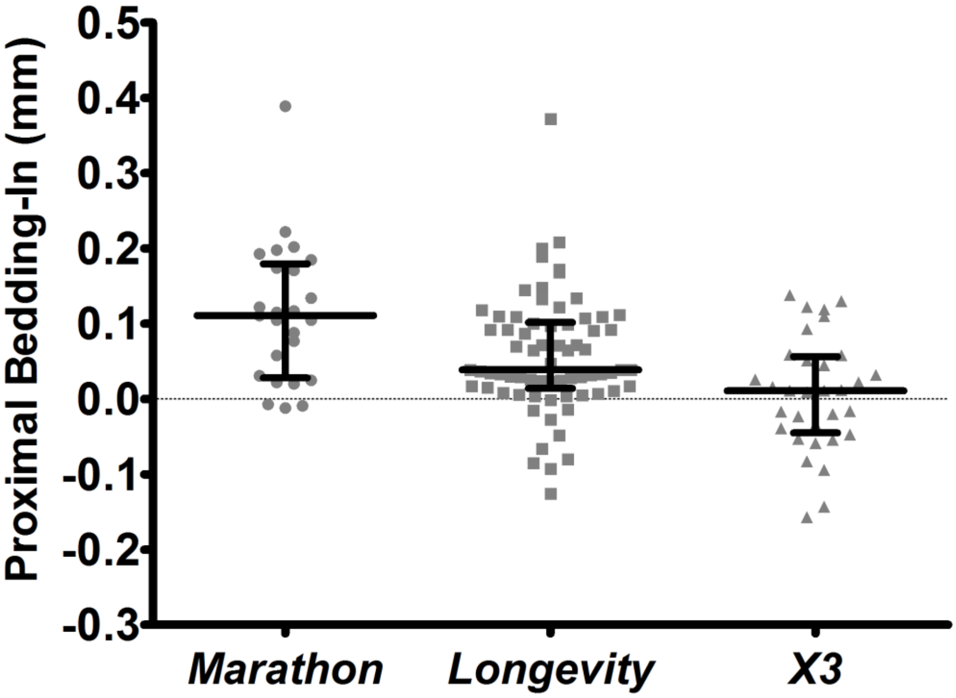

Figure 4.21: Proximal bedding-in (median, interquartile range) within the first year, by XLPE type

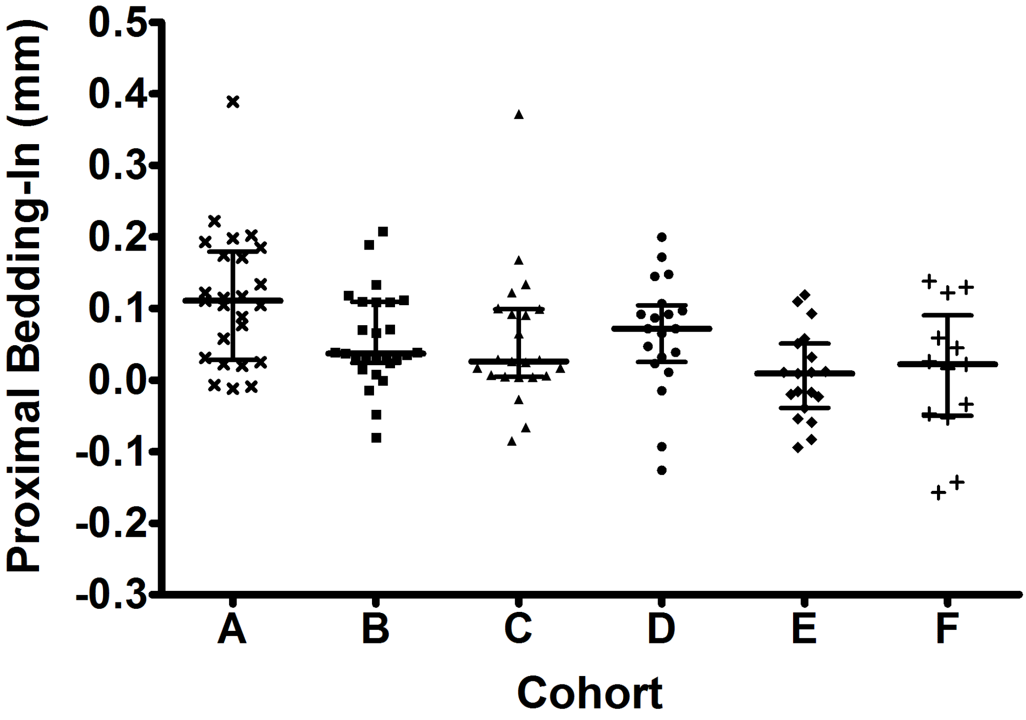

Figure 4.22: Proximal bedding-in (median, interquartile range) within the first year, by cohort

4.10.4 Wear Rate Between One and Two Years

The median proximal wear rate between one and two years is presented for each cohort in Table 4.22 (Figure 4.23). Medial, proximal, anterior, 2D and 3D wear rates between one and two years were not significantly associated with XLPE type, sex acetabular component outer diameter, inclination, BMI or age (Figures 4.23, 4.24 and 4.25).

Table 4.22: Proximal wear rate between one and two years (mm/yr) by cohort

Wear rate between 1 and 2 years (mm/yr)						
	A	B	C	D	E	F
Median	-0.002	0.011	-0.016	0.017	0.015	0.014
Mean	0.006	0.016	0.010	0.024	0.023	0.019
SD	0.083	0.066-	0.082	0.068	0.079	0.094
Range	-0.177 to 0.178	-0.143 to 0.167	-0.183 to 0.213	-0.100 to 0.218	-0.130 to 0.214	-0.146 to 0.157

*6 years for Cohort A

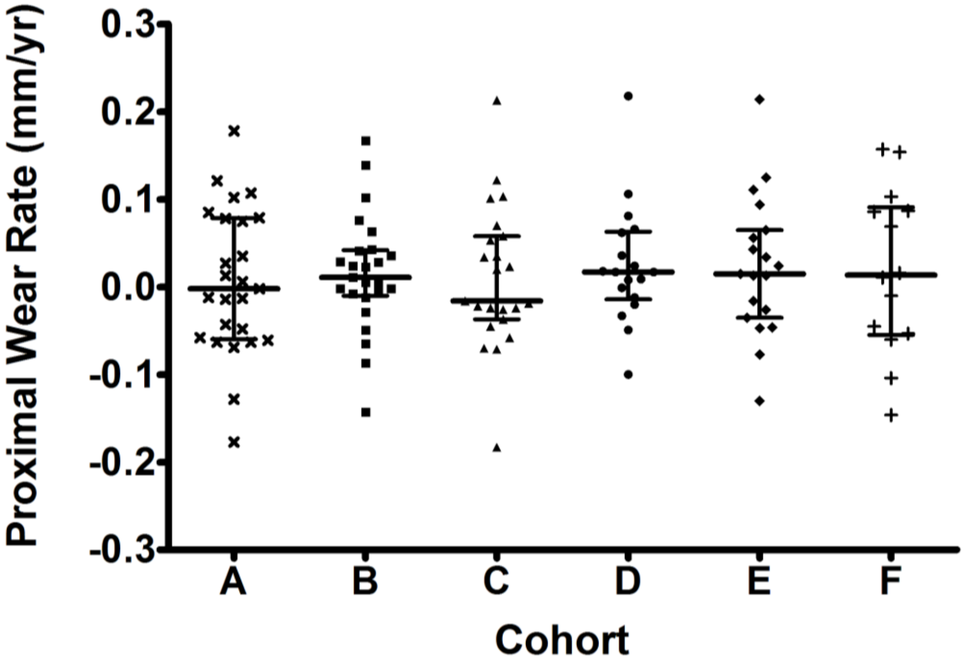

Figure 4.23: Proximal wear rate (median, interquartile range) between one and two years, by cohort

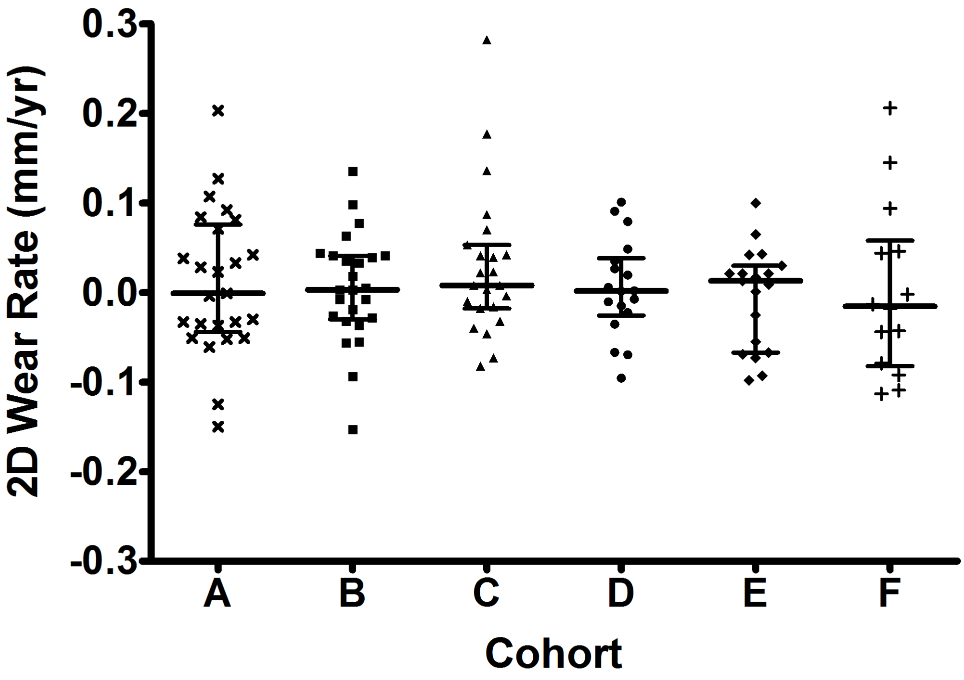

Figure 4.24: 2D wear rate (median, interquartile range) between one and two years, by cohort

