Acetabular Component Migration Following Revision Total Hip Replacement

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Sometimes it's not enough to know what things mean,
sometimes you have to know what things don't mean.

- *Bob Dylan*

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ABSTRACT

Background:

The most common reason for revision of the acetabular component after total hip replacement (THR) is loosening. Identifying a surrogate, such as early migration, that could predict the long-term performance of revision acetabular components and techniques is important given the introduction of new implants and techniques. Radiostereometric Analysis (RSA) and Ein-Bild Roentgen Analyse (EBRA-Cup) are the only validated methods to measure component migration that can predict long-term survivorship of primary THR implants. The advantage of EBRA-Cup is that it can be performed retrospectively, and therefore, is currently arguably the best method to establish thresholds for component migration that predict component loosening. The advantage of RSA is that it is the most accurate method to measure component migration and the current gold standard. If EBRA-Cup established thresholds of migration could be applied to RSA measurements, RSA could be used to predict loosening of revision acetabular components and therefore assess the early performance of various components as well as the effect that variation in technique can have on the performance of components.

Aims:

The aims of this thesis were:

(1) to undertake a scoping review of all studies that used RSA, to measure the migration of acetabular components used at revision THR.

(2) To determine the amount of acetabular component proximal translation and sagittal rotation as measured by EBRA-Cup after revision THR to predict and (3) diagnose aseptic loosing at re-revision surgery.

(4) To determine the accuracy of EBRA-Cup measurements of uncemented acetabular component migration after revision THR, and (5) to compare the number of cases identified using EBRA-Cup and RSA as having proximally migrated above and below 1mm at 2 years post-operatively.

(6) To compare the migration of the revision acetabular system thought to have the best results to treat severe bone defects, using porous tantalum acetabular components, with the EBRA established migration thresholds, and (7) to determine

the effect that modifying the surgical technique to implant the porous acetabular components in these cases has on the amount of early component migration.

Methods:

(1) A systematic search was performed on PubMed, Scopus and Embase to identify all publications that measured the migration of acetabular components following revision THR using RSA.

(2/3) EBRA-Cup was used to retrospectively measure the migration of 94 uncemented acetabular components used at revision THR, until re-revision surgery. The cohort was divided into two patient groups: Group A, included revision acetabular components that were found to be not loose at re-revision THR (52 components); and Group B, the revision acetabular components that were found to be loose at re-revision (42 components).

(4/5) The migration of 76 revision acetabular components was measured, and compared, using both RSA and EBRA-Cup and using radiographs taken at the same time points.

(6/7) RSA was utilized to measure the migration of 55 porous tantalum components used to treat severe, Paprosky III, acetabular defects at revision surgery. The component migration after a surgical technique change was compared to those preceding.

Results:

(1) The systematic literature search found seventeen publications. Uncemented acetabular components and components used to treat smaller defects had lower amounts of early migration. Several recommendations were made to improve the reporting of future RSA results to allow comparison between publications and to allow future systematic reviews and meta-analyses.

(2) The mean proximal translation and sagittal rotation, measured by EBRA-Cup, were significantly higher for acetabular components that were found loose compared with those that were not loose at re-revision ($p < 0.02$). Proximal translation > 1.0 mm within 24 months had a positive predictive value (PPV) of

90% and a specificity of 94%, but a sensitivity of 64%, for a revision acetabular component to be loose at re-revision.

(3) Thresholds of 2.5 mm proximal translation or 2° sagittal rotation (EBRA-Cup) in combination with radiolucency criteria had a sensitivity of 93% and specificity of 88% to diagnose aseptic loosening.

(4/5) EBRA-Cup can accurately measure migration of uncemented acetabular components used at revision THR. The presence of pelvic discontinuity, significantly influenced the accuracy of EBRA-Cup measurements. EBRA-Cup and RSA had good agreement on classification of components that migrated above or below 1mm at 2 years, with 100% sensitivity and 87% specificity.

(6) Of the 55 components used to reconstruct Paprosky III acetabular defects, 7 migrated more than the early threshold that predicts later loosening (>1 mm) and of these 5 had been re-revised for loosening at the time of the latest follow-up.

(7) At 2 years, the absolute median proximal translation of components with enhanced inferior fixation was |0.3| mm (range, |0.1| to |0.9| mm), which was significantly lower than |0.4| mm (range, |0.03| to |16.4| mm) for those without enhanced inferior fixation ($p = 0.04$).

Conclusion:

Improved reporting of RSA migration results of acetabular components used at revision THR is required. A 1mm threshold of early proximal migration reliably predicts re-revision for aseptic loosening of acetabular components used at revision THR. Furthermore, using the same method, thresholds of migration were established that are diagnostic of aseptic loosening of acetabular components used at revision THR at any time point. EBRA-Cup measurements of acetabular component migration following revision THR was shown to be accurate when compared with RSA measurements. The use of these thresholds in a prospective cohort of patients that underwent reconstruction of severe acetabular defects was shown to be effective to improve the surgical technique and early stability of the acetabular components investigated.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

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John M. Abrahams

September, 2019

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"As we express our gratitude, we must never forget that the highest form of appreciation is not to utter words, but to live by them."

- John F. Kennedy

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DEDICATION

“*Love never fails. But whether there are prophecies, they will fail; whether there are tongues, they will cease; whether there is knowledge, it will vanish away. For we know in part and we prophesy in part. But when that which is perfect has come, then that which is in part will be done away. When I was a child, I spoke as a child, I understood as a child, I thought as a child; but when I became a man, I put away childish things. For now we see in a mirror, dimly, but then face to face. Now I know in part, but then I shall know just as I also am known. And now abide faith, hope, love, these three; but the greatest of these is love.”*

- 1 Corinthians 8-13

I would like to dedicate this thesis to my wife and best friend Marina, who has supported me, believed in me, and encouraged me in my pursuits. Marina’s love and devotion has helped me become a more rounded individual. She has helped me in the easy times and also in the difficult ones. I am very excited for our future.

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PUBLICATIONS ARISING FROM THIS THESIS

1. **Abrahams JM**, Callary SA, Munn Z, Won Jang S, Huang Q, Howie DW, Solomon LB. Acetabular Component Migration Measured using Radiostereometric Analysis following Revision Total Hip Arthroplasty: A Scoping Review**. Accepted for publication by JBJS Reviews on 18th December 2019.**

2. Kim YS, **Abrahams JM**, Callary SA, De Ieso C, Costi K, Howie DW, Solomon LB. Proximal translation of > 1 mm within the first two years of revision total hip arthroplasty correctly predicts whether or not an acetabular component is loose in 80% of cases: a case-control study with confirmed intra-operative outcomes. **Bone Joint J. 2017; 99-B(4):465-474.**

3. **Abrahams JM**, Kim YS, Callary SA, De Ieso C, Costi K, Howie DW, Solomon LB. The diagnostic performance of radiographic criteria to detect aseptic acetabular component loosening after revision total hip arthroplasty. **Bone Joint J. 2017; 99-B(4):458-464.**

4. **Abrahams JM**, Callary SA, Hewitt J, Won Jang S, Howie DW, Solomon LB. Good agreement of RSA and EBRA-Cup measurements of acetabular component migration after revision THA. **J Orthop Res. 2020 Feb 10. doi: 10.1002/jor.24623.**

5. Solomon LB, **Abrahams JM**, Callary SA, Howie DW. The Stability of Porous Tantalum Acetabular Components used at revision total hip arthroplasty to treat severe acetabular defects. **JBJS. 2018;100(22):1926-1933.**

ABBREVIATIONS

THR	Total Hip Replacement
THA	Total Hip Arthroplasty
RSA	Radiostereometric Analysis, also known in earlier literature as Roentgen stereophotogrammetric analysis
EBRA	Ein-Bild-Roentgen-Analyse
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
mm	Millimetre
TMARS	Trabecular Metal Acetabular Revision System
UHMWPE	Ultra High Molecular Weight Polyethylene
HXLPE	Highly Cross-Linked Polyethylene
yr	Year
SD	Standard Deviation
CI	Confidence Interval
CN	Condition Number
PPV	Positive Predictive Value
NPV	Negative Predictive Value
AP	Anteroposterior
ROC	Receiver Operating Characteristics
AUC	Area Under Curve
IQR	Interquartile Range
GP	Gustilo-Pasternak Classification of Acetabular Defects
AAOS	American Academy of Orthopaedic Surgeons
PACS	Picture Archiving and Communication System

THESIS OVERVIEW

The research included in this thesis had seven aims.

The first aim was to undertake a scoping review, using a systematic search, of all studies that used radiostereometric analysis (RSA) and Ein-Bild-Roentgen-Analyse (EBRA-Cup) to measure the migration of acetabular components used at revision THR. A scoping review of the RSA studies was undertaken. The statistical reporting, methodology, implants and migration within the RSA studies were compared and are presented in Chapter 2.

The second aim was to determine the sensitivity, specificity and predictive values of previously reported thresholds of proximal translation and sagittal rotation after revision THR at various times during early follow-up with re-revision for aseptic loosening. This was done by measuring the migration, using EBRA-Cup, of a case-control cohort of acetabular components used at revision THR until eventual re-revision THR. The results of this are presented in Chapter 3.

The third aim was to determine the diagnostic performance of radiographic criteria to detect aseptic acetabular loosening after revision total hip replacement (THR). The predictive values of different thresholds of migration and of the presence of radiolucent lines were determined. The results of this are presented in Chapter 4.

The fourth aim was to determine the accuracy of EBRA-Cup measurements of uncemented acetabular component migration after revision THR. The results of this are presented in Chapter 5.

The fifth aim was to compare the number of cases identified using EBRA-Cup and RSA that proximally migrated above and below 1mm at 2 years post-operatively. The results of this are presented in Chapter 5.

The sixth aim was to compare the migration of porous tantalum acetabular components to treat severe bone defects, with the EBRA established migration thresholds for revision acetabular components. The results of this are presented in Chapter 6.

The seventh aim was to determine the effect on migration by enhancing the inferior fixation of the porous acetabular components used in hips with severe acetabular defects. The results of this are presented in Chapter 6.

CHAPTER ONE

Introduction

1.1 - Total Hip Replacement

Since the first attempt to replace the bearing surfaces of the human hip, there have been many different designs of implants and many failures with a need to subsequently treat these failures.

The modern Total Hip Replacement (THR) was introduced by Sir John Charnley in 1960 after much experimentation with different designs that were analogous to the hemiarthroplasty and hip resurfacing. The current THR includes replacing the acetabular bearing surface with a concave implant and replacing the femoral bearing surface with a new ball articulation in the form of a stemmed femoral component. Sir Charnley developed and tested a polytetrafluoroethylene acetabular component that was serrated to allow for bone ongrowth. He reported on a series of 97 hips in 1961[1] and was able to report "negligible wear" and "good results" based on plain radiographs and clinical findings at 10 months of follow-up. However, in a Letter to the Editor in 1966[2], Sir Charnley described how he had abandoned polytetrafluoroethylene in November of 1962, less than a year since his publication on its use because of catastrophic failure due to excessive wear, and its associated serious soft tissue reactions.

Since abandoning polytetrafluoroethylene, Sir Charnley developed ultra-high molecular weight polyethylene (UHMWPE), otherwise described as high-density polyethylene. Based on ex-vivo testing he thought it could last "150 years in the hip joint compared with 2.5 years for polytetrafluoroethylene"[2]. The modern day THR has not been able to be durable for 150 years, and it would be very difficult to prove that any implant would indeed be durable for this duration of time. The 2018 Australian Orthopaedic Association National Joint Replacement Registry *(AOANJRR)* reported a revision rate of 12.4% at 17 years for primary hips with UHMWPE[3].

Despite the substantial improvement in wear characteristics, UHMWPE and highly cross linked polyethylene (HXLPE) have been shown to still be prone to wear, and subsequently cause periprosthetic osteolysis, which may contribute to the late loss of fixation of the acetabular component[4-7]. The process of aseptic loosening has been shown to be a process that occurs from the time of implantation[8]. Acetabular implants may be loose, in the absence of osteolysis, because of the failure of initial good ingrowth or ongrowth of uncemented acetabular components that can lead to either fibrous encapsulation of the implant that is not durable, or no fixation at all that may lead eventual failure. For cemented acetabular components, debonding between a poor cement-bone interface or cement-implant interface due to surgical technique, cement and or implant factors may lead to loosening[9].

There is a strong need for a phased introduction of new implants, with early reporting on their performance which needs to include sensitive techniques that can accurately predict their longevity[10]. This was evident for all early failures of new implants, from the historical example of Sir Charnley's initial THR to the recent failure of the ASR metal-on-metal THR[11].

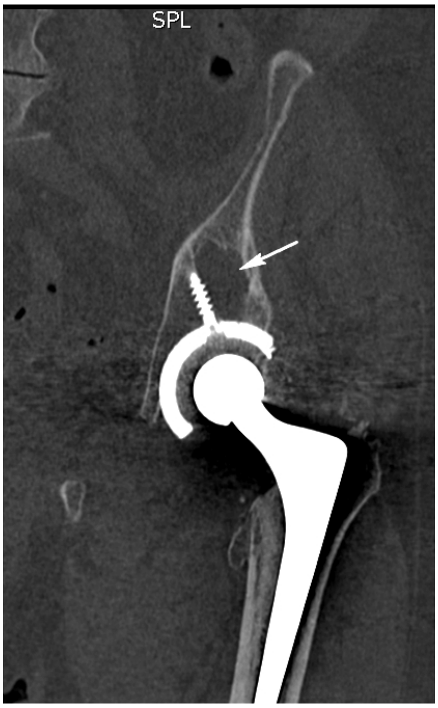
The consequences of a THR that has failed are patient suffering and complications that commonly lead to a revision THR, which is often complicated by poorer structural and biological conditions. Despite significant improvement in the durability of primary THR, with many implants having more than 95% survival at 10 years, revision THR is not as successful[3]. In the 2018 report of the AOANJRR, the acetabular component following revision THR had a reported re-revision rate of 36.3% at 10 years[3].

1.2 - Revision Total Hip Replacement

1.2.1 - Reasons for Revision of a primary THR

1.2.1.1 - Loosening and Osteolysis

According to the 2018 AOANJRR[3], loosening and/or osteolysis are the most common reasons for revision of a primary THR performed for osteoarthritis, representing 25% of revisions. The mechanism by which this develops has been attributed to a number of reasons; historically the most common reason for loosening is osteolysis. The resulting wear particles that form from degradation of the polyethylene liner have been implicated in an inflammatory cascade that results in an infiltration of matrix metalloproteases and various collagenases. In turn, an upregulation of cell signalling pathways has been implicated in the differentiation of osteoclasts which are directly responsible for osteolysis[4-7]. Whilst this has long been seen with UHMWPE, newer generation HXLPE, whilst forming less wear particles, has still been implicated in the same process[12]. The resultant osteolysis degrades peri-prosthetic bone and, as a result, there is displacement and loss of fixation of the implant, as seen in Figure 1.2.1. Since the introduction of UHMWPE, the rate of revision due to osteolysis has been decreasing, although the process still affects many older implants that remain *in situ*.



1.2.1 – Coronal CT image of a pelvis and proximal femur with a primary THR incorporating an UHMWPE liner in situ. The white arrow points towards a large supra-acetabular osteolytic defect.