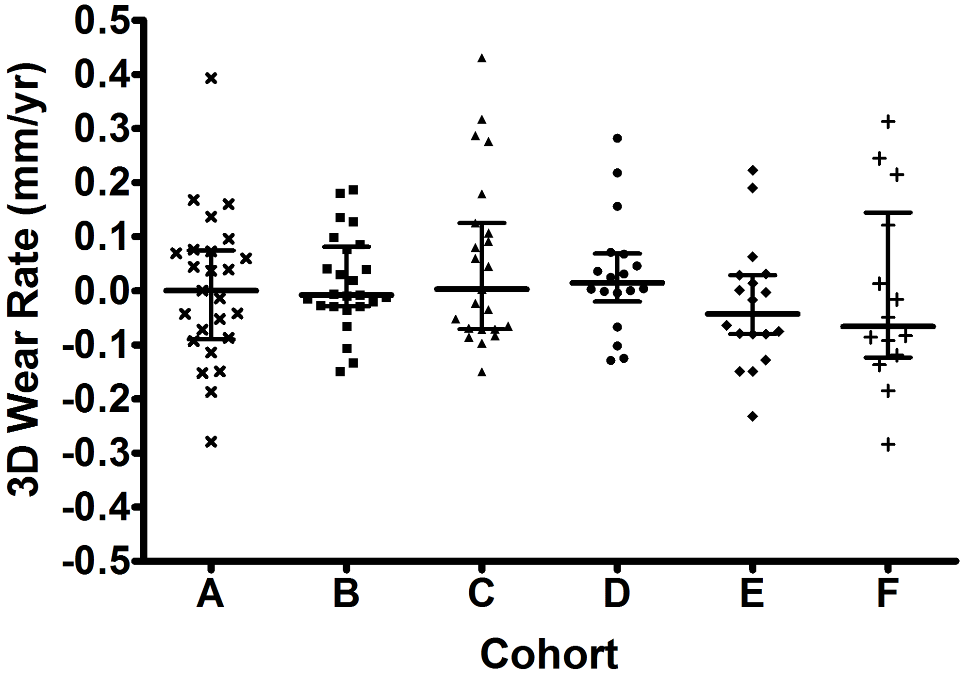

Figure 4.25: 3D wear rate (median, interquartile range) between one and two years, by cohort

4.10.5 Wear Rate between One and Five Years

The median proximal wear rate between one and five years is presented for each cohort in Table 4.23 and Figure 4.26. There was no association between XLPE type or sex and medial, proximal or anterior wear between one and five years. The 2D and

3D wear rate between one and five years was significantly associated with XLPE type (p=0.0262 and p=0.0027 respectively) (Figures 4.27 and 4.28). Marathon XLPE had the highest median 2D and 3D wear rate compared to Longevity and X3 (Figures 4.29 and 4.30).

Table 4.23: Proximal wear rate between one and five years (mm/yr) by cohort

Wear rate between 1 and 5* years (mm/yr)						
	A	B	C	D	E	F
Median	0.009	0.003	-0.002	0.004	0.004	-0.004
Mean	0.014	0.003	0.003	-0.001	0.001	-0.003
SD	0.021	0.022	0.014	0.025	0.018	0.027
Range	-0.015 to 0.063	-0.045 to 0.048	-0.014 to 0.032	-0.049 to 0.034	-0.033 to 0.033	-0.052 to 0.032

*6 years for Cohort A

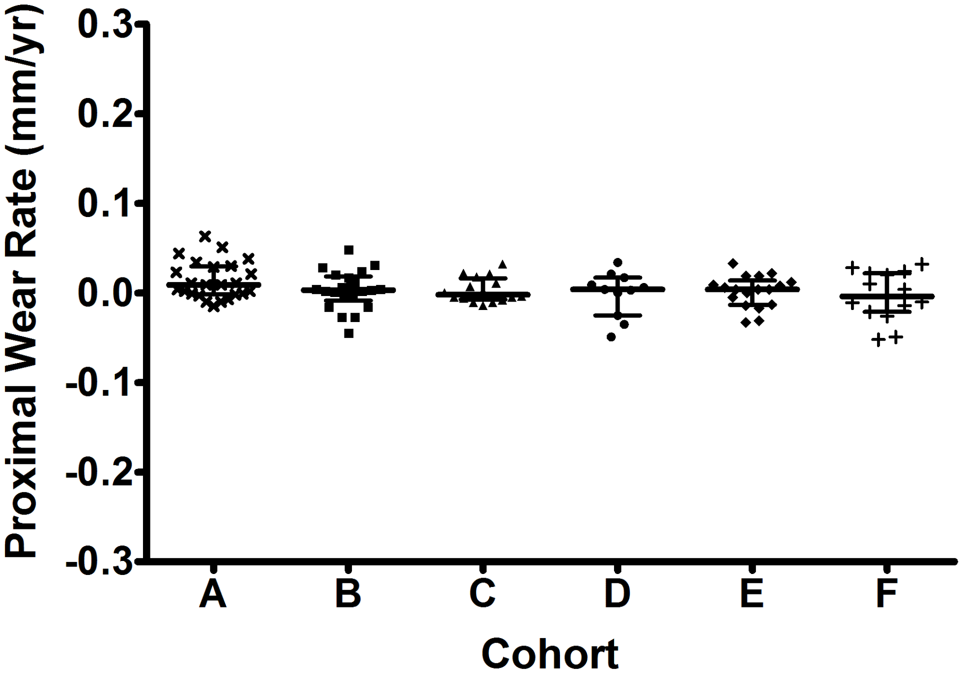

Figure 4.26: Proximal wear rate (median, interquartile range) between one and five years, by cohort

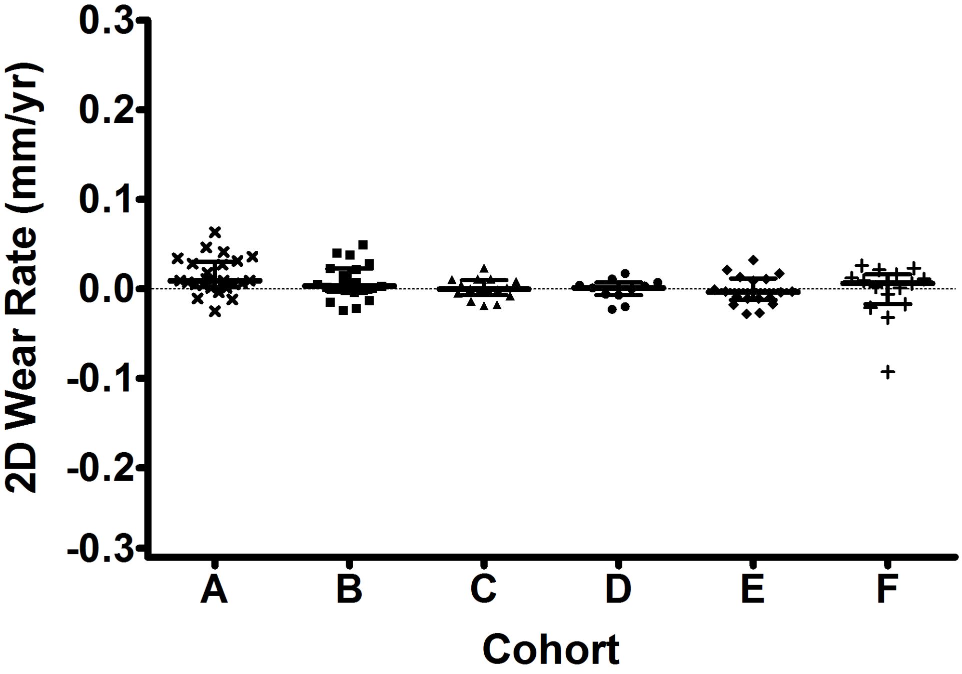

Figure 4.27: 2D wear rate (median, interquartile range) between one and five years, by cohort

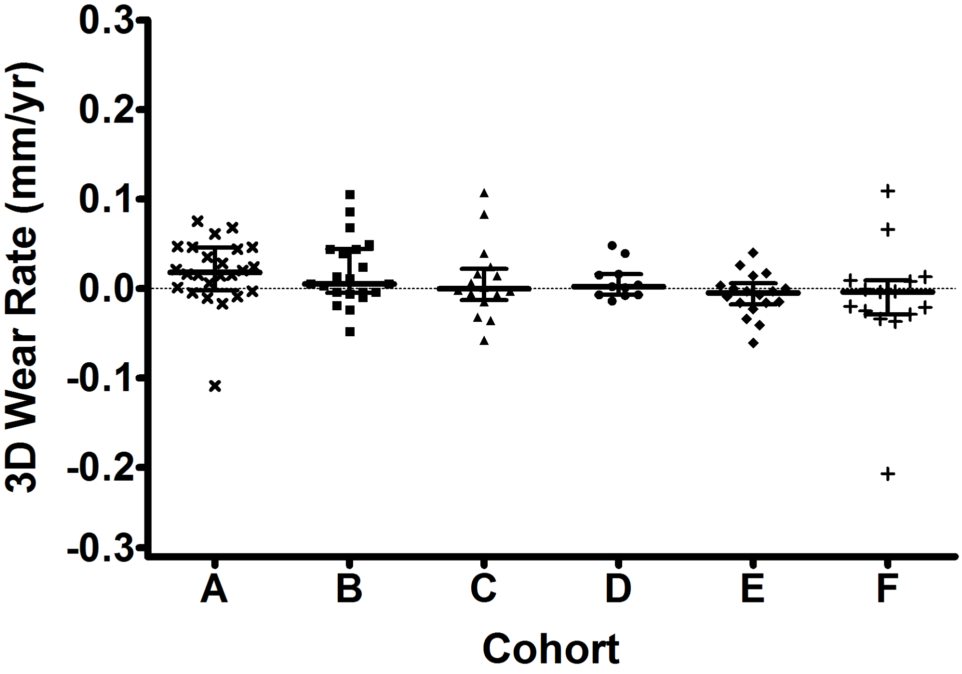

Figure 4.28: 3D wear rate (median, interquartile range) between one and five years, by cohort