The aetiology of aseptic loosening is due to multiple pathologies. Osteolysis may contribute to a late cause. However, the process of loosening may also begin from the time of implantation in the absence of osteolysis caused by wear particles. In uncemented acetabular components, loosening may take place due to poor bone ingrowth into, or ongrowth onto, the acetabular component. This may take place in cases where the acetabular component develops fibrous ingrowth/ongrowth. One reason for poor ingrowth or development of fibrous fixation has been related to the initial stability and micromotion at the bone-implant interface, with minimal micromotion less than 20 to 40 microns being optimal for bone ingrowth[13]. The material surface properties of acetabular components have been shown to have a significant effect on their initial ingrowth/ongrowth[14]. This is due to a number of reasons. First, depending on the surface of the acetabular component, acetabular components with surfaces that have a low co-efficient of friction may not allow for sufficient grip of host-bone that leads to excessive micromotion due to torsional forces in the normal gait cycle[15]. Secondly, acetabular components that have smooth coatings have low potential for ingrowth or ongrowth[16]. The coating itself may not be sufficiently osteoconductive or inductive to allow ingrowth/ongrowth depending on the size of the porosity. A porosity of 100 to 400 microns has been established as being optimal. Thirdly, the metallurgy of the alloy used to manufacture the acetabular component may not support osteogenesis. Fourthly, loading has been shown to be strongly related to bone ingrowth/ongrowth[17]. Depending on the geometrical design of the acetabular component and the surgical technique, it is also possible for uneven loading of the implant, which may only support sporadic areas of ingrowth/ongrowth[17]. Fourth, the degree of press-fit has been shown to have an influence on the early stability and the amount of micromotion that is generated at the bone-implant interface[15]. Fifth, augmentation of the cup with screw fixation has been shown to further reduce micromotion and is thought to promote bone ingrowth or ongrowth[18]. Finally, depending on the manufacturing properties of the acetabular component, it is possible for debonding of the coating to occur due to fatigue shear stresses generated at the coating-bone interface[19]. The material properties of the coating and manufacturing process have been implicated in premature failure[20], with early implants coated with hydroxyapatite (HA) undergoing resorption of the coating and losing bone-implant interlock due to lack of integration with the underlying metal substrate[21]. In retrieval studies, HA coated acetabular components were found to have significant debonding of the HA coating from the underlying acetabular component[22].

The manufacturing process has been implicated in premature failure of uncemented acetabular components, with grit blasted implants that are typically sprayed with ceramic and or glass particles having been found to have residual manufacturing particles that contribute to third body wear and foreign body reactions[23-26].

With regards to cemented acetabular components, long term stability in primary THR is achieved by good osteointegration of the cement mantle with host bone[27]. There may be a number of causes as to why the cement-bone interface may fail. First, depending on the pressurisation of the cement, it may not be possible to achieve good penetration of the cement that allows good initial stability and long term interdigitation of the cement with host cancellous bone[28]. It has been shown that cases with poor cement pressurisation have increased early migration as determined with RSA[29]. The timing of cement insertion has been shown to have an effect, due to the viscosity of the cement which changes over time of insertion[30]. Adequate preparation of host bone has also been shown to affect the initial stability[31], with cases that have a large amount of circulating blood compromising the bone-cement interface[32]. The quality of the radiographic appearance of the bone-cement interface has been linked to its mechanical stability in retrieved specimens[9]. Additionally, head size has been shown to have a significant effect on the forces that are distributed through the cement-bone interface and can lead to premature failure[33]. Debonding of the cement-prosthesis interface may also occur, either due to cement properties, or properties of the acetabular component that may have caused poor cement adhesion.

1.2.1.2 - Dislocation

The second most common reason for revision THR is dislocation, accounting for 21.1% of revisions[3]. The reasons for early dislocation include component malposition and infection, whereas later dislocations are due to liner wear, abductor dysfunction and capsular insufficiency [34]. If these patients require revision surgery they may undergo component explantation, which can cause bone loss. The use of larger articulations has reduced the rate of early dislocation[35] by increasing the head-to-neck ratio, subsequently increasing the amount of hip motion that occurs prior to impingement between the neck and edge of the acetabular component and the jump distance required for the components to dislocate.

1.2.1.3 - Infection

Infection of prosthetic joints is becoming increasingly more common due to the prevalence of multidrug resistant organisms and older patient age at time of index surgery. Infection is currently reported as the third most common reason for revision at 18.1%[3]. The presence of infection may cause development of necrotic and/or osteomyelytic bone, and, during revision surgery, bone loss may occur during explantation of the implants and debridement. Furthermore, it is common for a patient with infection to require staged procedures that often entail multiple procedures that cause bone loss and damage to soft tissue. Therefore, at time of implantation of the definitive implant at revision THR, treating bone loss is a challenge.

1.2.2 - Issues Encountered at Revision THR

Issues encountered at revision THR include treating existing bone loss as well as poorer bone and soft tissue quality.

1.2.2.1 - Bone loss

At revision THR, depending on the degree of bone loss, it may be difficult to achieve press fit fixation of the acetabular component and contact with bleeding host bone of sufficient quality. It has been reported that at least 50% of bleeding host bone is required to develop a significant amount of bone ingrowth or ongrowth for acceptable long-term outcomes[36-38]. In cases with poor quality host bone, for example as may occur in the presence of osteoporosis, the biological ability for host bone integration is reduced[39] and excessive micromotion or gross motion of the implant may occur that may further hinder ingrowth or ongrowth[40]. Depending on the severity of bone loss, particularly in the context of an uncontained defect, it may be difficult to achieve the initial stability required for bone ongrowth or ingrowth to occur. This may subsequently lead to no ingrowth or ongrowth whatsoever and eventual failure or to fibrous ingrowth that may be susceptible to early loosening. In cases with severe bone loss, the anterior and/or posterior columns may be compromised, the superior defect may extend well into the iliac wing and pelvic discontinuity may be present. In cases with severe defects such as a Paprosky III[41] defect, the bone loss is likely to extend to the roof of the sciatic notch, above which the bone thins to the outer and inner table, leaving very little bone with which to stabilise and anchor the reconstruction[42].

1.2.2.1.1 - Classification systems of Acetabular Defects

There are multiple classification systems that have been described to classify acetabular bone loss for academic comparison and to guide reconstruction options. The five most common classifications are described below.

1.2.2.1.1.1 - Gustilo-Pasternak Classification System

The Gustilo-Pasternak classification was described in 1988 by Gustilo et al[43]. This classification was derived from examination of a series of 57 hips that underwent revision due to failed femoral cemented component loosening. The study described four grades of acetabular defects based on radiographic findings, as shown in Table 1.2.1.

Type	Description
I	Lucent line around the acetabular component, minimal bone loss.
II	Severe acetabular enlargement. Marked thinning of the acetabulum.
III	Anterior, superior and/or central bone loss causing instability of the implant.
IV	Acetabular collapse with fracture or severe bone loss.

Table 1.2.1 - Gustilo-Pasternak Classification System of Acetabular Defects

1.2.2.1.1.2 - American Academy of Orthopedic Surgeons Classification System (AAOS)

The AAOS classification (Table 1.2.2) was originally described in 1989 by D'Antonio et al, and was based on the agreement of the American Academy of Orthopedic Surgeons (AAOS) hip committee that a standard nomenclature was required to guide reconstruction strategies for defects of the acetabulum[44]. Since the original description, a simplified version, described by D'Antonio in 1992, has been popularised[45]. Unlike other classification systems, it describes arthrodesis despite the fact that this is not necessarily associated with a deficiency, because of the technical difficulty in establishing the location of the true acetabulum.

Type	Description
I	Loss of part of the acetabular rim or medial wall
II	Volumetric loss in the bony substance of the acetabular cavity
III	Combination of segmental bone loss and cavitary deficiency
IV	Complete separation between the superior and inferior acetabulum
V	Arthrodesis

Table 1.2.2 – American Academy of Orthopaedic Surgeons Classification System of Acetabular Defects

1.2.2.1.1.3 - Paprosky System

Paprosky et al in 1994[41, 46] described a classification system for acetabular defects, with the aim being to guide treatment. The system was based on a six-year follow-up of 147 hip replacements that underwent revision with uncemented acetabular components. The classification uses a combination of radiographic and intraoperative findings and has since had its intra- and inter-observer error validated[47]. Unlike other classification systems, it uses more subjective criteria for its descriptions that allows for lower interobserver error and subsequent comparison of patient cohorts.

Grade	Description
I	Minimal bone loss, no component migration, and intact acetabular walls
II	Moderate bone loss with distortion of the acetabular hemisphere but preservation of the anterior and posterior acetabular columns, with less than 2 cm of acetabular component migration
IIA	Direct superior bone loss
IIB	Superolateral bone loss
IIC	Medial bone loss
III	Severe bone loss resulting in major destruction of the acetabular rim and supporting structures, with component migration >3 cm superiorly
IIIA	Bone loss pattern from 10 o'clock to 2 o'clock position. Moderate destruction of tear drop (medial wall of tear drop still present) with moderate lysis of ischium
IIIB	Bone loss pattern from 9 o'clock to 5 o'clock position with obliteration of teardrop and severe lysis of ischium

Table 1.2.3 – Paprosky Classification System of Acetabular Defects

1.2.2.1.1.4 - Gross Classification

Gross et al described an acetabular defect classification system in 1996 based on the type of bone graft required to reconstruct an acetabular defect at revision [48]. Unlike other classification systems, the Gross classification is based on the presence of a contained or a noncontained defect, which is further subdivided. Gross described initial results for 130 hips with a minimum of 5 years follow-up.

Type	Classification
I	Contained defect with intact rim and columns
II	Noncontained
IIA	Shelf/minor column Loss of <50% of host acetabulum in contact with cup
IIB	Major column >50% loss of acetabulum that is in contact with the cup. Loss of one or both columns

Table 1.2.4 – Gross Classification System of Acetabular Defects

1.2.2.1.1.5 - Saleh Classification

Saleh and Gross et al described in 2001 a classification system based on radiological signs, rather than intraoperative findings[49, 50]. It is based on the original Gross classification with more detailed descriptions of the radiological findings associated with each defect grade.

Type	Description
I	No notable loss of bone stock. Amount of bone loss is less than that which would require a revision component. There has been no migration of the primary component into the ilium, and both columns are largely intact.
II	Contained loss of bone stock. There is cavitary or volumetric enlargement of the acetabulum. If the cup does extend beyond the ilioischial line (protrusio), the defect can still be considered type II provided that the columns are intact.
III	Uncontained (segmental) loss of bone stock involving <50% of the acetabulum, primarily affecting either the anterior or the posterior column. Bone loss is considered uncontained if it is not amenable to treatment with morselized bone graft. The sum of all segments of bone loss in either the anterior or the posterior column allows ≥50% cup coverage by host bone (as assessed preoperatively with templates).
IV	Uncontained (segmental) loss of bone stock >50% of the acetabulum affecting both the anterior and the posterior column. Type IV is identical to type III except that the sum of the segmental bone loss in the columns exceeds 50%. There is no pelvic discontinuity.
V	Acetabular defect with contained loss of bone stock in association with pelvic discontinuity. Any pelvic discontinuity is considered a type-V defect regardless of the amount of bone loss.

Table 1.2.5 – Saleh Classification System of Acetabular Defects

1.2.2.2 - Bone and Soft Tissue Quality

Due to the presence of osteolysis, prior infection or osteoporosis, reduced bone quality is common at revision. Bone density is often lower, which increases the likelihood of poor fixation. Sclerotic bone which is devoid of a good blood supply may lead to poor ingrowth/ongrowth and/or bone-cement interface[51]. Scar tissue affects the quality of repair, which may lead to increased risk of dislocation and decreased hip function. The reduced quality of soft tissue increases the risk of infection[52].

Because of the potential for variability of existing bone stock and quality, there are several treatment options that have been tried in the past and new implants and systems are constantly *being introduced in attempts* to address the shortcomings of existing technology.

1.2.2.3 - Reconstruction Options

Acetabular component fixation involves either cemented or uncemented fixation. The use of uncemented reconstructions relies on initial stability of the reconstruction being augmented by long term bone ingrowth or ongrowth on a porous, porous-coated or fibre mesh coated metal backed acetabular component. The AOANJRR does not report the most common type of components used at revision in Australia or their re-operation rate. However, the Swedish Hip Joint Registry (SHJR)[53] has reported that in 2017 the most common type of implant used at acetabular component revision in Sweden was the Trabecular Metal Acetabular Revision System (Zimmer Pty Ltd, Warsaw, IN, USA).

Cemented fixation of the acetabular component relies on bonding an acetabular component into the acetabulum using bone cement. In cases where the component is being implanted directly into native host-bone, the stability is achieved by the cement interdigitisation with host bone that allows for long term stability and mechanical interlock[27]. At revision, impaction bone grafting has been used to restore bone stock; in this situation, tight packing of a contained defect with cancellous bone chips is performed before the acetabular component is then cemented. This allows for a good graft-cement interlock that provides initial stability while the graft incorporates into the host bone[54]. The durability of cemented acetabular components has been shown to be significantly affected by pressurisation of cement at time of implantation[29]. The presence of large and uncontained defects makes it difficult to achieve satisfactory pressurisation. The use of a cemented reconstruction at revision THR has decreased in favour of uncemented reconstructions with the SHJR reporting increased use of uncemented reconstructions[53] over the last twelve years.

1.2.2.3.1 - Type of bone graft

Bone graft used to treat existing acetabular defects at revision may either be morselised or bulk allografts. The purpose of bone graft is to restore bone stock to the acetabulum. The use of large structural grafts has been attempted but found to be associated with a high failure rate due to eventual graft collapse and resorption of the graft[55].

There is an increased demand for bone graft and a relative shortage in available allograft material. The use of artificial graft substitute has been documented in several studies of revision THR[56-58] because of its increased availability, relatively lower cost, longer shelf life, and ease of use. Current synthetic bone graft materials include bone graft substitutes such as calcium phosphate, tricalcium phosphate, calcium sulphate and coralline hydroxyapatite.

1.2.3 - Assessment of Acetabular Components after Revision THR

1.2.3.1 - Use of Re-Revision as an Outcome in Registry Data

The introduction of new implants and/or fixation methods are often based on theoretical benefits or are preceded by ex-vivo testing. Assessing in vivo performance has traditionally relied on patient outcomes, clinical outcomes and/or re-revision as an endpoint and a key performance indicator. Reporting outcomes in this manner requires long term follow-up at least a decade following its introduction, by which stage it is likely to have been implanted in a large number of patients and may even be superseded by newer designs. Importantly, outcome data based on re-revision rates, such as those reported by national registries, are not likely to reflect the true performance of the implant following revision surgery. This is because patients may not be re-revised due to failing general health or surgeon refusal because of the lack of reconstruction options available. Furthermore, patients who have undergone revision are likely to have been older and are therefore more likely to be lost to follow-up because of inability to attend or death.

1.2.3.2 - Plain Radiographic Assessment

Radiographic outcome reports have traditionally been based on obvious component migration or hardware failure that would be indicative of loosening, and the criteria for reporting these findings are varied and dependant on the observer. Some studies have used a change in acetabular component position greater than 6mm or 10° as indicative of failure, which is the threshold required to visually determine obvious component migration without use of computerised methods[59].

The presence of radiolucencies, described as a black line or region around the acetabular component, have been previously described by Charnley[60] in cemented THR, the use of which has been described to monitor progression of osteolysis and as an indication of loosening. The use of radiolucencies as an indication of loosening in uncemented THR is not reliable, as in uncemented reconstructions the acetabular component may not be seated directly on the host bone from time of operation, in particular in the region of Zone 2[61], and the acetabular component may have a greater ability to move into the defect. At revision THR there may be radiolucencies immediately following surgery due to bone defects, and these may be hard to assess and monitor on serial radiographs.

Acetabular component migration on radiographs can be assessed using three methods, namely radiostereometric analysis (RSA), Ein-Bild-Roentgen-Analyse (EBRA-Cup) or manual (non-computerised) "pen and ruler" methods. Whilst non-computerised methods were traditionally performed on hard copy radiographs, the availability of digital radiology PACS software has allowed potentially more accurate measurements. However, the basic principle behind the measurement technique and inability to identify an acetabular bone reference point reproducibly and correct for changes in pelvic tilt remain the main sources of inaccuracy.

1.2.3.3 - Radiostereometric Analysis (RSA)

1.2.3.3.1 - History of RSA

Radiostereometric analysis is a technique to measure the three-dimensional movement of an object within the human body using radiographs. The earliest example of RSA was in 1897, when Dennis described a technique to locate a "bullet in the brain case" using a setup of two x-rays that were taken perpendicular to each other from a known distance. Goran Selvik described in his PhD thesis the "Study of kinematics of the skeletal system" when he was working on modern RSA methodology to measure changes in organ or implant position. Since its initial development, RSA was initially used in various applications from craniofacial surgery, to spine surgery. However, RSA gained popularity during the 1990s when its application became more widespread in the analysis of implants used in arthroplasty.