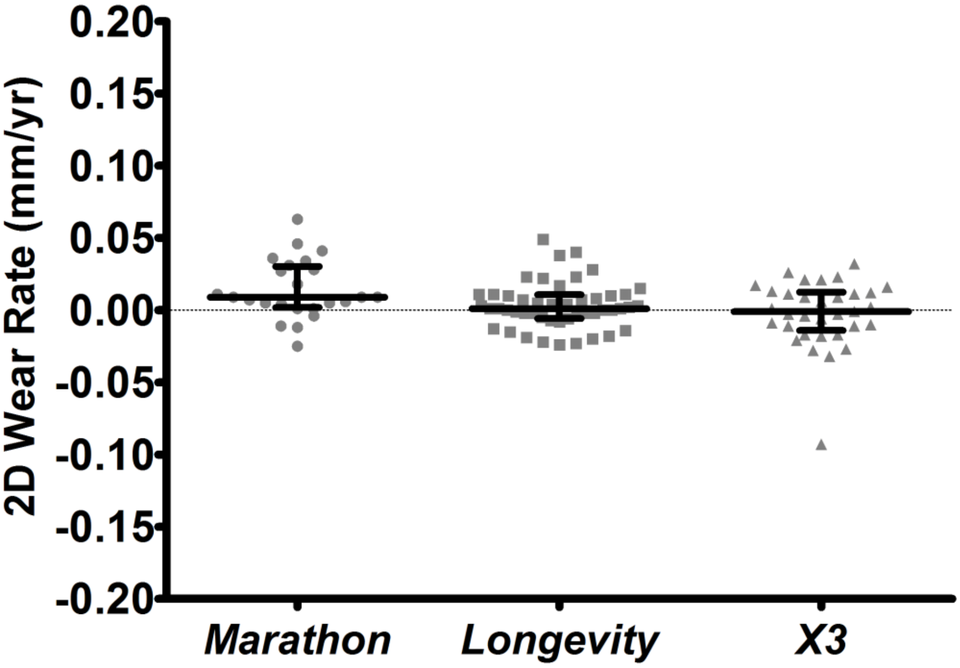

Figure 4.29: The 2D wear rate (median, interquartile range) between one and five years, by XLPE type

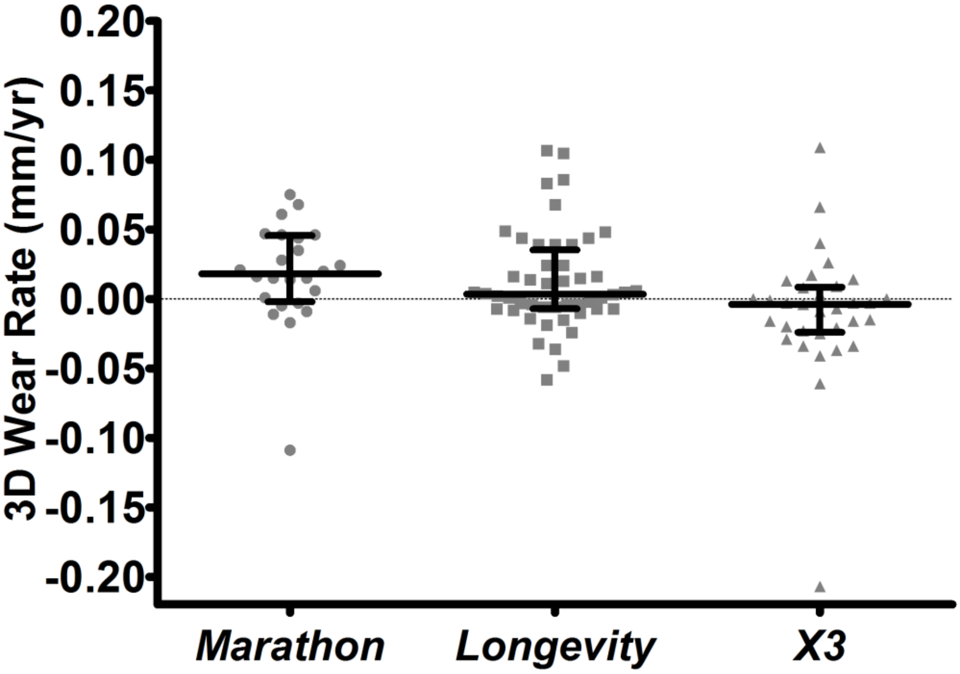

Figure 4.30: The 3D wear rate (median, interquartile range) between one and five years, by XLPE type

It is important to note the reduced range of wear rates found at five years compared to two years, as wear rate decreases over time in our study (Figure 4.31).

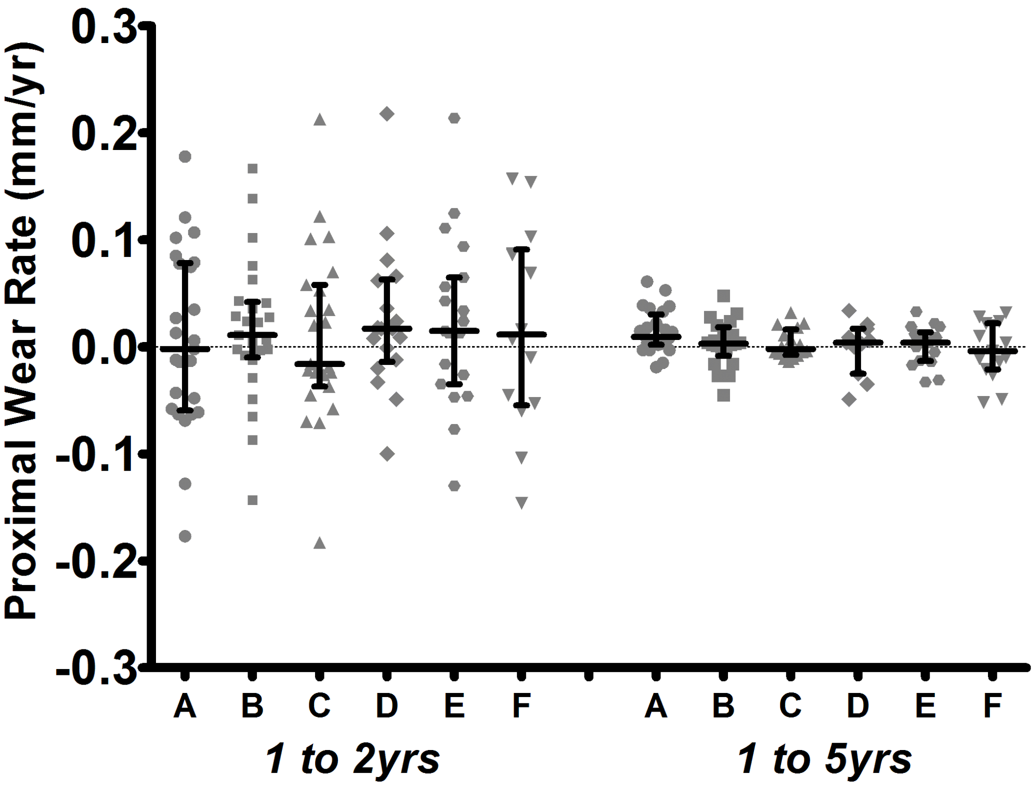

Figure 4.31: The proximal wear rate (median, interquartile range) for each individual in all six cohorts combined between one and two years, and between one and five years

There was no strong correlation between acetabular component outer diameter, inclination, BMI or age and the wear rate between one and two or five years in any axis. The following Figures 4.32, 4.33 and 4.34 show scatterplots of acetabular component outer diameter, BMI and age against proximal wear between one and five years. Acetabular component inclination was compared to medial wear rate between one and five years to demonstrate there was no trend for an increased lateral wear rate with a higher inclination (Figure 4.35).

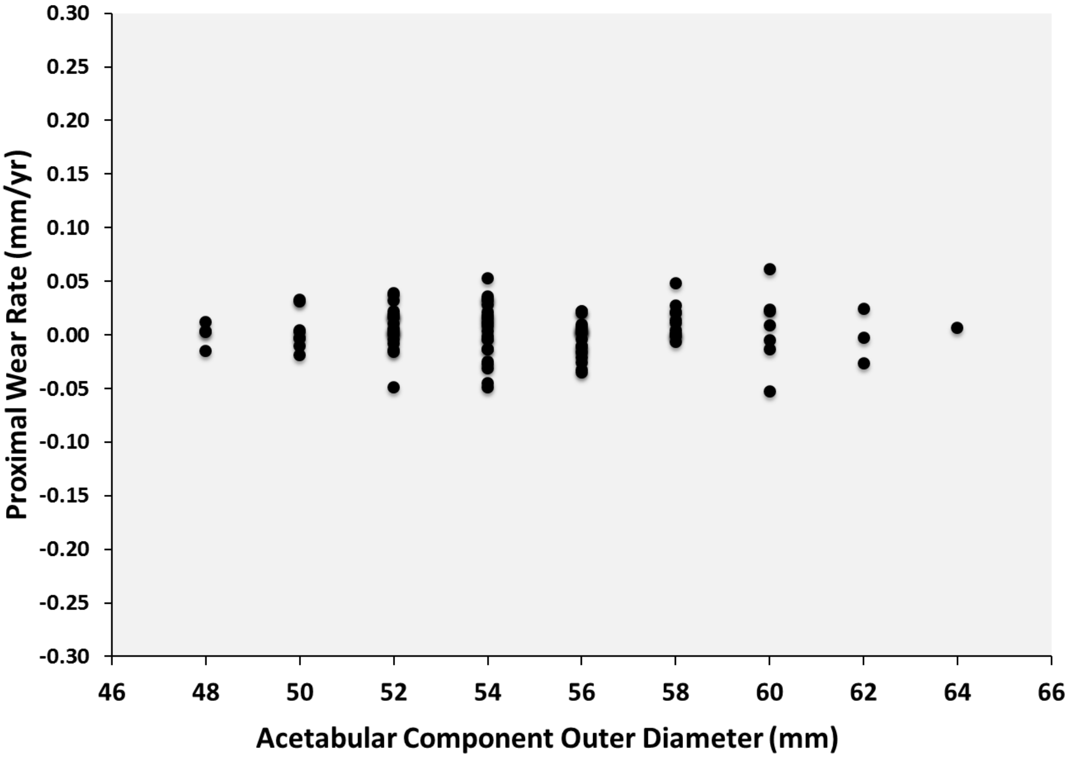

Figure 4.32: Proximal wear rate between one and five years versus acetabular component outer diameter

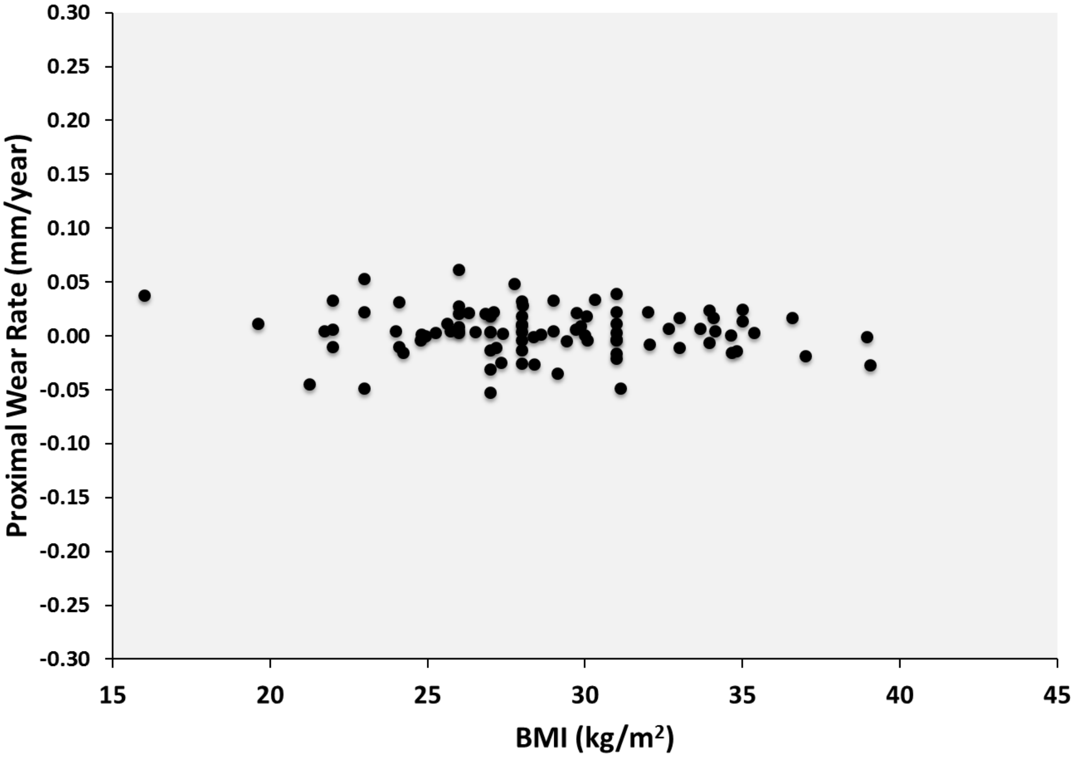

Figure 4.33: Proximal wear rate between one and five years versus BMI

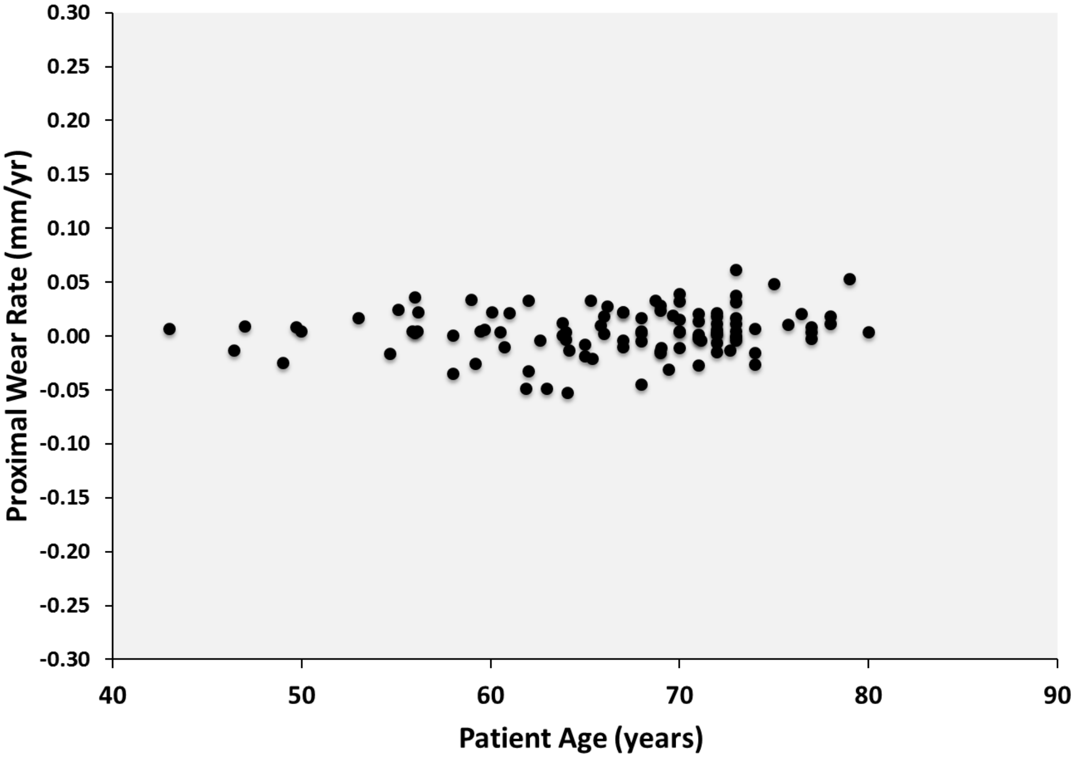

Figure 4.34: 3D wear rate between one and five years versus patient age

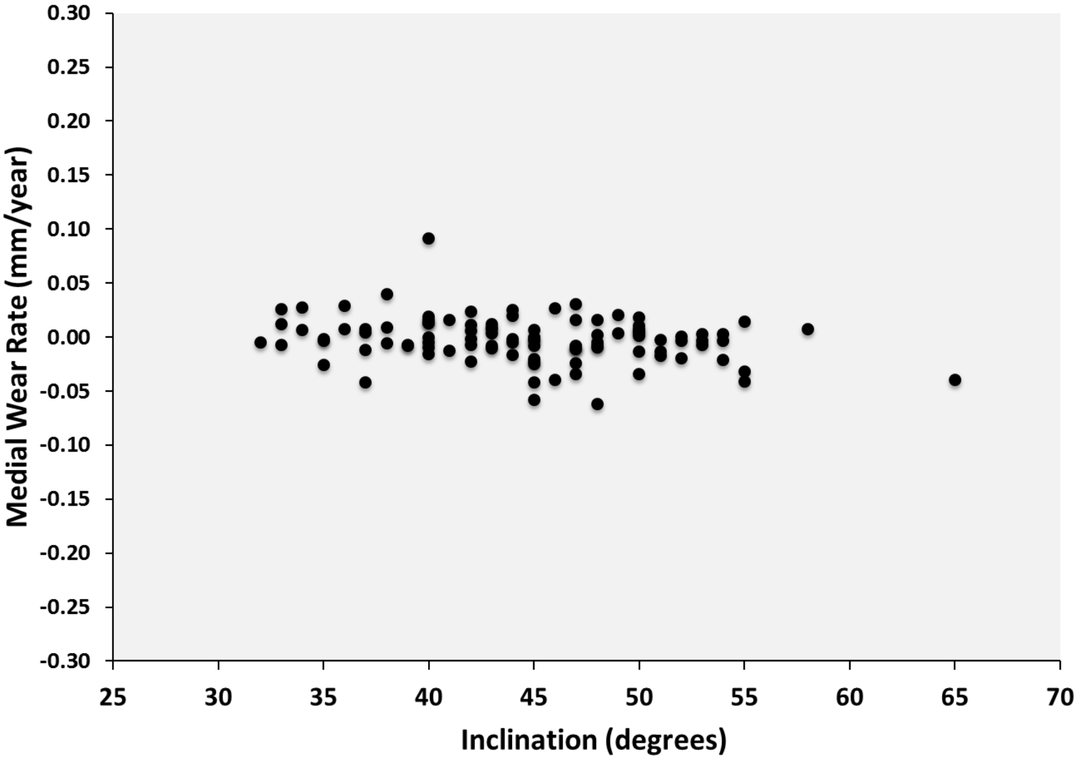

Figure 4.35: Medial wear rate between one and five years versus acetabular component inclination

4.10.6 *Wear Rates above 0.1 mm/yr*

A review of the literature found that osteolysis is infrequent when wear rates are less than 0.1 mm/yr and almost absent below 0.05 mm/yr (Dumbleton et al., 2002). The numbers of patients in each cohort who had a wear rate above either 0.05 mm/yr or 0.1 mm/yr at two and five years are presented in Table 4.24, as is the total number of patients across all cohorts. Although at two years 15%, 9% and 19% of patients had, respectively a proximal, 2D or 3D wear rate exceeding 0.1 mm/yr, at five years no patient had a proximal or 2D wear rate exceeding 0.1 mm/yr and only three of 105 patients (one patient from each of Cohorts B, C and F) had a 3D wear rate exceeding 0.1 mm/yr.