The RSA technique compares the migration of two rigid bodies relative to each other in the six degrees of freedom. The rigid bodies may be composed of either a group of tantalum markers, an implant or a combination thereof. Because of the lack of well-defined skeletal reference markers, spherical beads of known diameter are commonly inserted at time of operation in bone that is not expected to change in morphology. A rigid body would not be created across a fracture or a growth plate, as the beads would likely change in position over time. Dual simultaneous radiographs focused on the region of interest are taken in front of a calibration cage, as shown in Figure 1.2.2.

Figure 1.2.2 – Pictures of the calibration cage used for RSA examinations, (a) Side and (b) top view.

Using software, the calibration markers can be identified, as are the tantalum markers in the skeletal body of interest and, in the case of an implant, the outline of the implant can be traced to form a model-based rigid body.

1.2.3.3.2 - Quality Control

The accuracy of RSA is primarily derived from the accurate and reliable detection of the rigid bodies that are not prone to soft tissue shadowing, or poor identification because of the high absorption of x-rays. However, if tantalum markers are not sufficiently dispersed, they may not create a sufficient rigid body to meet the high accuracy expected of RSA. The dispersion of markers can be assessed within the software by a condition number (CN) for each rigid body, which is a measure of the spread of markers that form a rigid body. Markers that are well dispersed in all axes of space form a body that can be better used to make comparisons. Markers that are situated close together or only dispersed in a single axis do not allow for good comparison in all axes of movement. A condition number that is lower indicates good configuration of markers to form a rigid body[62].

1.2.3.3.3 - Issues with RSA

The RSA technique relies on optimal bead placement and visualisation. The formation of a rigid body is improved when markers are well dispersed and in an irregular pattern. Optimal placement of bone markers may be difficult in the revision scenario where there may be a lot of hardware that obstructs viewing each bead in both oblique views. Secondly, the bone markers may be subject to displacement depending on the remodelling of the pelvis and the rigid body may change morphology over time, which reduces the accuracy and precision of the measurements.

Because of the need for specialised dual radiographs and a calibration cage, follow-up is difficult for patients for whom it is difficult to travel to the specialised centre due to distance or frailty. RSA can only be performed prospectively because of the need for marker insertion intraoperatively and taking specialised radiographs post-operatively with a calibrated cage.

1.2.3.4 - Ein-Bild-Roentgen-Analyse

Ein-Bild-Roentgen-Analyse (EBRA-Cup) was described by Krismer et al and is a technique to measure acetabular component migration based on excluding non-compatible radiographs due to pelvic tilt or rotation[63]. The technique relies on comparing a minimum of three plain AP pelvis radiographs and using the centre of the ellipse of the outline of the acetabular component, which is then compared to reference lines based on anatomical landmarks. The technique has a documented difference of 0.26 mm (SD 0.31) for medial migration and 0.39 mm (SD 0.32) for proximal migration when compared to RSA[64].

1.2.3.4.1 - Limitations of EBRA

The EBRA technique is prone to variability based on the inaccuracy associated with labelling bone landmarks that may not be well defined and observer dependant. Furthermore, it relies on having comparable radiographs, the likelihood of which may be influenced by multiple variables such as patient positioning, machine setup and exposure.

1.2.3.5 – Non-Computerised (Manual) Techniques

There are a number of techniques that have been described to measure component migration manually using pencil and ruler, that do not use a computed algorithm to process results. Although they are considered to be the most inaccurate measures of migration, their advantages include the ease of use and accessibility of the technique.

The Sutherland method, described by Sutherland et al[65], uses the sacroiliac line, the ilioischial line and the teardrop line as references. Proximal translation of the acetabular component is represented by change in the distance from the midpoint of the acetabular component to the inter-teardrop line, medial translation is represented by the change in distance from the midpoint of the acetabular component to the ilioischial line, and change in inclination is defined as the change in angle between the rim of the acetabular component and the sacroiliac line, as shown in Figure 1.2.3.

The Nunn method, described by Nunn et al in 1989[66] uses the inter-teardrop line and the teardrop as reference lines, Figure 1.2.4.

The Wetherell method was described by Wetherell et al[67] and suggested different reference lines that were less likely to be affected by pelvic tilt and rotation. The ilioischial line is substituted by the obturator brim line and the teardrop line is substituted by the sacroiliac-symphysis line, Figure 1.2.5.

A study by Illchman et al[68, 69] demonstrated that the Sutherland method had a mean difference compared to RSA of 0.73mm (SD 0.67mm) for medial translation and 0.72mm (SD 0.80mm) for measurements of proximal translation. The Nunn method had a mean difference compared to RSA of 0.58mm (SD 0.70mm) for medial translation and 0.76mm (SD 0.71mm) for measurements of proximal translation. The Wetherell method had a mean difference compared to RSA of 0.52mm (SD 0.40mm) for medial translation and 1.04mm (SD 0.80mm) for measurements of proximal translation.

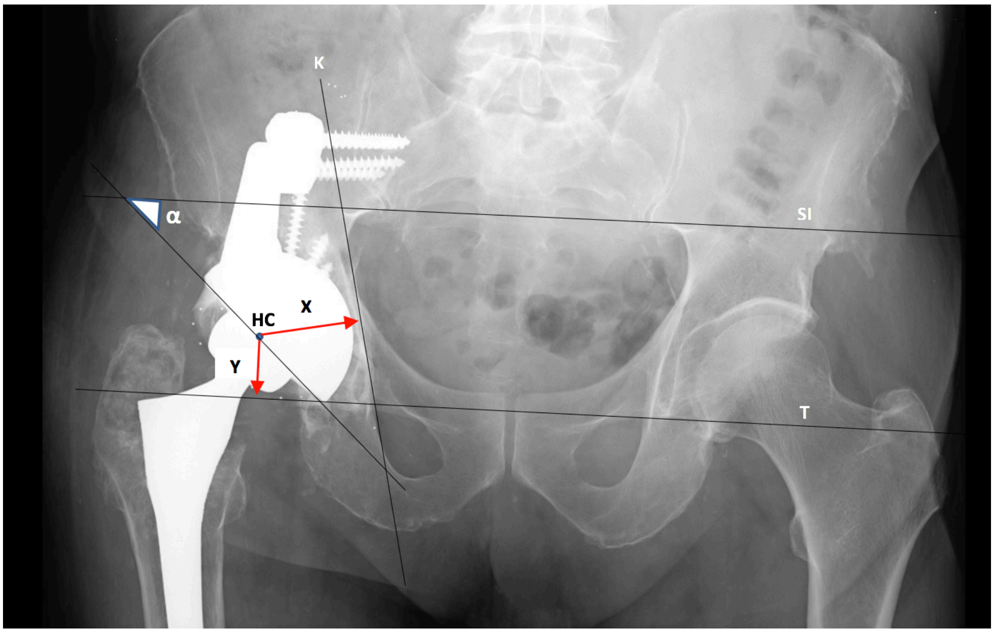


Figure 1.2.3 – The Reference lines used for the Sutherland method. K represents the ilioischial line. SI represents the sacroiliac line. T represents the inter-teardrop line. The change in α represents the change in inclination. HC represents the centre of rotation of the acetabular component. The change in Y represents the proximal translation of the acetabular component. The change in X represents the medial translation of the acetabular component.

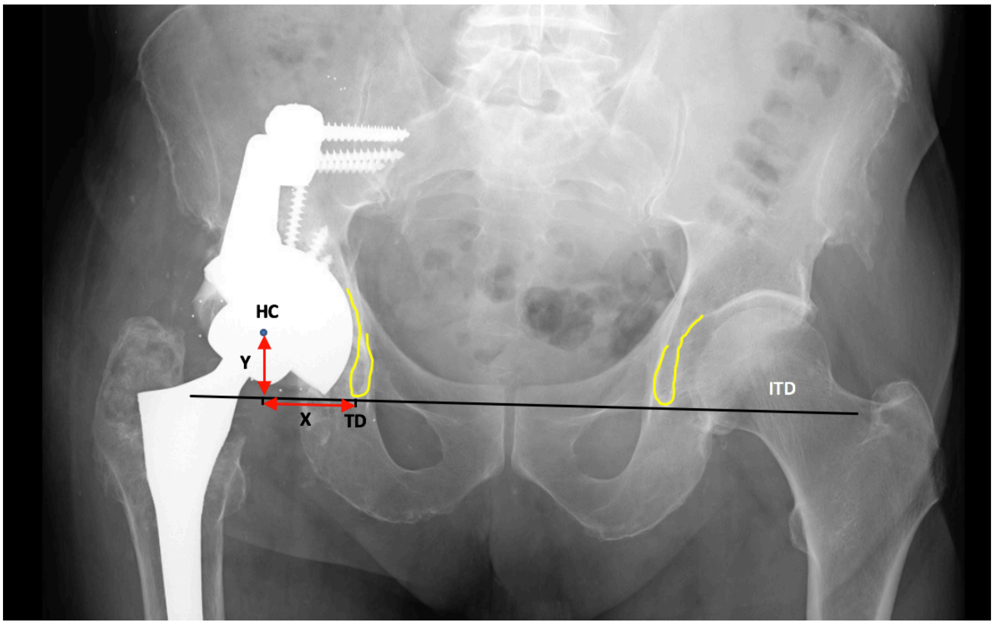


Figure 1.2.4 – The reference lines used for the Nunn method. ITD represents the inter-teardrop line. The yellow lines are the outline of the teardrop. TD represents the centre of the teardrop on the ITD. HC represents the centre of rotation of the acetabular component. The change in Y represents the proximal translation of the acetabular component. The change in X represents the medial translation of the acetabular component.

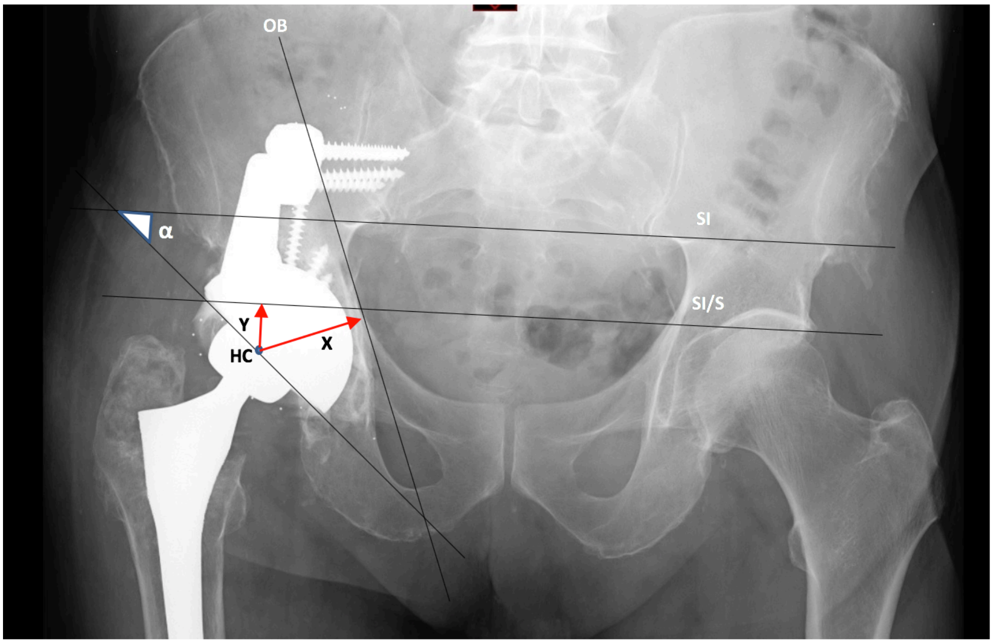


Figure 1.2.5 – The reference lines used for the Weatherall method. The change in α represents the change in inclination. OB represents the obturator brim line. SI represents the sacroiliac line. SI/S represents the sacroiliac-symphysis line, which is the midpoint between the SI line and the pubic symphysis. HC represents the centre of rotation of the acetabular component. The change in Y represents the proximal translation of the acetabular component. The change in X represents the medial translation of the acetabular component.

1.2.3.6 - Early Migration and use of Thresholds to Predict Later Loosening

Early migration at two years using all three measurement methods has been shown to be associated with later revision[70-72]. However, following revision THR, no study has established whether or not migration of acetabular components can predict later loosening or what amount of migration is deemed to be acceptable and not acceptable.

To date, the majority of RSA studies of revision THR have been used to report on a direct intervention with comparison to a control group, with few publications reporting migration of a new implant[73-76].

There are multiple reasons that migration of acetabular components following revision THR is likely to be higher than that following primary THR. First, there is poorer initial fixation at revision that may be dependent on screw fixation, rather than on rim press-fit which is the case in primary THR. Secondly, poorer bone quality at revision, secondary to sclerosis, previous stress shielding or osteolysis, is likely to affect the bone density and subsequently may cause a higher amount of early migration as the component sets into a new position following weight bearing. Thirdly, at revision THR, bone graft is more commonly used which may re-model over time.

Migration threshold limits that have been used at primary THR have been reported in two ways. First, the mean migration of the cohort at two years is thought to be very useful to compare overall performance of a homogenous cohort. Second, a threshold can be applied to individual cases at a certain time point. Even following primary THR, these existing thresholds have only been derived using limited clinical follow-up and non-matched cohorts. Pijls et al[72] determined a threshold of a mean of <0.2mm at two years as acceptable for a cohort, with a mean of 0.2-1.0mm being at risk of failure and >1.0mm being unacceptable. Unfortunately, this threshold was determined by comparing the early migration in RSA studies with survival statistics of the same implants from other studies that reported longer term outcomes.

Individual thresholds have been determined by examining primary cemented acetabular components[77]. With regards to these individual thresholds, the limitation is that there is short follow-up, with few known outcomes at revision THR. It is very possible for the thresholds to change considerably with extended follow-up.

The current thresholds established for early acetabular component migration in the literature are described in Table 1.2.6.

Threshold Described	Migration Measurement Methodology	Acetabular Components Analysed	Number of Hips with Confirmation of Loosening at Revision Surgery	Prediction
Mean migration <0.2mm at 2 years[72]	RSA	Primary Cemented and Uncemented Hips	Not Applicable (Meta-analysis study)	10-year survivorship
Individual migration <1.0mm within 2 years[70]	EBRA	Primary Cemented and Uncemented Hips	13/120	8-year survivorship
Individual migration < 1.29 to 1.76mm or rotation <2.53°[77]	RSA	Primary cemented	2/41	Component failure
Migration <3.4mm at two years[71]	Manual Measurement described by Nunn et al	Primary Uncemented	3/179	Re-revision rate at 6.5 years

Table 1.2.6 – Thresholds of migration for acetabular components

1.2.4 - Phased introduction of new implants

There were 220 new acetabular and femoral component combinations introduced in Australia in 2017[78]. Historically there have been a number of implants that were reported to have excellent early clinical results followed by an unacceptable number of failures[79]. Malchau et al[80] were the first to propose that new implants should be introduced to market in a phased manner that limits exposure of potentially poor performing implants. This should begin with a study using RSA, followed by a well-defined cohort study and subsequent registry analysis, with widespread adoption of the new implant only if the early results are deemed acceptable. The phased introduction process is yet to be performed for a revision implant. Additionally, a recent systematic review identified that 25% of implants available to surgeons for primary THR have no evidence base for their use, and 17% of acetabular components that were implanted have no supporting evidence[81]. The European Union has implemented new medical device regulations that will require new implants to have a minimum 10 year follow-up in registry or examination in a study, and more rigorous standards of post-marketing surveillance[82].

The benefits of a stepwise introduction of new implants and techniques cannot be overemphasised. An analysis of the introduction of ASR implants showed that they were not introduced in a stepwise approach, and that the large-scale failure could have been avoided had a stepwise introduction been followed[83]. Despite disasters like the poor introduction and early revision of most ASR implants, the practice of not using a stepwise introduction of new implants continues. For example, the Versafit cup DM by Medacta International has been used in 558 primary hips in Australia since its introduction approximately 6 years ago. In the 2018 AOANJRR[3] report, the Versafit DM implant was newly identified as having a higher than expected rate of revision. No RSA study has been published on the early migration of the Versafit DM cup. The reasons for revision were described as being predominantly due to loosening, infection and fracture. Despite it not being a very popular implant, the use of this implant could have been minimised if it were introduced in a phased manner beginning with a limited study of 20 patients with RSA. It may have been likely that this would have shown a higher than anticipated amount of early migration for an uncemented acetabular component.