These data are a further indication that the wear rate of XLPE plateaus over time. Of importance, however, is the finding that very few patients had a wear between one and five years above the threshold rate considered to be a risk factor for the development of osteolysis with conventional UHMWPE.

Table 4.24: The number of patients in each cohort who had a wear rate above either 0.05 mm/yr or 0/1 mm/yr at two and five years

Wear rate between one and two years	**A (n=25)**	**B (n=25)**	**C (n=23)**	**D (n=18)**	**E (n=19)**	**F (n=14)**	**Total (%) (n= 125)**
Prox >0.05 mm/yr	8	5	7	5	6	6	37 (30)
Prox >0.1 mm/yr	4	3	4	2	3	3	19 (15)
2D >0.05 mm/yr	7	4	6	3	2	3	25 (20)
2D >0.1 mm/yr	3	1	3	1	1	2	11 (9)
3D >0.05 mm/yr	9	7	10	5	3	4	38 (31)
3D >0.1 mm/yr	4	4	7	3	2	4	24 (19)
Wear rate between one and five years	**A (n=24)**	**B (n=21)**	**C (n=16)**	**D (n=11)**	**E (n=18)**	**F (n=15)**	**Total (%) (n= 105)**
Prox >0.05 mm/yr	2	0	0	0	0	0	2 (2)
Prox >0.1 mm/yr	0	0	0	0	0	0	0
2D >0.05 mm/yr	1	0	0	0	0	0	1 (1)
2D >0.1 mm/yr	0	0	0	0	0	0	0
3D >0.05 mm/yr	4	3	2	0	0	1	10 (10)
3D >0.1 mm/yr	0	1	1	0	0	1	3 (3)

4.11 DISCUSSION

4.11.1 Comparison to Other RSA Studies of XLPE

The individual RSA data were only available for the cohorts examined as part of this thesis. The mean proximal and 3D FHP, bedding-in and wear rates at different follow-up are compared to those RSA studies of XLPE wear reported in the literature in Tables 4.25 and 4.26. Cohorts are listed as reported in the scoping review (1 to 12). Studies of new third generation XLPE components with added antioxidants were not included for comparison. Four additional papers have been published since the scoping review that report longer term wear results of Cohorts 5, 6, 7, 8, 11 and 12 (Ayers et al., 2015; Glyn-Jones et al., 2015; Jonsson et al., 2015; Nebergall et al., 2016) and the proximal and 3D results for these studies have been added within Tables 4.25 and 4.26. Each of these studies reported low wear rates. Of particular interest is the study by Nebergall et al. (2016) because this study represents the longest follow-up of an RSA cohort in the literature to date. Specifically, at 13 years follow-up for Longevity XLPE liners with 28 and 36mm articulations, the proximal wear rate was 0.00 mm/year. However, this wear rate was based on only six patients with 28mm articulations and six patients with 36mm articulations. Two new cohorts of patients with XLPE components were added to the literature since the scoping review was undertaken (Gascoyne et al., 2014; Flatoy et al., 2015). These are shown in Tables 4.25 and 4.26 as Cohorts 13 and 14, comprising 19 hips with X3 XLPE liners at five years follow-up and 22 hips with Marathon XLPE liners at two years follow-up respectively.

The proximal and 3D wear rates reported in the six cohorts in this thesis were similar to those reported in other RSA studies of XLPE. Cohort A had a higher mean proximal bedding-in compared to most other cohorts. Cohorts 1, 2 and 7 reported a higher than expected mean 3D wear rate at two years which is likely to be due to the fact that these wear rates were calculated between three months and two years, not between one and two years. Hence, some bedding-in may have been included within these early wear rate results.

Table 4.25: Proximal FHP, bedding-in and wear rate reported for each cohort in each follow-up report

Cohort #	Follow-up (yrs)	Publication	Proximal		
			Femoral Head Penetration [a] (mm)	**Bedding-In [b] (mm)**	**Wear Rate [c] (mm/yr)**
1	2	(Digas et al., 2003)	0.13 (0.03 to 0.31) [d]	0.1 [d]	0.03 [f] (3-24m) [e]
	3	(Digas et al., 2004)	0.13 (-0.02 to 0.30) [d]	0.1 [d,g]	0.03 [f] (3-36m) [e]
	5	(Digas et al., 2007)	0.15 (-0.10 to 0.86) [d]	0.1 [d,g]	0.02 [f] (3-60m) [e]
	10	(Johanson et al., 2012)	0.15 [g]	0.1 [d,g]	0.01 (SE 0.00) (2-10y)[d]
2	2	(Digas et al., 2004)	0.08 (-0.03 to 0.28) [d]	0.08 [d]	0.03 [f] (3-24m) [e]
	5	(Digas et al., 2007)	0.08 (-0.02 to 0.24) [d]	0.08 [d,g]	0.02 [f] (3-60m) [e]
3	3	(Rohrl et al., 2005)	NR	0.05 (0-2m)	0.01 (2-24m)
	6	(Rohrl et al., 2007)	0.08 (CI 0.02 to 0.13)	0.06 [g]	0.01 (2-72m)
	10	(Rohrl et al., 2012)	0.07 (CI-0.02 to 0.15)	0.06 [g]	0.00 (2-120m)
4	2	(Zhou et al., 2006)	0.07 [g]	0.06 [g]	0.01 (2-24m)
5	3	(Bragdon et al., 2007)	0.06 [h] (SE 0.03)	0.06 [h] (SE 0.04)	0.03 [h] (SE 0.02)
	13 [i]	(Nebergall et al., 2016)	0.08 (SE 0.03)	0.07 (SE 0.03)	0.01 [f] (SE 0.00)
6	3	(Bragdon et al., 2007)	0.06 [h] (SE 0.06)	0.07 [h] (SE 0.02)	0.00 [h] (SE 0.06)
	13 [i]	(Nebergall et al., 2016)	0.03 (SE 0.02)	0.04 (SE 0.02)	0.00 [f] (SE 0.00)
7	2	(Glyn-Jones et al., 2008a)	NR	NR	0.06 (SD 0.07) (3-24m)
	3	(Glyn-Jones et al., 2008b)	NR	0.17 [g]	0.02 [g]
	7	(Thomas et al., 2011)	NR	NR	0.01 (CI ±0.03)
	10 [i]	(Glyn-Jones et al., 2015)	NR	NR	0.00 (CI ±0.03)
8	2	(Ayers et al., 2009)	0.07 [h] (-0.04 to 0.19)	0.07 (-0.14 to 0.16)	0.02 [g]
	5 [i]	(Ayers et al., 2015)	0.08 [h] (SE ±0.01)	0.07 [h] (SE ±0.02)	0.00 [h]
11	2	(Kadar et al., 2011)	0.09 (CI 0.06 to 0.12)	0.06 [g]	0.03
	5 [i]	(Jonsson et al., 2015)	0.12 (SD 0.16)	0.06 (SD 0.08)	0.02 (SD 0.03)
12	2	(Kadar et al., 2011)	0.08 (CI 0.04 to 0.12)	0.06 [g]	0.02
	5 [i]	(Jonsson et al., 2015)	0.10 (SD 0.10)	0.06 (SD 0.07)	0.01 (SD 0.01)
13	5 [i]	(Gascoyne et al., 2014)	0.03 [h]	NR	0.00 [h] (CI 0.00 to 0.00)
14	2 [i]	(Flatoy et al., 2015)	0.11[h](CI 0.09 to 0.14)	NR	0.04 [h]
Current Thesis Cohorts					
A	2	(Campbell et al., 2010a)	0.12 (-0.10 to 0.38)	0.11 (-0.01 to 0.39)	0.01 (-0.18 to 0.18)
	6	(Callary et al., 2013a)	0.19 (0.00 to 0.51)	0.11 (-0.01 to 0.39)	0.01 (-0.02 to 0.06)
B	2		0.07 (-0.06 to 0.25)	0.06 (-0.08 to 0.21)	0.02 (-0.14 to 0.17)
	3	(Howie et al., 2016)	0.07 (-0.08 to 0.25)	0.06 (-0.08 to 0.21)	0.01 (-0.05 to 0.07)
	5		0.08 (-0.08 to 0.33)	0.06 (-0.08 to 0.21)	0.00 (-0.04 to 0.05)
C	2		0.06 (-0.18 to 0.48)	0.05 (-0.09 to 0.37)	0.01 (-0.18 to 0.21)
	3	(Howie et al., 2016)	0.04 (-0.13 to 0.47)	0.05 (-0.09 to 0.37)	0.00 (-0.07 to 0.07)
	5		0.06 (-0.07 to 0.38)	0.05 (-0.09 to 0.37)	0.00 (-0.01 to 0.03)
D	2		0.08 (0.00 to 0.23)	0.06 (-0.13 to 0.20)	0.02 (-0.10 to 0.22)
	3		0.08 (-0.02 to 0.21)	0.06 (-0.13 to 0.20)	0.00 (-0.08 to 0.11)
	5		0.05 (-0.09 to 0.13)	0.06 (-0.13 to 0.20)	0.00 (-0.05 to 0.03)
E	2	(Campbell et al., 2010b)	0.02 (-0.07 to 0.16)	0.01 (-0.09 to 0.12)	0.02 (-0.13 to 0.21)
	5	(Callary et al., 2013b)	0.02 (-0.11 to 0.13)	0.01 (-0.09 to 0.12)	0.00 (-0.03 to 0.03)
F	2		0.02 (-0.06 to 0.12)	0.01 (-0.16 to 0.14)	0.01 (-0.15 to 0.16)
	5	(Callary et al., 2016)	-0.01 (-0.19 to 0.16)	0.01 (-0.16 to 0.14)	0.00 (-0.05 to 0.03)

CI: 95% confidence interval
NR: not reported.

[a] Initial to final follow-up unless otherwise noted; mean (range).

[b] Initial examination to 1-year follow-up unless otherwise noted; mean (range).

[c] Annual rate from 1-year follow-up to final follow-up unless otherwise noted; mean (range).