1.2.5 - Systematic review on acetabular reconstruction types at revision surgery

A recent systematic review on construct options used at revision THR by Baauw et al[84] showed that porous tantalum acetabular components used in combination with a cage or augment have demonstrated the best clinical results based on a review of the literature. To date, however, there have been no RSA studies or studies that have used other sensitive radiographic techniques that have established the early migration of these components.

1.3 - Rationale of Present Work

Revision THR has poor performance to date with regards to the survivorship of the acetabular component. This is likely because of the large variability in treatment options, biology and anatomy, as well as poor early surveillance of new implants. Therefore, there is a need to determine if, as in primary THR:

(1) early migration is a reliable predictor of late outcomes following acetabular reconstruction at revision THR,

(2) if the most widely used and "promising" acetabular component at revision, the porous tantalum acetabular components, has acceptable early migration, and

(3) how the performance of porous tantalum acetabular components compares with migration studies of other acetabular components used at revision THR.

CHAPTER TWO

Acetabular Component Migration Measured using Radiostereometric Analysis following Revision Total Hip Arthroplasty: A Scoping Review

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Joint registries are unable to provide accurate representations on performance of acetabular components used at revision THR because of the large variability of patient factors and the data collected by joint registries is limited. Joint registries are only able to detect re-revision rates, which may not accurately represent the true proportion of unsatisfactory reconstructions.

A recent review found that RSA and EBRA are the only validated methods to measure component migration that can predict long-term survivorship of primary THR implants[85]. The advantage of EBRA is that it can be done retrospectively, and therefore it is the only method that can be used to correlate the migration of implants that were re-revised with their intraoperative loosening status at the time of re-revision. Therefore, EBRA is currently the best method to establish thresholds for component migration that predict component loosening. RSA is the most accurate technique to measure component migration and has been shown to be a predictor of late term outcomes in a recent systematic review[85].

To assess the effect of implant and patient factors on early acetabular component stability following revision THR, it would therefore be ideal to identify and compare the amount of early migration reported in RSA and EBRA studies and how these studies have been conducted. A search of major databases has found that there are currently no scoping or systematic reviews that address this topic and that there are not enough publications reporting on EBRA measurements of revision acetabular cup migration to perform a review. Therefore, this chapter presents the results of a scoping review, using a systematic search, of all RSA studies that measured the migration of acetabular components used at revision THR to assess the characteristics of these studies, including the current surgical reconstruction methods.

The findings of this scoping review are presented in the form of the submitted manuscript.

Statement of Authorship

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Name of Principal Author (Candidate)	John M Abrahams
Contribution to the Paper	Performed scoping review, collected data from publications included, ensured accuracy of data, wrote the initial draft manuscript.
Overall percentage (%)	60
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 24/9/19

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	Z. Munn
Contribution to the Paper	Provided advice on the systematic search criteria, assisted with the scoping review methodology, proofread and contributed to the manuscript.
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Name of Co-Author	S. A. Callary
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JBJS Reviews

Acetabular Component Migration Measured using Radiostereometric Analysis (RSA) following Revision Total Hip Arthroplasty (THA): A Scoping Review

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Acetabular Component Migration Measured using Radiostereometric Analysis (RSA) following Revision Total Hip Arthroplasty (THA): A Scoping Review

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Take Home Points:

- RSA studies of acetabular component migration following revision THA have a large variation in their methodology, reporting of results and may not be directly comparable. Standardisation of RSA reporting is recommended.
- There was a trend for cemented acetabular components to have larger amounts of early proximal migration than uncemented acetabular components. Results of cemented and uncemented components should be reported separately.
- Cohorts that addressed larger acetabular defects were associated with a larger amount of early migration.
- Reporting the migration result at one and two years may enable poor performing implants to be identified earlier.

Abstract

Background and Purpose: Evaluating the performance of acetabular components following revision total hip arthroplasty (THA) using registry data is challenging due to the smaller incidence of revision relative to primary THA, and the individual differences including the number of previous revisions, bone defects treated and surgical techniques used. Radiostereometric analysis (RSA) measurement of early migration is a recognised surrogate marker used to predict the long-term performance of acetabular components. We undertook a scoping review of all RSA studies that measured acetabular component migration following revision THA. We investigated the effect of the acetabular component design and existing acetabular bone defect size on acetabular component migration following revision THA.

Materials and Methods: A systematic search of Pubmed, Scopus and Embase was undertaken to identify all RSA studies of acetabular components following revision THA. Exclusion criteria included patients that had a cage rather than an acetabular component in contact with host bone and revisions following hemiarthroplasty, or radiotherapy or tumour excision.

Results: Seventeen publications involving 26 patient cohorts were identified. Ten cohorts reported a mean or median proximal migration at two years between 0.21 and 2.10mm. Inconsistent inclusion criteria and methods of reporting RSA results limited the sub analysis of the effect of implant and patient factors on component migration. Uncemented acetabular components tended to exhibit lower proximal migration at two years, compared with cemented components. Acetabular components used to treat more severe bone defects were associated with higher amounts of early migration. Where comparison was possible, the mean proximal migration at one year was similar to that at two years for the same cohort.

Interpretation: The mean or median proximal migration reported at two years for each cohort was greater than the 0.2mm threshold recommended for acetabular components used at primary THA. Uncemented acetabular components and components used to treat smaller

defects had lower amounts of early migration. Cemented and uncemented acetabular components migrate differently and therefore should be examined separately. Several recommendations are made to improve the reporting of RSA studies of acetabular migration following revision THA and enable future identification of poorly performing implants and surgical techniques.

Introduction

Revision total hip arthroplasty (THA) is more complex and has more complications than primary THA[1]. With a re-revision rate of 36.3% at 10 years[2], the survivorship of acetabular components used during first revision THA is poor. Achieving satisfactory initial stability of revision acetabular components in revision THA is more difficult than in primary THA. Furthermore, revision THA may involve reconstruction of severe bone defects leading to increased risk of failure of revision acetabular components[3].

Assessing the survivorship of implants used at revision THA is difficult due to the variety of additional surgical challenges including existing bone defects, differences in the number of previous revision **operations,** variety of surgical techniques used and treating older patients who have more comorbidities. The orthopaedic community therefore often relies on the results of smaller single-institution clinical studies to report on the success of implants or changes in surgical technique. Comparing the results of cohort studies is difficult due to the inconsistent inclusion criteria, variation in the manner of reporting results and the considerable delay between the introduction of surgical changes and publication of long-term results.

A recent review found only two validated surrogate methods to predict long-term success of THA implants, namely Radiostereometric Analysis (RSA) and Ein Bild Roentgen Analyse (EBRA) measurements of early migration and wear[4]. Early migration of acetabular components **within the first two years** measured on radiographs using sensitive methods **have** been shown to be a good predictor for later loosening following primary[5-7] and revision THA[8,9]. RSA is the most accurate method to measure migration and requires only a relatively small number of study participants and a short follow-up period, allowing early identification of poorly performing implants[10]. To assess the effect of implant, surgical and patient factors on early acetabular component stability following revision THA, it would therefore be ideal to compare the amount of early migration reported in RSA studies. However, a search of major databases identified no reviews that address this topic. A scoping review using systematic search methodology was chosen because our aim aligned with one of the key reasons for conducting scoping reviews, namely to identify the characteristics of studies in a certain field[11]. Unlike traditional reviews of interventions, scoping reviews are conducted with the aim of broadly identifying the types of studies available in a field and identifying their characteristics[11]. Therefore, we undertook a scoping review, using a systematic search, of all RSA studies that measured the migration of acetabular components used at revision THA.

Methods

The review was conducted according to the Joanna Briggs Institute's guidelines[12] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Review Extension[13]. A protocol was developed prior to conducting the review. On 5 December 2018 a systematic search was undertaken to identify RSA studies that have investigated acetabular component migration following revision THA. A search was performed on PubMed, Scopus and Embase according to the following strings: PUBMED ((((Arthroplasty, Replacement, Hip[mh] OR "hip arthroplasty"[tiab] OR "arthroplasty"[tiab] OR "hip replacement"[tiab])) AND (Revision[tiab] OR redo[tiab] OR reoperation[tiab] OR "re-do"[tiab] OR "re-operation"[tiab])) AND ("acetabular component"[tiab] OR cup[tiab] OR acetabular[tiab])) AND (Radiostereometric analysis*[tiab] OR radiostereometry analysis*[tiab] OR Roentgen stereophotogrammetric*[tiab] OR RSA[tiab]) EMBASE: ('hip arthroplasty'/de OR 'hip replacement'/de OR 'hip arthroplasty':ti,ab OR 'hip replacement':ti,ab) AND (revision:ti,ab

OR redo:ti,ab OR reoperation:ti,ab OR 're-do':ti,ab OR 're-operation':ti,ab) AND ('acetabular component':ti,ab OR cup:ti,ab OR acetabular:ti,ab) AND (roentgen:ti,ab OR 'radiostereometric analysis':ti,ab OR 'radiostereometry analysis':ti,ab OR 'roentgen stereophotogrammetric':ti,ab OR 'rsa':ti,ab) SCOPUS: (({hip arthroplasty} OR {hip replacement}) AND (revision OR redo OR reoperation OR {re-do} OR {re-operation}) AND ({acetabular component} OR cup OR acetabular) AND (migrat* OR movement OR rotat* OR inclination OR translation) AND ({radiostereometric analysis} OR {Roentgen stereophotogrammetric} OR {radiostereometry analysis} OR {RSA})). Search terms were chosen based on the different names used to describe RSA studies.

Inclusion Criteria

The review considered all RSA studies published in English that had measured the migration of acetabular components following revision THA, with no restrictions based on when or where the study was conducted. The concept was the characteristics and results of studies that had used RSA to measure the migration of acetabular components following revision THA. All study designs other than case reports were considered. A revision THA was defined as a procedure that included the replacement of an existing acetabular component. Following the search, all citations were imported into reference management software. At least two authors conducted the screening and selection of studies for inclusion in the review.

Exclusion Criteria

Studies were excluded if the revision THA involved reconstruction with a cage where the acetabular component was not in contact with host bone and revisions following radiotherapy, tumour excision and hemiarthroplasty. Duplicate publications, theses, conference proceedings, and abstracts were all excluded.

Extraction and Analysis

Data extracted from the studies included details of the patient cohort, the RSA methodology used, proximal migration, sagittal rotation, re-revision rate for aseptic loosening, and number of hips that were identified as being radiographically loose but not re-revised. A cohort was defined as a group of patients within each study who received the same acetabular implant. Where possible, raw migration data were extracted from papers directly, either through tables or from graphs.

Results

The systematic search identified 17 publications that reported on 26 cohorts of revision THA according to acetabular component design[9,15-30] (Figure 1). The included publications, cohorts, type of fixation used, acetabular component used, use of bone graft and defect classification are presented in Table 1.

Thirteen cohorts included uncemented acetabular components and thirteen included cemented components. The mean age of each cohort varied from 56 to 77 years. The median number of hips in each cohort was 19, ranging from 5 to 244. Where documented, all studies used the UmRSA software (RSA Biomedical, Umea, Sweden) for the analysis of radiographs. A total of twelve different acetabular components designs were used within 22 cohorts, four cohorts did not report the acetabular component used (Cohorts 1, 2, 17, 18).

Of the seventeen publications only three were randomised **controlled** trials that are classified as a Level 1 study. The remaining 14 publications were all cohort studies (Level 2 or 3) in which patients were prospectively enrolled as part of RSA methodology.

Migration reported for each cohort by acetabular component design

While 16 of 17 publications reported a mean/median proximal migration at two years, only ten of the 26 cohorts reported proximal migration at two years by acetabular component design (Table 2). The mean proximal migration of these ten cohorts varied between 0.21 to 2.10mm. Mean sagittal rotation at two years was only reported for four cohorts by acetabular component design. Of the sixteen cohorts that did not report proximal migration at two years by implant design, the migration of 15 cohorts (four cemented, four uncemented, seven mixed fixation type) were actually reported in combination with another cohort within a publication (Table 1).

The reported mean proximal migration of uncemented components (five individual cohorts, two combined cohorts) varied between 0.21 and 0.90mm (Figure 2). The reported proximal migration of cemented components (five individual cohorts, two combined cohorts) varied between 0.40 and 2.50 mm (Figure 2).

There were eight cohorts that reported mean or median migration at both one and two years. Seven of these eight cohorts would have the classified the migration in the same risk category at one year as they would have at two years according to Pijls et al[5]. The means at one and two years were all within 0.40mm of each other, with the exception of Cohorts 2 and 5 which had a lower mean migration at two years (0.75mm and 2.10mm) compared to one year (1.30mm and 2.80mm), (Table 2).

Ten cohorts reported individual migration data at two years that allowed comparison to the 1mm threshold previously described by Kim et al[8] and Klerken et al[9] (Table 1). Using this threshold, it was possible to identify that the percentage of individual components above 1mm within each of these cohorts varied between 6 and 66%.

The effect of the acetabular bone defect classification on mean proximal migration was investigated in and reported for only three cohorts (cohorts 2, 6 and 26). In all three cohorts more severe defects were associated with increased early migration. Four of the 17 publications investigated the effect of the type and amount of bone graft on migration. Excluding the publications that examined additives to bone graft, only one determined that the type of bone graft had an effect on migration[22], whilst three found no significant difference[15,20, 21]. Ten of the 17 publications described the previous number of revisions and none reported the migration according to previous number of revisions, although three publications only included first time revisions.

Discussion:

The survivorship of acetabular components used at revision THA is poor. The Australian Orthopaedic Association National Joint Replacement Registry has reported a 36.3% re-revision rate of the acetabular component at ten years following first time revision THA[2]. New implants and modified surgical techniques continue to be introduced. Institutional cohort studies are of limited value because they require a long follow-up period by which time the studied implant may no longer be in clinical use. Early migration of the acetabular component has been shown to predict later loosening after primary[5] and revision THA[8].

Our systematic search identified seventeen publications that measured the migration of acetabular components following revision THA using the most accurate measurement method, RSA[31]. However, acetabular components design and reconstruction techniques used varied across studies and were used to treat a range of bone defects. It is known that multiple factors may influence the migration of acetabular components, such as fixation type, implant design, and the use of different bone grafts to treat acetabular bone defects of varying severity. Our scoping review indicates that a subsequent full meta-analysis of the effect of these factors on acetabular component migration measured by RSA is not currently feasible due to the relatively small cohorts studied, the fact that many studies did not report the migration according to acetabular component design, and the varying bone defect severity or use of bone graft. The recommendations identified by this review will assist in performing a meta-analysis as more studies are undertaken.

Comparison of published cohort results to existing migration thresholds

A review of short-term RSA studies matched with long term clinical results determined that cohorts of acetabular components used at primary THA with a mean proximal migration of less than 0.2mm at two years were associated with revision rates for loosening of less than 5% at ten years[5], this being deemed to be clinically 'acceptable'. Mean proximal migration of 0.2 to 1.0mm was considered 'at risk' of revision rates in excess of 5% at ten years and a mean proximal migration exceeding 1.0mm was considered 'unacceptable' as it was associated with a rate of revision exceeding 5% at ten years[5]. No cohort in this scoping review had a mean proximal migration at two years considered to be clinically 'acceptable'. Four publications[19,20,23,24] in this review reported a mean proximal migration greater than 1.0mm at two years which would be deemed to be 'unacceptable' (Figure 2). This may be due to the inferior condition of host bone at revision THA which potentially may affect initial component stability.

Our review identified eight cohorts for which a mean proximal migration was reported at both one and two years. In seven of these cohorts, the mean or median at one year was classified in the same risk category as the two year result according to Pijls et al[5]. Cohort two was categorised differently, and this was likely due to fewer patients in Cohort 2 being reviewed at the longer follow-up, including two components that had migrated >1mm at one year[15]. While further validation of using the mean migration at one year as a threshold would be required, earlier identification of poorer performing acetabular components would potentially reduce their frequency of use and thus re-revision rates. Based on findings of this review, it is therefore recommended that future RSA studies report migration results at one and two years (Table 3).

Reporting RSA results: Absolute values

Twelve of seventeen publications reported a mean proximal migration based on signed values. At revision THA, a negative (distal) proximal migration is as relevant as a positive (proximal) value. The reason for a negative value may be related to the centre of rotation moving distally secondary to rotation. It may also occur due to loss of superior fixation. Mean or median values that are derived from signed values are likely to be smaller in magnitude than means derived from absolute values. Valstar et al[32] recommended that signed values be used because of possible methodological errors. However, this may be more relevant when measuring primary THA components as it is uncommon to have such components migrate large amounts distally. In contrast, Derbyshire et al[33] recommended that the mean or median of the absolute values be used to prevent reporting a mean of zero, despite a large range. Based on findings of this review, it is recommended that both absolute and signed values be reported to enable improved comparison across the literature (Table 3).

Reporting RSA results: Mean, median and individual data

If migration values are not normally distributed, the mean reported for the cohort is likely to be significantly affected by components exhibiting larger migrations, particularly if sample sizes are relatively small. For example, Cohort 26's migration results were not normally distributed as a result of seven components migrating >1.0mm. Subsequently, the median (0.3mm) was smaller than the mean (0.9mm). While it is more appropriate to report medians rather than means when values are not normally distributed, the additional reporting of mean values allows comparison with existing thresholds that are based on mean migration (Table 3).

Individual migration data were reported for ten of 26 cohorts by acetabular component design. Reporting of migration values individually for all components examined allows the identification of outliers and comparison with other studies. Individual proximal migration exceeding 1.0mm at two years has been shown to predict aseptic loosening of acetabular components at re-revision surgery in 80% of cases[8]. The use of thresholds based on individual data may indicate expected re-revision rate for loosening.

Component migration according to fixation type

There was a trend for uncemented acetabular components to have a lower mean migration at two years than cemented components (Figure 2, Table 2). The only two cohorts that reported an 'unacceptable' mean proximal migration at two years, namely exceeding 1mm, both used a cemented acetabular component. Two additional publications[19,20] confirmed this trend, reporting a significantly larger amount of proximal migration for cemented components compared to that with uncemented components (Figure 2). The reason for this finding may be that at revision THA it is more difficult to achieve good cement interdigitisation within sclerotic bone and in the presence of large uncontained defects.

Three publications in our review combined the migration results of cemented and uncemented components. Reporting the mean migration of a heterogeneous cohort obscures any potential differences between specific sub cohorts of patients. Based on the findings of this review, it is recommended that uncemented and cemented reconstructions be reported separately (Table 3).

It is important to acknowledge that despite the trend towards greater early migration of cemented components identified in this review, the long-term effect on survivorship is unknown due to the lack of long-term follow-up studies. All RSA studies in this review presented short term results, with eleven publications having a mean follow-up of two years and the remaining six studies having a mean follow-up of three to five years.

Comparison of the migration according to implant type and defect severity treated

The acetabular component with the lowest mean proximal migration at two years was **an uncemented hydroxyapatite coated** component (mean 0.21mm, Cohort 5, Table 2). These results should be interpreted cautiously due to the various differences within the cohorts, for example, the low migration of cohort 5 may be due to treating relatively less severe bone defects (GP I or II).[34]

A recent systematic review of acetabular components used at revision THA identified TMARS as having the most promising clinical results[35]. The mean proximal migration of the TMARS components in our review was 0.25mm and 0.90mm (Cohorts 24 and 26 respectively). Cohort 26 reported only on severe defects (Paprosky IIIA and IIIB)[36] which likely influenced the results. Our review identified that acetabular components used to reconstruct more severe defects migrated more at two years and therefore it is recommended that migration be reported by defect type.

The most commonly reported defect classification was by Gustillo-Pasternack[34], which was used in thirteen of the seventeen publications included in this review. However, other classification systems, such as the one described by Paprosky et al[36], are considered superior because of the use of more objective descriptions, the ability to differentiate between an intact rim and the ability to describe the presence of intact anterior/posterior columns[37].

Reporting RSA results: Initial follow-up time point

While the majority of studies undertook the initial RSA exam within the first eleven days of revision surgery, three publications did not describe at what time point it was undertaken and one publication reported that the baseline examination was done between one and three weeks following surgery. Studies that do not perform the initial RSA examination within the first week may inadvertently report a lower amount of migration that may not be comparable to other studies or allow assessment using established thresholds. Ornstein et al[26] measured acetabular component migration with RSA every week for the first six weeks post-operatively and concluded that the initial examination should be taken as soon as possible and prior to patient weight bearing. Based on the findings of this review, it is recommended that the baseline RSA examination should occur prior to weight bearing, and the timing of it should be reported (Table 3).

There are some limitations of this review, with the first limitation being the diversity and lack of standardisation of the RSA studies included in the review. Furthermore, only a relatively small number of publications were available for review and all only involved short-term follow-up. Although a protocol was adhered to and a systematic search was undertaken, it is nevertheless possible that some studies may have been missed.

In conclusion, this scoping review of RSA studies identified a wide variety of different surgical techniques and acetabular components used to treat acetabular components at revision THA. There was a trend for cemented reconstructions to have larger amounts of early migration than uncemented reconstructions, as did reconstructions of more severe acetabular bone defects. A number of recommendations have been made based on this review, which will improve the reporting of future RSA studies.

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FIGURE LEGENDS:

Figure 1:

Flow chart of the systematic literature search and exclusion of articles.

Figure 2:

Mean proximal migration at two years for cemented and uncemented acetabular components. Solid symbols = Reported individual cohort by implant design; Hollow symbols = Reported combined cohorts

TABLE LEGENDS:

Table 1:

Publications included in the scoping review with cohort details including type of fixation used, acetabular component used, use of bone graft, defect classification and proximal migration at two years.

Table 2:

The mean proximal migration and sagittal rotation reported for each cohort at one and two years.

Table 3.

Recommendations to enhance reporting of RSA acetabular migration studies.

Table 1

Publication	Cohort	Acetabular Component Design	Number of hips	Mean follow-up (range) (years)	Mean Age (range)	Fixation Type	Bone Graft	Acetabular Defect Grades Gustilo Pasternak (I/II/III/IV)	Mean Proximal Migration at 2 years (mm)	No. Hips migrated >1mm at 2 years
Snorrason and Karrholm[28] 1990	1	NR	15	2	64 (45-78)	Cemented	NR	7/8/0/0	0.82	NR
Franzen et al. 1993[15]	2	NR	17	1.6 (1-2)	63 (44-78)	Cemented	Bone graft n=7	4/12/1/0	0.75	7/17
Nivbrant et al. 1996[22]	3	Harris Galante I (Zimmer)	32	2	66 (39-83)	Uncemented	Bulk allograft n=5 Morselised bone graft n=26 No graft n=29	23/25/10/2	0.36	NR
	4	Harris Galante II (Zimmer)	28	2						NR
Nivbrant and Karrholm 1997[21]	5	ABG (Howmedica)	29	1.9 (1-2)	65 (30-83)	Uncemented	Morselised bone graft n=23, Morselised + bulk graft n=2	7/18/4/0	0.21	NR
Ornstein et al. 1999[23] & Ornstein et al. 2006[25]	6	Exeter low profile (Howmedica)	21[23];17[25]	2[23];5[25]	74* (56-87) [23];73 (56-81) [25]	Cemented	Impacted morselized allograft used where appropriate	6/6/9/0[23];5/6/6/0[25]	2.10	14/21
Ornstein et al. 2000[26]	7	Exeter low profile (Howmedica)	5	6 weeks	68 (47-76)	Cemented	Impacted morselized allograft	0/5/0/0	NR	NR
Ornstein et al. 2003[24]	8	Exeter low profile	9	2	73* (61-84)	Cemented	Impacted morselized allograft used where appropriate	1/10/1/0	2.50*	8/12
	9	Lubinus socket	3	2						
Khan et al. 2006[17]	10	Trident Constrained (Stryker)	30	2.7 (2-4.8)	73.1 (46-91)	Uncemented	NR	NR	0.37	NR
Kärrholm et al. 2006[16]	11	Harris-Galante II(Zimmer)	14	3	NR	Uncemented	Impacted morselised bone graft mixed with OP-1 n=7,	3 (3-4)*	NR	5/20

	12	Trilogy (Zimmer)					Impacted morselised bone graft n=7		NR	
	13	Reflection (Smith and Nephew)	6	3	NR	Cemented	Impacted morselised bone graft mixed with OP-1 n=3, Impacted morselised bone graft n=3		NR	
Khan et al. 2007[18]	14	Trident Constrained (Stryker)	107	3 (2-4.8)	76.9 (32-93)	Uncemented	Morselised allograft n=65, Morselised allograft and bulk allograft n=2	NR	0.57	NR
Saari et al. 2014[27]	15	Trilogy (Zimmer)	14	3	61 (35-80)	Uncemented	Impacted morselised bone graft where necessary	3 (3-4)*	NR	NR
	16	Ogee (Depuy)	27	3		Cemented	Impaction allograft n=27		NR	NR
Klerken et al 2015[9]	17	NR	244	2-20	64 (SD 12.6)	Uncemented	Impacted morselised bone graft, n=259	86/119/94/12, NR=1	NR	NR
	18	NR	68			Cemented			NR	NR
Mohaddes et al. 2017[19]	19	Harris Galante (Zimmer)	16	NR (0.25-17)	61 (33-77)	Uncemented	Impacted morselised bone grafting n=16	1/6/12/1	0.71	NR
	20	Multi-hole Trilogy (Zimmer)	4			Uncemented	Impacted morselised bone grafting n=4			NR
	21	Reflection Cup (Smith and Nephew)	24		56 (38-79)	Cemented	Impacted morselised bone grafting n=24	0/9/10/8	1.39	NR
	22	Charnley Ogee Cup (DePuy)	3			Cemented	Impacted morselised bone grafting n=3			NR
Mohaddes et al. 2017[20]	23	ZCA (Zimmer)	19	2	69 (40-77)	Cemented	Impacted morselised bone graft, n=38	4/6/9/0	1.45	6/15
	24	TM Component	23	2	68	Uncemented		6/10/7/0	0.25	1/16

		(Zimmer)			(42-79)					
Zampelis et al. 2018[30]	25	Exeter (Howmedica)	18	2	72 (55-85)	Cemented	Impacted morselized allograft with clodronate n=9 Impacted morselized allograft n=9	Paprosky IIA/IIB = 9/9	0.40	NR
Solomon et al. 2018[29]	26	TMARS (Zimmer)	55	4 (2-12)	69* (35-89)	Uncemented	Bone allograft where appropriate	Paprosky IIIA/IIIB= 28/27	0.90	7/55

NR= Not reported; *Median values

Table 2

Mode of Acetabular Component Fixation	Cohort	Number of Acetabular Components	Mean Proximal Migration at one year (mm)	Mean Proximal Migration at two years (mm)	Mean Sagittal Rotation at one year (°)	Mean Sagittal Rotation at two years (°)
Cemented Only	1	15	0.47	0.82	NR	NR
	2	17	1.30	0.75	NR	NR
	6	21	1.8*	2.10*	NR	NR
	7	5	NR	NR	NR	NR
	8	9	NR#	NR#	NR	NR
	9	3	NR#	NR#	NR	NR
	13	6	NR#	NR#	NR	NR
	16	27	NR#	NR#	NR	NR
	18	68	NR#	NR#	NR	NR
	21	24	NR#	NR#	NR	NR
	22	3	NR#	NR#	NR	NR
	23	19	1.16*	1.45*	NR	NR
	25	18	0.40	0.40	0.03	0.10
Uncemented Only	3	32	NR#	NR#	NR	NR
	4	28	NR#	NR#	NR	NR
	5	29	NR	0.21	NR	0.64
	10	30	0.49	0.37	1.70	2.32
	11	NR	NR#	NR#	NR	NR
	12	NR	NR#	NR#	NR	NR
	14	107	0.49	0.57	1.12	1.58
	15	14	NR#	NR#	NR	NR
	17	244	NR#	NR#	NR	NR
	19	16	NR#	NR#	NR	NR

	20	4	NR#	NR#	NR	NR
	24	23	0.21*	0.25*	NR	NR
	26	55	NR	0.9	NR	NR

NR = Not Reported; * = Median, # Migration data for this cohort was only reported in combination with another cohort

Table 3

Recommendations to enhance reporting of RSA migration studies:
1. Report one year and two year proximal migration and sagittal rotation results
2. Report absolute and signed migration results
3. Report median and mean values of the cohort
4. Present individual migration curves for each hip to allow identification of outliers that exceeded established thresholds
5. Report migration according to implant type used
6. Report migration according to defect type treated
7. Report when the baseline RSA examination occurred, preferably in the first week prior to weight bearing