[d] Supine

[e] Standing

[f] Manually calculated to be rate/year from a reported value given after bedding-in.

[g] Visualized from graph

[h] Median

[i] Additional publication added to scoping review data

Table 4.26: 3D FHP, bedding-in and wear rate reported for each cohort in each follow-up report

Cohort #	Follow-up (yrs)	Publication	3D		
			Femoral Head Penetration [a] (mm)	**Bedding-In [b] (mm)**	**Wear Rate [c] (mm/yr)**
1	2	(Digas et al., 2003)	0.18 (0.07 to 0.35) [d]	0.15 d	0.11 [f] (3-24m) [e]
	3	(Digas et al., 2004)	0.23 (0.04 to 0.41) [d]	0.18 [d,g]	0.09 [f] (3-26m) [e]
	5	(Digas et al., 2007)	0.23 (0.02 to 0.91) [d]	NR	0.04 [f] (3-60m) [e]
	10	(Johanson et al., 2012)	0.22 [d,g]	0.18 [d,g]	0.01 (SE 0.00)(2-10yr)[d]
2	2	(Digas et al., 2004)	0.22 (0.05 to 0.40) [d]	0.25 [d]	0.19 [f] (3-24m) [e]
	5	(Digas et al., 2007)	0.20 (0.10 to 0.61) [d]	0.24 [d]	0.07 [f] (3-60m) [e]
3	3	(Rohrl et al., 2005)	0.17 (CI 0.06 to 0.28)	NR	NR
	6	(Rohrl et al., 2007)	0.23 (CI 0.10 to 0.35)	NR	0.03 (2-72m)
	10	(Rohrl et al., 2012)	0.20 (CI 0.03 to 0.36)	0.19 [g]	0.00 [f] (2-120m)
4	2	(Zhou et al., 2006)	0.19 [g]	0.15 [g]	0.03 [f] (2-24m)
5	3	(Bragdon et al., 2007)	NR	NR	NR
	13 [i]	(Nebergall et al., 2016)	NR	NR	NR
6	3	(Bragdon et al., 2007)	NR	NR	NR
	13 [i]	(Nebergall et al., 2016)	NR	NR	NR
7	2	(Glyn-Jones et al., 2008a)	0.31 (SD 0.18)	0.30 [g]	0.06 (SD 0.06) (3-24m)
	3	(Glyn-Jones et al., 2008b)	0.35 (SD 0.14)	0.26 (SD 0.17)	0.03 (SD 0.06)
	7	(Thomas et al., 2011)	0.33 (CI ±0.10)	0.29 (CI ±0.07)	0.01 (CI ±0.02)
	10 [i]	(Glyn-Jones et al., 2015)	0.33 (CI ±0.10)	NR	0.00 (CI ±0.00)
8	2	(Ayers et al., 2009)	NR	NR	NR
11	2	(Kadar et al., 2011)	0.19 (CI 0.15 to 0.23)	NR	NR
	5 [i]	(Jonsson et al., 2015)	NR	NR	NR
12	2	(Kadar et al., 2011)	0.18 (CI 0.13 to 0.22)	NR	NR
	5 [i]	(Jonsson et al., 2015)	NR	NR	NR
13	5 [i]	(Gascoyne et al., 2014)	0.20 [h]	NR	-0.01 (CI 0.00 to 0.00)
14	2 [i]	(Flatoy et al., 2015)	0.14[h] (CI 0.12 to0.16)	NR	NR
Current Thesis Cohorts					
A	2	(Campbell et al., 2010a)	0.23 (0.02 to 0.84)	0.23 (0.06 to 0.93)	0.00 (-0.28 to 0.39)
	6	(Callary et al., 2013a)	0.32 (0.05 to 0.60)	0.23 (0.06 to 0.93)	0.02 (-0.11 to 0.08)
B	2		0.17 (0.03 to 0.36)	0.16 (0.05 to 0.40)	0.02 (-0.15 to 0.19)
	3	(Howie et al., 2016)	0.22 (0.02 to 0.79)	0.16 (0.05 to 0.40)	0.04 (-0.11 to 0.36)
	5		0.21 (0.05 to 0.56)	0.16 (0.05 to 0.40)	0.02 (-0.05 to 0.10)
C	2		0.25 (0.05 to 0.82)	0.20 (0.07 to 0.73)	0.05 (-0.15 to 0.43)
	3	(Howie et al., 2016)	0.22 (0.04 to 0.73)	0.20 (0.07 to 0.73)	0.01 (-0.10 to 0.14)
	5		0.26 (0.07 to 0.82)	0.20 (0.07 to 0.73)	0.01 (-0.06 to 0.10)
D	2		0.20 (0.07 to 0.42)	0.18 (0.08 to 0.38)	0.03 (-0.13 to 0.28)
	3		0.17 (0.06 to 0.43)	0.18 (0.08 to 0.38	-0.1 (-0.11 to 0.10)
	5		0.21 (0.09 to 0.47)	0.18 (0.08 to 0.38	0.01 (-0.02 to 0.05)
E	2	(Campbell et al., 2010b)	0.15 (0.07 to 0.26)	0.18 (0.02 to 0.32)	-0.03 (-0.23 to 0.22)
	5	(Callary et al., 2013b)	0.15 (0.04 to 0.32)	0.18 (0.02 to 0.32)	-0.01 (-0.06 to 0.04)
F	2		0.21 (0.11 to 0.43)	0.24 (0.09 to 0.55)	-0.01 (-0.28 to 0.31)
	5	(Callary et al., 2016)	0.18 (0.05 to 0.38)	0.24 (0.09 to 0.55)	-0.01 (-0.21 to 0.11)

CI: 95% confidence interval
NR: not reported.

[a] Initial to final follow-up unless otherwise noted; mean (range).

[b] Initial examination to 1-year follow-up unless otherwise noted; mean (range).

[c] Annual rate from 1-year follow-up to final follow-up unless otherwise noted; mean (range).

[d] Supine

[e] Standing

[f] Manually calculated to be rate/year from a reported value given after bedding-in.

[g] Visualized from graph

[h] Median

[i] Additional publication added to scoping review data

4.11.2 Different XLPE components

Small differences may exist in the *in vivo* wear rates of different XLPE liners because of different polyethylene stock and manufacturing methods being used. Of all published RSA studies to date, the wear rate of seven different XLPE components have been investigated. Of the studies undertaken as part of this thesis, two publications were the first to report the wear rate of Marathon and X3 XLPE liners. Marathon XLPE liners (Cohort A) were found to have a higher amount of proximal bedding-in within the first year compared to the other XLPE liners in this thesis. Increased bedding-in may be due to manufacturing design and fit of the liner within the metal-backed shell or the mechanical properties of the liner that allow more permanent deformation during the early postoperative period. One recent study reported a significantly increased bedding-in with a remelted XLPE liner (0.234 mm) compared to an annealed XLPE liner (0.159 mm) and no difference in the wear rate thereafter up until latest follow-up at ten years (Hamai et al., 2016). Over time orthopaedic companies have improved the conformity of liners within the shell by improving design and associated locking mechanisms. The Marathon XLPE liner was also found to have a higher 2D and 3D wear rate between one and five years than the other XLPE liners. The only other RSA study of Marathon XLPE liners reported the highest median proximal wear rate of any XLPE component in the RSA literature (0.036 mm/yr, Table 4.25). This increased wear rate may be due to the fact that Marathon XLPE liner is manufactured with a lower level of gamma irradiation (5mRad) compared to other XLPE liners (Table 1.1). This XLPE liner requires further follow-up as this amount of proximal wear is similar to that of a conventional UHMWPE liner reported in an RSA study at two and five years (0.05 and 0.04 mm/year respectively) (Ayers et al., 2009; Ayers et al., 2015). It is interesting to note, however, that the number of hips with wear rates above the historical thresholds associated with osteolysis were not over represented in Cohort A, as seen in Table 4.24.

4.11.3 Direction

The direction of the FHP, bedding-in and wear rate was investigated in medial, proximal, anterior, 2D and 3D axes. The direction of wear in conventional UHMWPE liners was most commonly observed to be in a proximal direction (Dowling et al., 1978) or a proximal-lateral direction (Charnley et al., 1975). The majority of FHP in five cohorts examined at five years was proximal and no patient’s

FHP exceeded 0.3 mm medially or 0.3 mm laterally. The FHP in Cohort A between one week and six years was in a proximal direction for all patients and proximal-lateral for 16 of 24 patients. Only one study amongst all the published RSA wear studies of XLPE liners has reported results in medial axis and that study found the majority of the FHP at seven years to be in the proximal-lateral direction (Thomas et al., 2011).

4.11.4 Wear Rates Decrease over Time

Both in the six cohorts examined in this thesis and in the other published RSA studies of XLPE, the wear rate decreased as more years were included in follow-up. That the range of results also decreased over time indicates that there is very little additional FHP occurring after one year and, because the measured FHP value at longer term follow-up is being divided by more years, this results in a decreased wear rate. For example, the reported 3D wear rate of the Crossfire liner was 0.033 mm/yr at 6 years (Rohrl et al., 2007), but this decreased to 0.002 mm/yr at 10 years follow-up (Rohrl et al., 2012).

The decrease over time in both average wear rates and their range translates also to a reduction in the number of patients with wear rates above historical thresholds, as seen in Table 4.24, which is encouraging for the continued use of XLPE liners. Figure 4.36 below shows that of the six cohorts in this thesis, Cohort A (Marathon XLPE) was the only cohort in which the mean proximal wear rate increased over time. The higher proximal wear rate of Cohort A at five years may be due the Marathon XLPE liner being manufactured with a lower dose of gamma irradiation (50kGy). This irradiation dose is at the lower range of PE components included as a XLPE and sometimes in the literature the Marathon XLPE liner is actually referred to a moderately cross-linked PE for this reason.

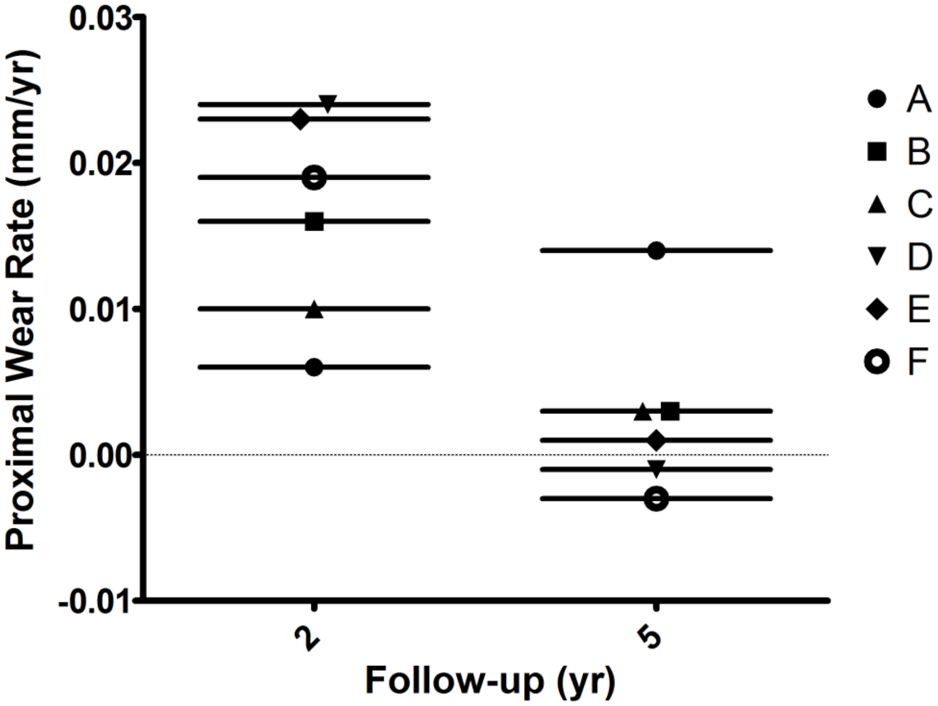

Figure 4.36: Mean proximal wear rate (mm/yr) between one and two or five years by cohort

4.11.5 Influence of Articulation Size on Wear of XLPE

Two of the manuscripts included in this Chapter directly examined the effect of articulation size on wear (Callary et al., 2016; Howie et al., 2016). Both found that larger articulations did not significantly increase the early wear rate *in vivo*.

4.11.6 Influence of Age on Wear of XLPE

The influence of age on wear rates was examined by comparing two cohorts of patients that differed only by age (40-64 years versus 65-74 years). No difference in wear rates were identified.

In the regression analysis of the wear data from all cohorts combined, there was no strong correlation between age and XLPE wear in any axis, suggesting that XLPE wear rates are not increased in younger patients, supporting the finding of low XLPE wear in young patients in a recent study (Garvin et al., 2015).

4.11.7 Strengths and Limitations

There were several limitations to the clinical wear studies. These included the relatively small sizes of the cohorts, the use of supine RSA examinations, inclusion of negative wear in the determination of mean and median values, the use of directionless vectorial sums for 2D and 3D wear measurements and very few volumetric estimations. Furthermore, the presence of periprosthetic osteolysis was not investigated in any cohort.

4.11.7.1 Nature of Cohorts

The six cohorts included relatively small numbers of patients. Importantly, however, unless specifically stated, *post hoc* power analyses confirmed adequate power for the analyses that were undertaken and reported in this thesis. Furthermore, the use of RSA to measure wear, which is internationally recognised as the most sensitive measure of wear and therefore regarded as the gold standard technique, permits the use of smaller samples than would be acceptable if other, less sensitive techniques were used. One limitation of RSA studies is the requirement for unique RSA radiographic examinations to be done prospectively. Patient follow-up at a centre with RSA equipment (calibration cage) is required. A number of patients are usually excluded over time from RSA studies for reasons relating specifically to RSA, over and above loss to follow-up due to death, illness or other reasons for inability to undergo RSA follow-up. For example, in an RSA study of cemented Marathon XLPE components (Cohort 14, Table 4.25), of 66 patients who completed their two year follow-up only 22 hips were included in RSA wear analyses at two years due to missing postoperative images, a CN>150, non-visible markers and a MERBF >0.3, (Flatoy et al., 2015).

The most appropriate study design to investigate the effects of implant, patient or surgical factors on XLPE wear is a randomised controlled trial within which the cohorts being compared vary with respect to one factor, such as the type of XLPE, patient age or articulation size. The comparison of Cohorts B and C to examine the effect of articulation size on XLPE wear and Cohorts B and D to examine the effect of patient age on wear fulfilled this requirement, given that other patient characteristics were comparable across these cohorts.

Examination of single surgeon cohorts are the next best option, followed by multiple regression analysis of a large sample of data pooled from multiple cohorts. The cohorts analysed as part of Chapter 4 collectively represent 125 hips with a recorded wear rate at 2 years and 105 hips at 5 years, the largest pool of individual XLPE wear data obtained using RSA. Importantly, RSA techniques were constant across all cohorts and all analyses were undertaken by one individual, namely the PhD candidate. The other published RSA cohorts lacked this consistency, as described in the systematic search detailed in Chapter 2. One limitation related to the use of pooled data was the potential disadvantage of confounding variables of interest. For example, Cohort A which was the only cohort with Marathon XLPE, showed the highest proximal wear at five years, which was most likely due to this type of XLPE undergoing the lowest level of gamma irradiation. Therefore, the results of the pooled analyses of the effects of other variables on wear may be confounded by the effect of XLPE type.

4.11.7.2 Supine RSA Examinations (see section 3.6.1.4)

All RSA radiographs across all cohorts analysed as part of this thesis were taken with the patient in a supine position. In an attempt to measure the femoral head in its deepest wear track within the acetabular component, some other studies have used standing rather than supine radiographs. One study found weight bearing radiographs increased the measured wear due to the femoral head sitting in the deepest part of its wear track (Smith et al., 1999). In contrast, another study found no difference in wear determined from weight bearing and supine radiographs (Moore et al., 2000). However, since then, three RSA studies have confirmed no statistically significant difference in XLPE wear measured from standing and supine XLPE radiographs (Digas et al., 2004; Bragdon et al., 2006; von Schewelov et al., 2006). For example, in patients who had both standing and supine RSA examinations, the proximal FHP between 3 months and 3 years did not differ between radiographs obtained from standing and supine examinations (Digas et al., 2004).

Standing examinations are proposed to be more important early in the postoperative period when the patient may have poor muscle tone and there may be some laxity in the hip joint (McCalden et al., 2005). However, standing RSA radiographs are more difficult to perform in the early postoperative period, particularly for older, unsteady or unwell patients. One study of XLPE wear attempted standing RSA examinations within seven days after the operation but found patients had too much discomfort and, as a result, reverted to the use of supine examinations (Digas et al., 2004). Standing radiographs of heavier patients also increase the likelihood of soft tissue overhang of the stomach in front of the area of interest resulting in poorer image quality.

4.11.7.3 Negative Wear Results

The results reported as part of this thesis have included a negative wear rate for a number of individuals within each cohort, which is common for radiographic studies of wear (McCalden et al., 2005). There are a number of reasons for these reported negative wear rates from radiographic measurements. First, the wear of XLPE is very low and some measurements are below the detectable limit of the radiographic measurement method. RSA was determined to be the most sensitive technique available to monitor *in vivo* FHP, as described in Chapter 3. The majority of proximal FHP measurements are positive and well above the detection limit of RSA. However, some negative wear rates were reported for these individuals because when bedding-in within the first year is excluded, the amount of penetration thereafter is very low.

Some studies have not included negative wear in their calculation of mean wear or have substituted the negative value with zero. However, inclusion of each individual result in the calculation of wear rates and their presentation in scatterplots provides the most accurate representation of the data. An adequately powered study allows for negative results, which should not significantly influence the calculated mean or median wear rates of the cohort (McCalden et al., 2005).

Along with accuracy and precision error, variation in the measurement methods and the small amount of wear being measured, negative wear rates may also be due to the femoral head not being seated in the deepest part of the acetabular liner at every examination. There are manufacturing tolerance errors in the production of both the femoral head and XLPE liner. Each prosthetic component is manufactured with both a tolerance limit and clearance limit. The tolerance limit is the error allowed in the manufacturing of each implant which means the femoral head may actually be slightly less than the diameter described and the liner may be larger than the diameter described. For example, if the inner diameter of the liner is meant to be 32mm it may be 31.99mm ± 0.01mm. The clearance limit is the intentional amount of difference between the outer diameter of the head and the inner diameter of the liner in order to allow lubricant within the articulation. This incongruent conformity of the femoral head within the liner allows the measurements to reflect where the femoral head happens to be in contact.

There may be other explanations for negative wear results including a small amount of expansion of the XLPE liner with the absorption of fluid and/or lipids. For example, two types of XLPE liners tested in a wear simulator showed wear rates of 1.5 and -1.4 mg/million cycles compared to control non-crosslinked PE (15.7 and 12.5 mg/million cycles) (D'Lima et al., 2003). The negative results showed a gain in weight of one type of XLPE due to fluid absorption and the authors acknowledged that the very small difference in wear rates between the XLPE designs are likely to be too small to be clinically significant (D'Lima et al., 2003).