Figure 1

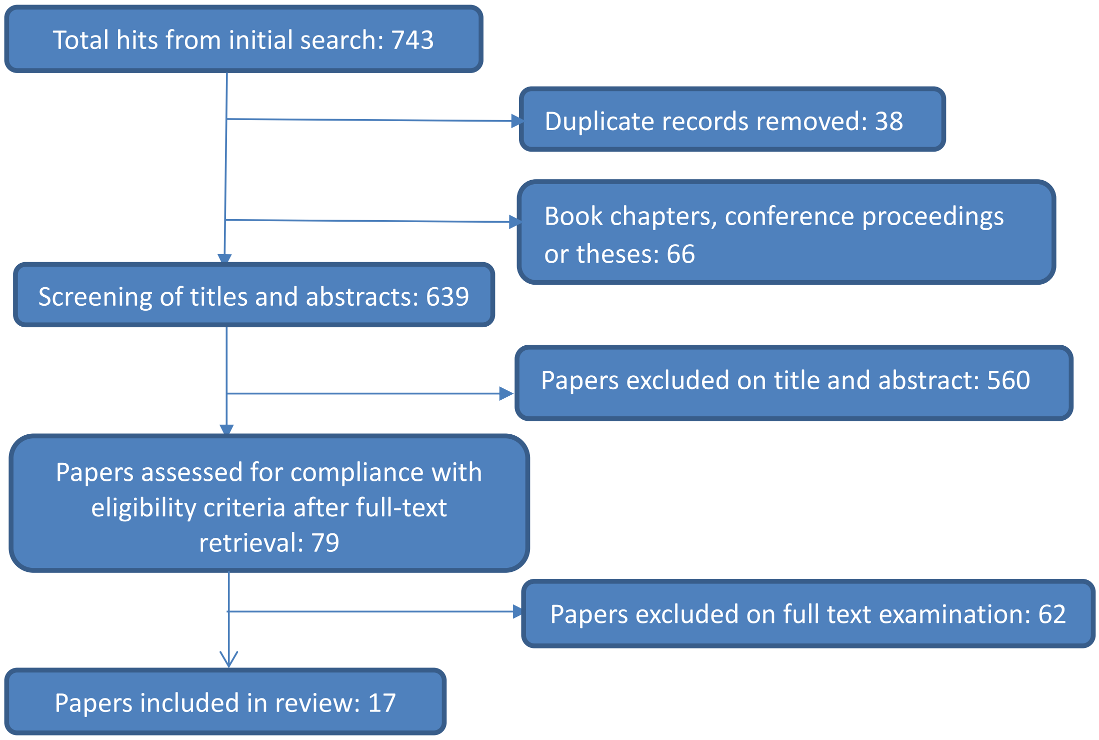
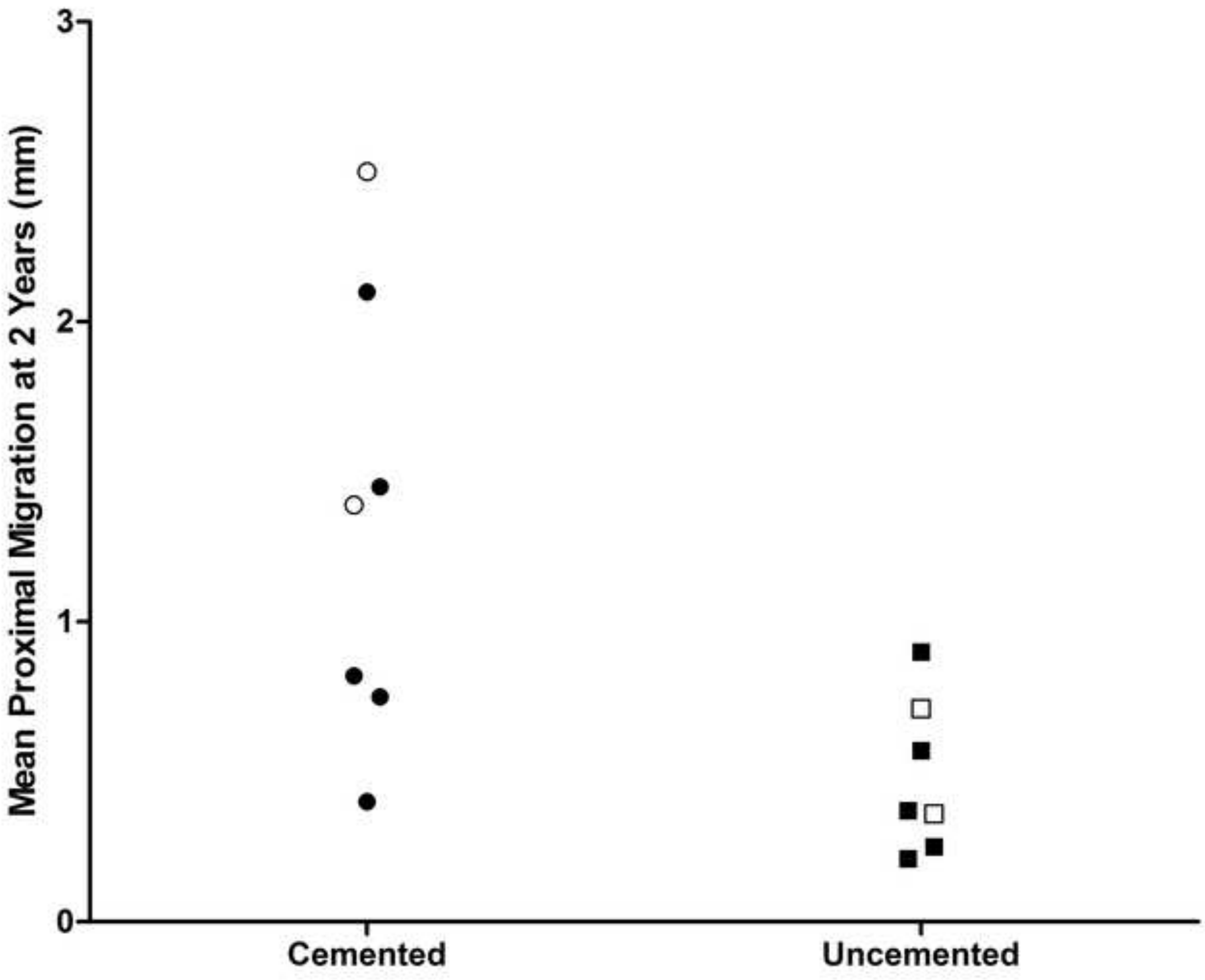

Total hits from initial search: 743
Duplicate records removed: 38
Book chapters, conference proceedings or theses: 66
Screening of titles and abstracts: 639
Papers excluded on title and abstract: 560
Papers assessed for compliance with eligibility criteria after full-text retrieval: 79
Papers excluded on full text examination: 62
Papers included in review: 17

Figure 2


3
2
1
0
Mean Proximal Migration at 2 Years (mm)
Cemented
Uncemented

CME Questions Submission Form

Enter all questions on this form. A total of 3 multiple-choice questions are required. Please review the *Guidelines for Creation of CME Questions* in the Author Resource Center section of the JBJS website before submitting your questions.

Manuscript number: REVIEWS-D-19-00170
Article title: Acetabular Component Migration Measured using Radiostereometric Analysis following Revision Total Hip Arthroplasty: A Scoping Review

Question 1

I. Does this question have an associated image or images?

☐ Yes ☒ No

(If YES – upload image(s) separately using the "CME Question Figure" item option in the Attach Files screen of Editorial Manager. Include a one to two sentence description of each figure here. All figures should be at least 5x7 inches with a resolution of 300 ppi.)

II. Question: (A patient-care scenario is preferred when appropriate; see *Guidelines* link above)

Which two techniques used to measure implant migration have been validated as surrogate methods to predict later loosening?

III. Options: *(In alphabetical or logical order.* ***Please do not use "all of the above" or "none of the above" as potential answer choices.****)*

A.	CT and RSA
B.	CT and MRI
C.	RSA and EBRA
D.	RSA and MRI
E.	EBRA and CT

IV. Answer: (must be *clearly* the best of the options)

☐ A. ☐ B. ☒ C. ☐ D. ☐ E.

V. Correct Answer Location: Please identify the manuscript section where the correct answer is located (e.g. "Results" or "Discussion")

Introduction

VI. Supporting Statement: Please include one sentence from the section identified above supporting the correct answer.

A recent review found only two validated surrogate methods to predict long-term success of THA implants, namely Radiostereometric Analysis (RSA) and Ein Bild Roentgen Analyse (EBRA) measurements of early migration and wear[4].

Question 2

V. Does this question have an associated image or images?

☐ Yes ☒ No

(If YES – upload image(s) separately using the "CME Question Figure" item option in the Attach Files screen of Editorial Manager. Include a one to two sentence description of each figure here. All figures should be at least 5x7 inches with a resolution of 300 ppi.)

VI. Question: (A patient-care scenario is preferred when appropriate; see *Guidelines* link above)

In our scoping review of RSA studies, which variable was found to be associated with increased amounts of early migration.

VII. Options: *(In alphabetical or logical order.* ***Please do not use "all of the above" or "none of the above" as potential answer choices.****)*

A.	Patient comorbidities
B.	Cemented acetabular fixation
C.	Screwless fixation
D.	Patient gender
E.	Number of previous revisions

VIII. Answer: (must be *clearly* the best of the options)

☐ A. ☒ B. ☐ C. ☐ D. ☐ E.

V. Correct Answer Location: Please identify the manuscript section where the correct answer is located (e.g. "Results" or "Discussion")

Discussion

VI. Supporting Statement: Please include one sentence from the section identified above supporting the correct answer.

There was a trend for uncemented acetabular components to have a lower mean migration at two years than cemented components

Question 3

IX. Does this question have an associated image or images?

☐ Yes ☒ No

(If YES – upload image(s) separately using the "CME Question Figure" item option in the Attach Files screen of Editorial Manager. Include a one to two sentence description of each figure here. All figures should be at least 5x7 inches with a resolution of 300 ppi.)

X. Question: (A patient-care scenario is preferred when appropriate; see *Guidelines* link above)

Which of the following is not a recommendation of this scoping review

XI. Options: *(In alphabetical or logical order.* ***Please do not use "all of the above" or "none of the above" as potential answer choices.****)*

A.	Report absolute and signed migration results
B.	Report one year and two year proximal migration and sagittal rotation results
C.	Report migration according to defect type treated
D.	Report proximal migration by gender
E.	Report median and mean values of the cohort

XII. Answer: (must be *clearly* the best of the options)

☐ A. ☐ B. ☐ C. ☒ D. ☐ E.

V. Correct Answer Location: Please identify the manuscript section where the correct answer is located (e.g. "Results" or "Discussion")

Table 3

VI. Supporting Statement: Please include one sentence from the section identified above supporting the correct answer.

Table 3 lists all recommendations except for option D.

CHAPTER THREE

Proximal translation of > 1 mm within the first two years of revision total hip arthroplasty correctly predicts whether or not an acetabular component is loose in 80% of cases.

As published in The Bone and Joint Journal, April 2017

To date, the acceptable limits of early migration for the acetabular component have been determined using homogeneous cohorts of primary THR. Revision THR presents many treatment challenges that are not present at primary THR such as the presence of bone defects, poorer host bone quality, use of bone grafts and an older patient's age that typically has greater medical co-morbidities. Additionally, particularly in severe cases of bone loss it may not be possible to achieve press-fit fixation as in primary THR. Because of the aforementioned factors, the initial stability and pattern of migration of acetabular components following revision THR is likely to be different from that of primary THR. Ideally, the development of an early migration threshold to predict long term outcomes would rely on confirmed intra-operative findings of loosening and not loosening. Therefore, the primary aim of this study was to measure the radiological migration of cementless acetabular components from revision to re-revision THR using EBRA-Cup. We used EBRA for these measurements as this technique allows for a retrospective analysis which was practical for our database that included the follow-up of patients undergoing a revision THR until their next re-revision, well before RSA was available at our institution. The secondary aim of the study was to determine the sensitivity, specificity and predictive values of previously reported thresholds of proximal translation and sagittal rotation after revision THR at various times during early follow-up.

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

Statement of Authorship

Title of Paper	Proximal translation of > 1 mm within the first two years of revision total hip arthroplasty correctly predicts whether or not an acetabular component is loose in 80% of cases
Publication Status	☒ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Bone Joint J 2017;99-B:465–74.

Principal Author

Name of Principal Author (Candidate)	John M Abrahams		
Contribution to the Paper	Ethics submission, Study design, Analysis of results, Wrote initial draft.		
Overall percentage (%)	60		
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	24/9/19

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	Y. S. Kim		
Contribution to the Paper	Data collection, Analysis of results, Edited manuscript to publication.		
Signature		Date	24/9/19

Name of Co-Author	S. A. Callary		
Contribution to the Paper	Planned the study, Analysis of results, Edited manuscript through to publication.		
Signature		Date	24/9/2019.

Name of Co-Author	K. Costi
Contribution to the Paper	Assisted with data collection, Critical review of manuscript.
Signature	Date 24/9/19

Name of Co-Author	C. De Ieso
Contribution to the Paper	Data collection, Analysis of results, Critical review of manuscript.
Signature	Date 24/9/19

Name of Co-Author	D. W. Howie
Contribution to the Paper	Planned the study, Interpretation of results, Critical review of manuscript.
Signature	Date 24/9/19

Name of Co-Author	L. B. Solomon
Contribution to the Paper	Planned the study, Ethics submission, Interpretation of results, Edited manuscript through to publication.
Signature	Date 24/9/19

■ HIP

Proximal translation of > 1 mm within the first two years of revision total hip arthroplasty correctly predicts whether or not an acetabular component is loose in 80% of cases

A CASE-CONTROL STUDY WITH CONFIRMED INTRA-OPERATIVE OUTCOMES

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Aims

The purpose of this study was to determine the sensitivity, specificity and predictive values of previously reported thresholds of proximal translation and sagittal rotation of cementless acetabular components used for revision total hip arthroplasty (THA) at various times during early follow-up.

Patients and Methods

Migration of cementless acetabular components was measured retrospectively in 84 patients (94 components) using Ein-Bild-Rontgen-Analyse (EBRA-Cup) in two groups of patients. In Group A, components were recorded as not being loose intra-operatively at re-revision THA (52 components/48 patients) and Group B components were recorded to be loose at re-revision (42 components/36 patients).

Results

The mean proximal translation and sagittal rotation were significantly higher in Group B than in Group A from three months onwards ($p < 0.02$). Proximal translation > 1.0 mm within 24 months had a positive predictive value (PPV) of 90% and a specificity of 94%, but a sensitivity of 64%. Proximal translation > 1.0 mm within the first 24 months correctly identified 76 of 94 (81%) of components to be either loose or not loose. However, ten components in Group B (24%) did not migrate proximally above 1.0 mm within the first 60 months.

Conclusion

The high PPV of EBRA-Cup measurements of proximal translation (90%) shows that this can be used in early follow-up to identify patients at risk of aseptic loosening. The absence of proximal translation within the first 60 months indicates a component is not likely to be loose at re-revision THA although it does not exclude late aseptic loosening as a cause of failure.

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The acetabular component is more commonly revised for aseptic loosening than the femoral component.[1] Most acetabular components currently used for revision total hip arthroplasty (THA) are cementless.[2] It has been suggested that aseptic loosening of the acetabular component can occur early because of inadequate fixation at the time of implantation or failure of bone ingrowth or ongrowth,[3] or late, secondary to loss of fixation from osteolysis.[4] Early migration of acetabular components used at primary THA may predict survivorship at 6.5 years[5] and ten years.[6] Sensitive radiological measurement techniques including radiostereometric analysis (RSA)[7] and Ein-Bild-Roentgen-Analyse (EBRA-Cup)[5,8] have been used to measure the early migration of acetabular components. Their ability to predict mid- to long-term loosening of the acetabular component at early follow-up can be used to identify poorly performing implants.

In a recent systematic review, early migration of the acetabular component after primary THA was found to be a predictor of late

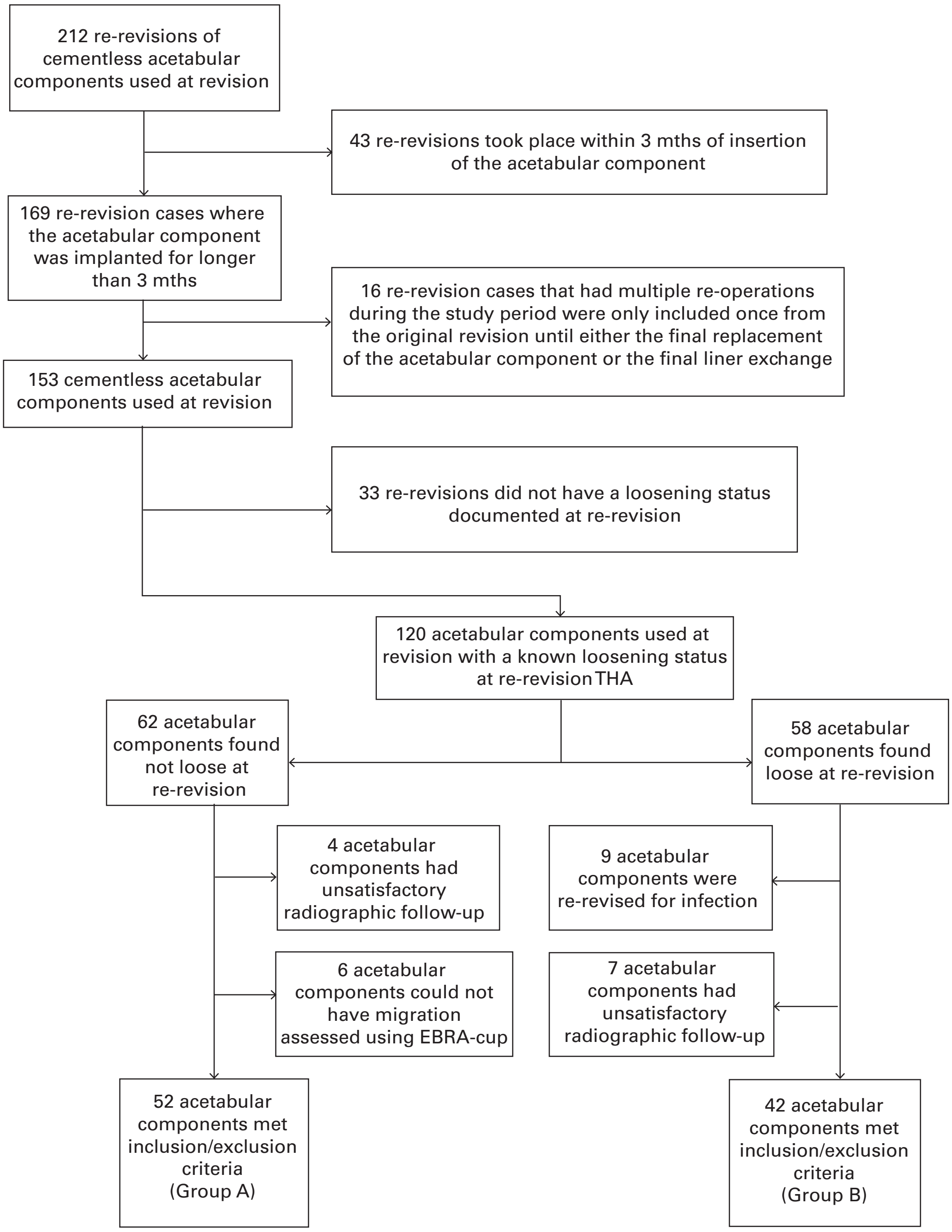

Fig. 1

Flowchart of acetabular components in the final analysis (THA, total hip arthroplasty; EBRA-Cup, Ein-Bild-Rontgen-Analyse).

revision.[6] This review matched the reported two-year migration with the ten-year survivorship according to the type of acetabular component. Ideally, early migration and survivorship should be measured within the same cohort of components.

To date, there are only three published cohort studies that have used sensitive radiological techniques in an attempt to correlate early migration of an acetabular component with mid-term component loosening.[5,9,10] In these three studies, only 16 out of 312,[10] two out of 41[9] and 13 out of 120[5] components had their loosening status confirmed intra-operatively at revision THA. The remaining unrevised acetabular components were assessed using plain radiographs and assumed to be either loose or not loose

Table I. Intra-operative loosening grade classification according to Howie et al[16]

Grade of loosening	Description
0	No loosening
1	Fluid movement only at interface
2	Slight movement, required hammering or strong leverage
3	Loose, removable by hand or gentle leverage

based on radiolucency criteria. An unconfirmed diagnosis of loosening limits the specificity of a study and may affect its ability to predict loosening on the basis of early migration.

Of the three studies mentioned above, only one investigated the migration of acetabular components used at revision THA, and reported on a combination of cemented and cementless revision acetabular components.[10] The migration of acetabular components used at revision THA may differ from those in a primary setting because of the presence of acetabular defects, the use of bone grafts, a poorer quality of host bone stock and an older patient. In addition, cemented and cementless components may migrate differently, especially at early follow-up[11] while cemented components may be more prone to later revision for aseptic loosening.[12]

The primary aim of this study was to measure the radiological migration of cementless acetabular components from revision to re-revision THA using EBRA-Cup. The secondary aim of the study was to determine the sensitivity, specificity and predictive values of previously reported thresholds of proximal translation and sagittal rotation after revision THA at various times during early follow-up.

Patients and Methods

After obtaining ethics committee approval from the Royal Adelaide Hospital, we undertook a case-control study of all patients who had undergone a second revision THA at our hospital between 1980 and 2015, using prospectively collected data.

All patients were allocated to one of two groups: Group A, in which the acetabular component was found to be not loose at re-revision, and Group B, in which the acetabular component was found to be loose at re-revision (Fig. 1). Re-revision THA was defined as an operation in which at least one prosthetic component was exchanged for a hip that had undergone previous revision of the acetabular component. Exclusion criteria were survival for less than three months, because osteointegration of the cementless acetabular component would have been unlikely,[13-15] and loosening status that was not documented intra-operatively at re-revision THA. Patients who had undergone multiple re-operations during the study period were only included once from the original revision until either the acetabular component had been replaced or until the final exchange of the liner.

Inclusion criteria for Group A were all patients with a revision cementless acetabular component who had undergone re-revision for any cause and were found not to have a loose acetabular component at operation. Loosening was assessed after at least 40% of the circumference of the bone implant interface had been exposed: acetabular component stability was tested according to the description of Howie et al[16] (Table I) after any screws had been removed. The grade of intra-operative loosening was documented at the time of re-revision on a standardised operating form that included a clear description of each grade of loosening.

Inclusion criteria for Group B were all patients with a revision cementless acetabular component which was confirmed to be loose at the time of re-revision. Exclusion criteria for Group B were patients with an acetabular component that was re-revised for infection. Infection was not an exclusion criterion for components in Group A as the stability of acetabular component had not been compromised.

Any patients with inadequate radiological follow-up were excluded. Inadequate radiological follow-up was defined as not having at least three anteroposterior (AP) radiographs of the pelvis available for review, including an immediate post-operative radiograph of the revision investigated and one prior to re-revision. Patients were also excluded if EBRA-Cup was unable to calculate migration because radiographs had been taken with different degrees of pelvic rotation and tilt.

EBRA-Cup measurements of migration were carried out using plain AP radiographs of the pelvis. Radiographs that had been taken before January 2000 and those that were only available as hard-copy images were digitally scanned at a 300 dpi, 12-bit resolution and saved to the hospital picture archiving and communication system (PACS). Radiographs were retrieved from the hospital PACS (Agfa IMPAX, AGFA-Gevaert N.V, Mortesl, Belgium) at the highest quality setting and were analysed with EBRA-Cup (Universität Innsbruck, Innsbruck, Austria). The standard landmarks used within EBRA-Cup as reference lines were the ischial tuberosities, the inferior obturator line, the ilio-ischial line and a horizontal line between the roof of the sciatic notches or the superior border of the sacral foramina. The size of the acetabular component and femoral head were recorded in the programme as part of the standard calibration process.

The proximal and medial translation and change in sagittal rotation were measured on each radiograph by a single observer (YSK). Migration values were generated by interpolation when a radiological examination did not exist by using the migration values immediately before and after the required time point. The time points chosen for analysis

Table II. Intra-observer error of Ein-Bild-Rontgen-Analyse measurements

	Medial translation (mm)	Proximal translation (mm)	Sagittal rotation
Mean	0.22	-0.08	-0.53°
95% confidence interval	0.05 to 0.39	-0.31 to 0.15	-1.02° to -0.05°

Table III. Patient demographics in each group including; gender, mean age at time of index revision procedure, mean time to re-revision, presence of bone graft, use of screws, pre-operative Paprosky grade[17] of the acetabular defect and intra-operative loosening grade at re-revision procedure

	Group A (not loose)	Group B (loose)
Components (patients) (n)	52 (48 patients)	42 (36 patients)
M:F	23:29	13:29
Mean age (yrs, range)	63 (33 to 82)	59 (27 to 79)
Mean time to re-revision (mths, range)	69 (4 to 235)	114 (4 to 233)
Loosening grade		
	Grade 0 = 52	
		Grade 1 = 2
		Grade 2 = 20
		Grade 3 = 20
Screws		
	25 in ilium only	21 in ilium only
	3 in ilium and ischium	2 in ilium and pubis
	1 in ilium and pubis	1 in pubis only
Cases with bone graft (n, %)	20 *(38)*	20 *(48)*
Pre-operative Paprosky Grade (n, %)		
	IIA 7 *(13)*	IIA 10 *(24)*
	IIB 13 *(25)*	IIB 5 *(12)*
	IIC 18 *(35)*	IIC 16 *(38)*
	IIIA 6 *(12)*	IIIA 3 *(7)*
	IIIB 8 *(15)*	IIIB 8 *(19)*

were those used routinely for clinical follow-up: 12, 24, 36 and 60 months from surgery.

The intra-observer error of the EBRA-Cup measurements was determined by repeated analysis at two-week intervals at every follow-up time point for 18 components by a single observer (YSK). Nine components from each group were selected at random using the 'RAND' function in Microsoft Excel (Microsoft, Redmond, Washington). Previous measurements were not made available to the observer for comparison. The intra-observer error was reported as the mean and 95% confidence intervals (CI). There were a total of 119, 110 and 109 radiological measurements available for comparison of medial, proximal translation and sagittal rotation respectively. The intra-observer error of EBRA-Cup measurements performed in this study is shown in Table II.

Acetabular defects present before the index revision were graded according to Paprosky et al[17] as described by Yu et al.[18]

Statistical analysis. Logistic regression analysis was used to examine the significance of the relationship of age at the time of operation, gender, side, component type, sagittal rotation, proximal translation and medial translation with intra-operative loosening outcome using SPSS version 20 (IBM, Armonk, New York).

A Mann-Whitney U test was carried out to determine if migration at three, six, 12, 24, 36 and 60 months was significantly different for the two groups using GraphPad Prism 6 (GraphPad Software, San Diego, California).

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of three previously described thresholds of proximal translation of 1.0 mm[5] and 1.8 mm[9] and sagittal rotation of 1° and 2.5°[9] were determined at 12, 24, 36, and 60 months. A combination of thresholds was also tested: 1.0 mm of proximal translation or 1.0° of sagittal rotation; and 1.8 mm of proximal translation or 2.5° of sagittal rotation.

Sensitivity was calculated as the proportion of cases in Group B that exceeded the given threshold. Specificity was calculated as the proportion of cases in Group A that did not exceed the threshold. A p-value < 0.05 was considered significant for all statistical tests.

Receiver operating characteristic (ROC) curves of maximal migration values within 24 months for proximal translation and sagittal rotation, for all cases in each group were generated using GraphPad Prism 6. Migration values for Group A were considered to be the 'negative result values' and those for Group B were considered to be 'positive result values'. The area under the ROC curve was used to determine the accuracy of using either translation

Table IV. Cause of re-revision for group A, not loose at time of re-operation

Cause of re-revision	n
Recurrent dislocation	16
Femoral component loosening	15
Infection	9
Ectopic bone	2
Femoral osteolysis	3
Periprosthetic femoral fracture	4
Unexplained pain	1
Loose acetabular line	1
Implant fracture	1

Table V. Logistic regression analysis of variables that predict aseptic loosening. An initial model showed that sagittal rotation was the only significant factor. In the final model time to re-revision, sagittal rotation and proximal migration were significant factors

Model	Odds ratio	p-value
Initial model		
Age (yrs)	0.993	0.839
Gender (female)	1.049	0.956
Side (left)	1.675	0.564
Time to re-revision	1.013	0.054
Medial migration	0.786	0.286
Sagittal rotation	1.702	0.022
Proximal migration	1.390	0.105
Final model		
Time to re-revision	1.013	0.042
Sagittal rotation	1.677	0.032
Proximal migration	1.389	0.042

or change in sagittal rotation to detect loosening. A test with 'very good' or 'excellent' diagnostic accuracy is defined as having an area under the curve of 0.8 to 0.9 or 0.9 to 1.0 respectively.[19]

Results

The 212 re-revision cases of cementless acetabular components used at re-revision were identified in department records during the study period. After all exclusion criteria, 52 acetabular components (48 patients) were included in Group A (not loose), and 42 acetabular components (36 patients) were included in Group B (loose) (Fig. 1).

The mean time to re-revision was shorter in Group A than in Group B (Table III). The most common causes of re-revision for cases in Group A were recurrent dislocation and loosening of the femoral component (Table IV). The most common type of acetabular component used in each Group was PCA (Howmedica, Rutherford, New Jersey) (see supplementary material).

A total of 804 AP radiographs were available for analysis. EBRA-Cup excluded radiographs with excessive pelvic tilt and or rotation. The number of radiographs that were excluded because of proximal translation, sagittal rotation and medial translation were 32 (4%), 98 (12%) and 20 (2.5%) respectively.

In the final logistic regression analysis model, proximal translation and sagittal rotation were significant predictors of loosening; medial translation was not (Table V). Consequently, only proximal translation and sagittal rotation were considered for further analysis.

The proximal translation and sagittal rotation with time for each of the 94 acetabular components in the two groups is shown in Figures 2 and 3. There was a significantly higher mean proximal translation (Table VI, Fig. 4) and mean sagittal rotation (Table VI, Fig. 5) in Group B than in Group A from three months onwards.

Proximal translation of > 1.0 mm within 24 months had a good PPV (90%) and specificity (94%) but an average sensitivity (64%) (Table VII). The sensitivity of using proximal translation > 1.0 mm as a threshold increased from 48% (20/42 loose acetabular components) at 12 months to 76% (32/42 loose acetabular components) at 60 months. Of the 42 components in Group B, ten (24%) had migrated < 1.0 mm within the first 60 months and were found to be loose at revision (see supplementary material). Four of these had not migrated > 1.0 mm at final follow-up prior to re-revision THA.

Proximal translation > 1.0 mm within the first two years correctly identified 76 of 94 (81%) components to be loose or not loose.

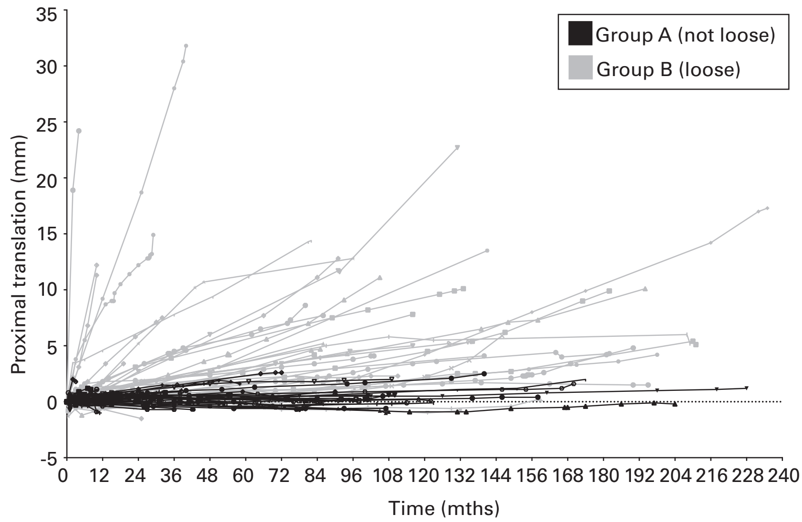

Fig. 2

Proximal translation over time for all cases. Cases in Group A are represented by the black lines. Cases in Group B are represented by the grey lines.

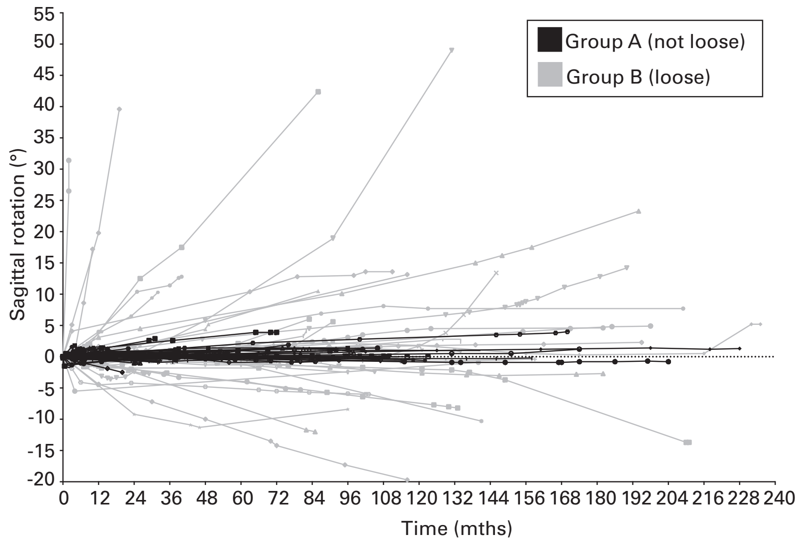

Fig. 3

Sagittal rotation over time for all cases. Cases in Group A are represented by the black lines. Cases in Group B are represented by the grey lines.

Using a combination of either proximal translation > 1.0 mm or sagittal rotation > 1.0° improved the sensitivity and NPV but decreased the specificity and PPV. Increasing the threshold of proximal translation to 1.8 mm or sagittal rotation to 2.5° increased the specificity and PPV but decreased the sensitivity and NPV (Table VII).

The area under the ROC curve for proximal translation within 24 months was 0.833. Using the generated sensitivity and specificity table, the optimal point was found to be > 1.05 mm with a sensitivity of 64%, specificity of 94% and a likelihood ratio of 11.14.

The area under the ROC curve for sagittal rotation within 24 months was 0.738, suggesting that it is a relatively less accurate test when compared with proximal translation. The optimal point for sagittal rotation was found to be > 1.15° with a sensitivity of 60%, specificity of 81% and a likelihood ratio of 3.10.