4.11.7.4 Directionless Vectorial Sums

RSA allows measurement of the FHP in medial, proximal and anterior directions relative to the calibration cage beneath the patient (Figure 4.13). Both 2D and 3D measurements are consistently reported for FHP measurements to allow comparison to previous published studies that have used different measurement methods. 2D and 3D FHP measurements are both vectorial sums that are directionless and absolute (positive) due to the way they are calculated. For example, 2D FHP is the vectorial sum of any movement in the proximal-distal and the medio-lateral axes. It therefore only describes the magnitude of the movement and not the direction, whether it is proximal or distal. 2D measurements, commonly referred to as linear, have been used most commonly in wear studies using measurement methods other than RSA (Callary et al., 2015). Proximal and 3D FHP are the most commonly reported wear measurements in RSA studies of XLPE components (Callary et al., 2015). However, 2D RSA measurements are likely to be more accurate than 3D because they do not include the out-of-plane z-axis which is associated with higher errors. A study of conventional UHMWPE components reported that 95% of hips recorded similar 2D and 3D FHP measurements, while the remaining 5% had 3D measurements three times greater than the 2D measurements (Sychterz et al., 1999). Hence while movement out of the anterior-posterior plane is uncommon, 3D FHP should be investigated when trying to identify outliers with higher amounts of wear. Medial, proximal, anterior, 2D and 3D measurements were analysed as part of the combined cohort results in this thesis, however, if no correlation with factors was identified, proximal, 2D and 3D results have been presented as they of the most interest and provide adequate detail to compare results to previous studies.

4.11.7.5 Volumetric Calculation from Linear Measurements

Volumetric wear is commonly calculated from the linear wear measurements derived from radiographs. While less frequently reported in the literature, volumetric wear rates are arguably more clinically relevant than linear wear rates, as the volume of wear particles is likely to be associated with the development of osteolysis. Volumetric estimations have therefore been calculated from linear measurements using the known surface area of the femoral head (πr^2) multiplied by the amount of linear wear. This assumes that the wear follows a cylindrical path and may underestimate the true amount of wear. This volumetric calculation also does not take into account the direction of the wear in reference to the opening of the acetabular liner. If the wear direction is out of the component or involves part of the cylinder of wear outside of the liner, the volume of wear may be overestimated (Chuter et al., 2007) For example, volumetric wear calculated from radiographic measurements did not correlate with fluid displacement measurements made on a series of retrieved implants (Chuter et al., 2007). Despite the limitations, the simple volumetric calculation has been used in wear studies, most notable two studies commonly cited for osteolytic thresholds (Oparaugo et al., 2001; Orishimo et al., 2003). Numerous more complicated mathematical formulae have been improved over time to adjust for the direction of wear (Kabo et al., 1993; Derbyshire, 1998; Kosak et al., 2003; Ilchmann et al., 2008; Wu et al., 2010). New methods correcting for direction of wear still may underestimate actual wear due to the multi-directional nature of wear. For example volumetric wear estimations from radiographic measurements taking direction into account were 8.5% less when the fluid displacement method was used on retrieved implants and up to 15% less when direction not taken into account (Kosak et al., 2003).

Volumetric wear calculations are considered more important when investigating the wear of different sized articulations. However, the clinical studies of XLPE wear within this thesis have in most cases avoided translating volumetric wear from linear wear due to the limitations in linear radiographic measurements. Furthermore, irrespective of the sophistication of the algorithms used to calculate volumetric wear, it remains an estimation and not a measurement that can be derived directly from radiographs (Ilchmann et al., 2008).

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CHAPTER FIVE

THESIS CONCLUSIONS

5.1 Major Study Findings

A study using a phantom hip model determined that RSA has superior accuracy and reduced variability compared to HAS, PolyWare and ROMAN methods when measuring 2D FHP within metal-backed acetabular components. This was the first study that had compared the accuracy of RSA to other commonly used software methods within the same *in vitro* phantom study. The superior accuracy of RSA allows much smaller cohorts to be used in RSA clinical wear studies than those utilizing other software programs. Articulation size did influence the accuracy of some measurement methods and this should be considered prior to using those methods in studies comparing the wear of different sized articulations. A comparison between methods of representing the acetabular component indicated that the specific method used did not influence the accuracy of RSA measurements.

Despite almost universal acceptance of the use of XLPE in acetabular components, a scoping review using a systematic search of the literature determined that XLPE wear in THR had been monitored using RSA in only 10 cohorts involving 209 hips, excluding the cohorts studied within this thesis. The scoping review confirmed the low wear rates of XLPE in THR. However, due to the variation in both the methodology and manner of reporting RSA results, a number of recommendations were made to enhance the reporting of RSA wear results. These included using the terms FHP to denote the penetration from the initial examination to the specified follow-up, bedding-in/creep to represent the FHP from the initial examination to the one year examination and wear to represent the annual wear rate between the one year examination and the specified follow-up. Presentation of the results should include specification of the axis of measurement, which should usually include proximal, 2D and 3D. Furthermore, data should also be presented in scatterplots because this allows a more detailed representation of all data. Importantly, this would enable retrospective identification of individuals with higher amounts of wear, if a relationship between XLPE wear and osteolysis were to be found in the future.

Clinical RSA studies were undertaken of primary THR confirmed the low wear rates of XLPE components at five years follow-up. Through comparisons between specific cohorts and the use of pooled data it was established that articulation size and patient age at time of THR did not influence the wear rate of XLPE liners at five years. Specifically, the first RCT to examine the effect of articulation size on XLPE wear showed that the proximal, medial, 2D and 3D wear rates of a 36mm metal-on-XLPE (Longevity) articulation between one and three years were low and not significantly greater than those of a 28mm metal-on-XLPE (Longevity) articulation. Similarly, the proximal, medial, 2D and 3D wear rates of X3 XLPE liners between one and five years of larger 36 and 40mm articulations were not significantly greater than those of a similar cohort of patients with 32mm articulations.

The very low proximal, 2D and 3D wear rates reported for younger patients were not significantly greater than those of older but otherwise comparable patients at three and five years follow-up. Proximal bedding-in within the first year tended to be higher in the younger cohort compared to the older cohort, but there was no difference in the proximal FHP at five years.

Analysis of the aggregate results from all cohorts in this thesis revealed that the Marathon XLPE liner, manufactured with 5mRad irradiation which is at the lower range of irradiation included as a XLPE liner, had a higher proximal bedding-in and a higher 2D and 3D wear rate between one and five years compared to Longevity and X3 XLPE liners, both of which were manufactured using higher levels of irradiation. All XLPE wear rates decreased when measured at five years compared to two years with the exception of those of Marathon XLPE liners. Patient sex, age, BMI, acetabular component outer diameter and acetabular component inclination were not significantly associated with bedding-in or wear rate at two or five years. The low early wear rates of XLPE identified in the cohorts examined as part of this thesis are similar to the wear rates of other cohorts identified through the scoping review. These low rates support the continued use of XLPE liners.

5.2 Future Studies

5.2.1 Longer Term Wear

The early adoption of new technologies is hard to resist (Leopold, 2014) as is evident by the continued introduction of new materials and designs in the manufacturing of prosthetic components for use in THR. National registries are important to determine the survival of implants by collating information across populations (Torosyan et al., 2015). However, registries focus on revision rates of THR and therefore, in most instances, many tens of thousands of THRs will have been undertaken before a poorly performing component is identified through an increased revision rate. A recent systematic review of studies evaluating surrogate measures for predicting long-term outcome in primary THR found only two validated measures, RSA and EBRA, each measuring polyethylene wear and implant migration (Malak et al., 2016). Monitoring wear and migration of implants with the most sensitive measurements such as RSA is important in the stepwise introduction of new implants but this has not always been adhered to by the orthopaedic community (Malchau et al., 2011).

In the short term, low XLPE wear rates have been demonstrated for both standard and larger articulations. This supports the use of larger articulations with XLPE liners which have been shown to reduce the risk of dislocation (Howie et al., 2012) in middle-aged and elderly patients who are at increased risk of dislocation. However, before the use of large articulations with XLPE liners can be widely encouraged in young patients, longer term studies are required to determine whether the identified low wear of XLPE in the short-term continues into the long-term. These longer term RSA studies should adhere to the guidelines described by Valstar et al (2005) and Callary et al. (2015).

5.2.2 Will Oxidation of XLPE Result in Increased Wear as Polyethylene Degrades?

Elevated oxidation at the rim of annealed and remelted XLPE liners has been reported to occur *in vivo* (Wannomae et al., 2006a; Wannomae et al., 2006b; Currier et al., 2010; MacDonald et al., 2011; Rowell et al., 2015), with maximum rim oxidation correlating significantly with time *in vivo* (Currier et al., 2007). An association between time *in vivo* and oxidation has also been reported by MacDonald et al (2011), who found an increase in oxidation over time in remelted XLPE liners and a decrease in ultimate strength at the bearing surface with increased implantation time of annealed XLPE liners. However, analyses of retrieved XLPE liners are compromised by the time lag between revision surgery and examination in the laboratory, during which the liners continue to oxidise in air (Muratoglu et al., 2010). Subtle changes in oxidation at the bearing surface of remelted XLPE liners have also been reported to occur *in vivo* (Wannomae et al., 2006a; Wannomae et al., 2006b; MacDonald et al., 2011). Concerns relating to potential oxidation of XLPE have led to the introduction of modified XLPE liners incorporating the use of anti-oxidants such as vitamin E (Gomez-Barrena et al., 2008). Future studies should include evaluation of the wear rate of new anti-oxidant XLPE liners in well-designed randomised controlled trials using RSA.

5.2.3 Relationship between XLPE and Osteolysis

The relationship between XLPE and the development of osteolysis remains unknown. Although the wear rate for each cohort in this thesis was well below 0.1 mm/yr, the osteolysis threshold suggested for conventional UHMWPE (Dumbleton et al., 2002), the benefit of the decreased wear rates of XLPE may be offset by an increase in the inflammatory profile of these wear particles compared with those from conventional PE (Illgen et al., 2009). The prevalence of peri-acetabular osteolysis around THR involving XLPE components varies in the literature because plain radiographs are not adequate for detection of osteolysis (Harris, 2003). To detect and measure the size of periprosthetic osteolytic lesions accurately, a CT scan of the hip is required (Stamenkov et al., 2003).

Future studies incorporating both RSA to measure XLPE wear and CT to determine the prevalence of osteolysis are required to determine definitively whether the low early wear of XLPE does indeed translate to low wear and a low incidence of osteolysis in the medium- to long-term. These studies will enable a comprehensive understanding of the relationship between XLPE wear and osteolysis.

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