Table VI. Mann-Whitney U test comparison of mean proximal translation and sagittal rotation at different time points within the first 60 months

Time	Mean proximal translation (95% CI) Group A	Mean proximal translation (95% CI) Group B	p-value for proximal translation comparison	Mean sagittal rotation (95% CI) Group A	Mean sagittal rotation (95% CI) Group B	p-value for sagittal rotation comparison
3 mths	0.2 (0.12 to 0.26)	1.3 (0.22 to 2.34)	< 0.0001	0.3 (0.16 to 0.45)	1.6 (0.15 to 3.02)	0.0114
6 mths	0.3 (0.21 to 0.36)	1.3 (0.69 to 1.84)	< 0.0001	0.4 (0.22 to 0.56)	1.8 (0.84 to 2.67)	0.0017
12 mths	0.3 (0.25 to 0.44)	1.5 (0.85 to 2.16)	< 0.0001	0.5 (0.26 to 0.77)	2.0 (0.89 to 3.07)	0.0013
24 mths	0.5 (0.36 to 0.66)	2.5 (1.31 to 3.66)	< 0.0001	0.5 (0.34 to 0.67)	3.1 (1.44 to 4.74)	0.0006
36 mths	0.5 (0.37 to 0.66)	3.1 (1.34 to 4.91)	< 0.0001	0.5 (0.33 to 0.76)	3.1 (1.75 to 4.36)	< 0.0001
60 mths	0.6 (0.30 to 0.80)	3.2 (2.12 to 4.19)	< 0.0001	0.8 (0.39 to 1.17)	4.4 (2.43 to 6.32)	< 0.0001

CI, confidence interval

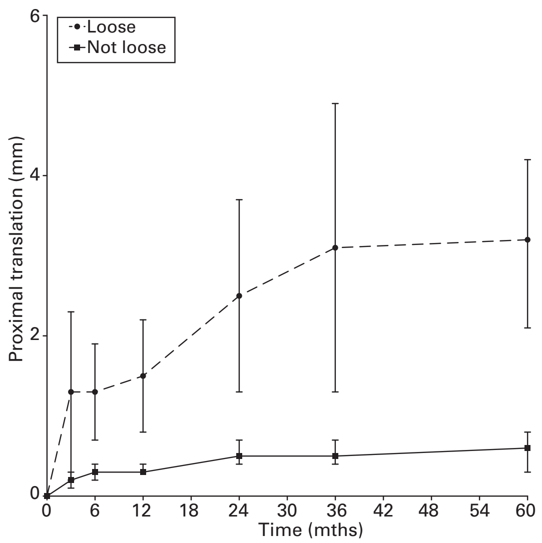

Fig. 4

Mean proximal translation of the acetabular component *versus* time for Group A (not loose) – solid line and Group B (loose) – dotted line.

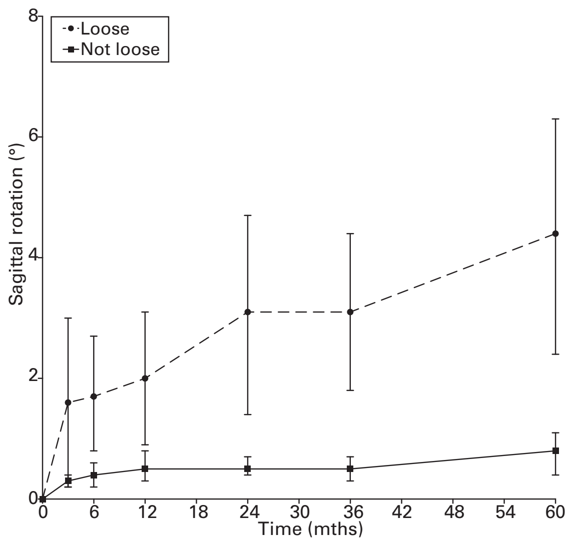

Fig. 5

Mean sagittal rotation of the acetabular component*versus* time for Group A (not loose) – solid line and Group B (loose) – dotted line

Discussion

This study is the first to correlate the early migration of cementless acetabular components used at revision THA with a confirmed intra-operative finding of loosening. Early proximal translation and sagittal rotation were found to be significant predictors of loosening. This suggests that irrespective of degree of bone loss and the reconstructive technique used at revision THA, initial stability is needed if the reconstruction is to be successful.

Loose components were found to have a higher mean proximal translation and sagittal rotation from three months onwards ($p < 0.02$). Using RSA studies of primary THA, Pijls et al[6] showed that cohorts with a mean proximal translation of > 1.0 mm at 24 months had an unacceptable rate of revision at ten years: cohorts with a mean proximal translation between 0.2 mm and 1.0 mm were considered to be at greater risk of revision.

The mean proximal translation at 24 months for Groups A and B were 0.5 mm (95% CI 0.4 to 0.7) and 2.5 mm (95% CI 1.3 to 3.7) respectively. The proximal translation in Group A may be higher than that in the meta-analysis of Pijls et al[6] because of potential differences in migration between primary and revision acetabular components. It may also have been affected by using EBRA-Cup rather than the more sensitive RSA to measure migration.

In an RSA study of acetabular components used for revision THA, Klerken et al[10] found that every millimetre of proximal translation at two years increased the risk of aseptic loosening by 37%. Similarly, our study showed that greater early proximal translation or sagittal rotation increased the risk of loosening.

Using a threshold of proximal translation > 1.0 mm within 24 months, the sensitivity of 64% and specificity of 94% were very similar to those reported for cementless components used at primary THA (62% and 91% respectively).[5] However, Krismer et al[5] reported a PPV of 56% compared with the 90% reported in our study. This may be because we confirmed whether or not a component was loose at operation. Poor PPVs at all time points resulted in Krismer

Table VII. Table showing sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for proximal translation (> 1.0 mm or 1.8 mm), sagittal rotation (> 1.0° or 2.5°) and combined criteria, within 12, 24, 36 and 60 months

	Migration							
	Proximal translation (1.0 mm)				**Proximal translation (1.8 mm)**			
Time (mths)	**12**	**24**	**36**	**60**	**12**	**24**	**36**	**60**
Group B detected (n)	20	27	30	32	9	16	23	27
Sensitivity (%)	*47.6*	*64.3*	*71.4*	*76.2*	*21.4*	*38.1*	*54.8*	*64.3*
Specificity (%)	*96.2*	*94.2*	*90.4*	*86.5*	*98.1*	*98.1*	*98.1*	*94.2*
PPV (%)	*90.9*	*90*	*85.7*	*82.1*	*90*	*94.1*	*95.8*	*90*
NPV (%)	*69.4*	*76.6*	*79.7*	*81.8*	*60.7*	*66.2*	*72.9*	*76.6*
	Sagittal rotation (1.0°)				**Sagittal rotation (2.5°)**			
Time (mths)	**12**	**24**	**36**	**60**	**12**	**24**	**36**	**60**
Group B detected (n)	20	26	29	36	14	16	22	23
Sensitivity (%)	*47.6*	*61.9*	*69*	*85.7*	*33.3*	*38.1*	*52.4*	*54.8*
Specificity (%)	*80.8*	*76.9*	*73.1*	*71.2*	*98.1*	*96.2*	*94.2*	*94.2*
PPV (%)	*66.7*	*68.4*	*67.4*	*70.6*	*93.3*	*88.9*	*88*	*88.5*
NPV (%)	*65.6*	*71.4*	*74.5*	*86*	*64.6*	*65.8*	*71*	*72.1*
	Combined criteria 1.0 mm or 1.0°				**Combined criteria 1.8 mm or 2.5°**			
Time (mths)	**12**	**24**	**36**	**60**	**12**	**24**	**36**	**60**
Group B detected (n)	24	31	35	39	16	21	26	29
Sensitivity (%)	*57.1*	*73.8*	*83.3*	*92.9*	*38.1*	*50*	*61.9*	*69*
Specificity (%)	*77.4*	*75*	*69.2*	*63.5*	*94.3*	*94.2*	*92.3*	*90.4*
PPV (%)	*68.6*	*70.5*	*68.6*	*67.2*	*88.9*	*87.5*	*86.7*	*85.3*
NPV (%)	*69.5*	*78*	*83.7*	*91.7*	*65.8*	*70*	*75*	*78.3*

et al[5] reporting the influence of migration on survivorship rather than on loosening.

Stocks et al[20] similarly reported a correlation between mean migration at 12 months and survivorship at 6.5 years in cohorts of acetabular components used at primary THA. The limitation of using survivorship or a revision rate at a certain time point is that it may be misleading because of the interval between the time when the patient is first symptomatic and when revision surgery is undertaken. This depends on many factors and may result in survivorship being months or years longer than the time at which the prosthesis loosens.

Increasing the proximal translation threshold to 1.8 mm within 24 months, as suggested by Nieuwenhuijse et al[9] did not significantly improve the predictive values in our study. Its specificity was similar (98% *versus* 100%) but the sensitivity was much lower (38% *versus* 73%) which may be because of differences in migration pattern between primary cemented and revision cementless components. We found the optimal threshold, as determined from a ROC curve, was > 1.0 mm within the first 24 months.

The use of early sagittal rotation (2.53°) as a predictor of acetabular component loosening has only been reported once. Its sensitivity within the first 24 months was 73% and its specificity 93%.[9] In our study, a threshold of 2.5° within 24 months had a much lower sensitivity (38%) and similar specificity (96%), again possibly due to differences in migration pattern between primary cemented and revision cementless prostheses. Using a lower threshold of sagittal rotation (> 1.0° within 24 months) improved the sensitivity to 62% but reduced the specificity to 68%. As an independent measure, sagittal rotation generally had a poorer PPV for loosening than did proximal translation. The area under the ROC curve was less for sagittal rotation than for proximal translation supporting its inferiority as a test.

Although prediction of acetabular component loosening is possible at 12 months, measurements made at 24 months markedly improve its sensitivity. Beyond this point sensitivity sequentially improves but specificity worsens, as was found by Krismer et al.[5] The sensitivity of proximal translation at 60 months in our study was 76% because ten acetabular components had migrated < 1.0 mm but were subsequently found to be loose. Seven of the ten had rotated > 1.0° in the sagittal plane within 60 months, suggesting that they failed by rotating on their axis. Caution should therefore be exercised when just using early proximal translation to predict long-term loosening. Of the ten components, six translated proximally > 1.0 mm (1.5 to 5.9) after 60 months. The lack of detection within 60 months can, therefore, be the result of late component migration and subsequent failure. Late migration may be caused by loss of fixation from poor bone ingrowth, fibrous encapsulation, polyethylene wear debris osteolysis or from hardware failure, all of which may not be associated with early migration.

This study has a number of limitations. First, the number of components investigated in each group is relatively small. It is, however, the largest radiological study of revision components confirmed by intra-operative assessment of fixation.

Secondly, many of the components investigated are no longer in clinical use. This problem will be encountered in any study that spans > 30 years. The purpose of our study was not to highlight the performance of individual types of implant, but to identify the patterns of migration of revision acetabular components.

Thirdly, EBRA-Cup measurements were undertaken retrospectively using all available radiographs. EBRA-Cup uses a ‘best fit curve’ depending on the number of radiographs included: our results may have been different if we had carried out a prospective analysis with fewer radiographs. Despite this, EBRA-Cup is the most sensitive retrospective radiological measurement method: RSA can only be used prospectively. The intra-observer error reported in the present study (95% CI +/- 0.23 mm) was better than that previously described in the literature (+/- 0.67 mm[8] and +/- 0.90 mm[21]). The level of precision in this study is sufficient to detect the clinically relevant threshold of 1 mm. The reason for the improved precision in this study may be attributed to the use of digital images and software analysis rather than a digitiser and pencil markings.

Fourthly, we used an intra-operative classification of loosening[16] which may be subject to intra-observer bias. For example, it may be difficult to differentiate an acetabular component with fluid movement (grade one) from one that is not loose (grade zero). However, only two patients had grade 1 loosening, and both had a pattern of migration similar to most of the other components in Group B.

Fifthly, Group A (not loose) had a shorter survivorship than Group B (loose) due to the different reasons for revision. The longer follow-up of Group B may have reduced the reported sensitivity as some components migrated late. Despite this, previous studies have shown that a cementless acetabular component which is left in place while the femoral component is revised has a high long-term survival.[22,23]

This study has shown that the thresholds of early migration are as applicable to revision arthroplasty as they are to primary arthroplasty. Proximal translation within two years correctly predicted 81% of acetabular components to be loose or not loose at re-revision THA. From three months onwards, the mean proximal translation and sagittal rotation of the acetabular components which were found to be loose at re-revision THA were significantly higher than those of those which were not loose. Proximal translation of a cementless acetabular component used at revision THA > 1.0 mm within the first 24 months had a high PPV for loosening. Migration thresholds may be used to assess the introduction of new acetabular components and as a clinical tool to guide follow-up. The absence of proximal translation within the first 60 months indicates that a component is not likely to be loose at re-revision THA although it does not exclude late aseptic loosening as a cause of failure.

Take home message:

- This study is the first to correlate the early migration of cementless acetabular components used at revision THA with a confirmed intra-operative finding of loosening.
- Proximal translation of > 1 mm within the first two years correctly predicted 80% of acetabular components to be loose or not loose following revision total hip arthroplasty.
- This study has shown that the thresholds of early migration are as applicable to revision arthroplasty as they are to primary arthroplasty.

Supplementary material

A table showing the type of acetabular component used in the index revision for all cases in each group and a figure showing proximal translation over time for ten cases in Group B can be found alongside the online version of this article at www.bjj.boneandjoint.org.uk

Author contributions:

Y. S. Kim: Data collection, Analysis of results, Edited manuscript to publication.
J. M. Abrahams: Ethics submission, Study design, Analysis of results, Wrote initial draft.
S. A. Callary: Planned the study, Analysis of results, Edited manuscript through to publication.
C. De Ieso: Data collection, Analysis of results, Critical review of manuscript.
K. Costi: Assisted with data collection, Critical review of manuscript.
D. W. Howie: Planned the study, Interpretation of results, Critical review of manuscript.
L. B. Solomon: Planned the study, Ethics submission, Interpretation of results, Edited manuscript through to publication.

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Table i. The type of acetabular component used in the index revision for all cases in each group

	Group A (not loose)	Group B (loose)
Trilogy (Zimmer, Warsaw, Indiana)	11	1
Lord (Benoist Girard, Bagneux, France)	0	6
PCA (Howmedica International, Limerick, Ireland)	14	16
TM (Zimmer)	9	6
Vitalock (Howmedica International)	12	6
Other	6	7

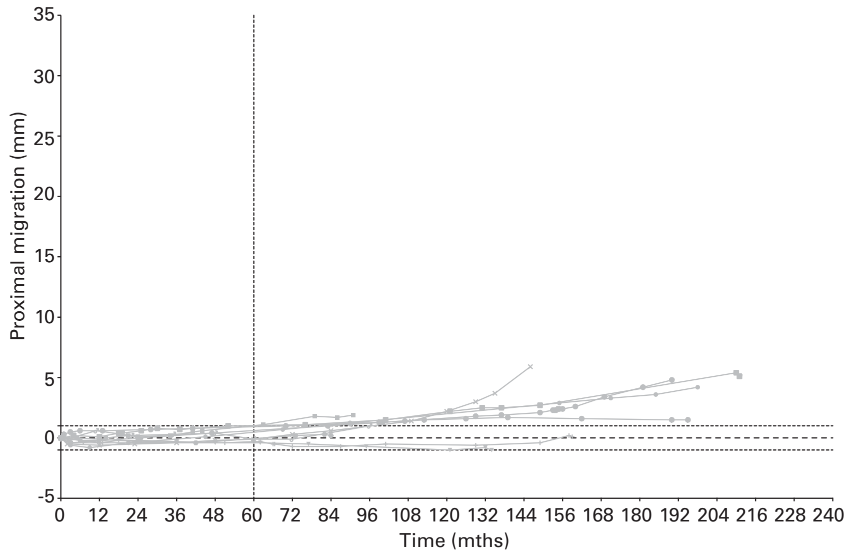

Fig. a

Proximal translation over time for the ten cases (Group B) that did not migrate > 1.0 mm within the first five years.

CHAPTER FOUR

The diagnostic performance of radiographic criteria to detect aseptic acetabular component loosening after revision total hip arthroplasty.

As published in The Bone and Joint Journal, April 2017

Whilst early migration is an important predictor for future failure, a threshold is required to determine the likelihood of failure in patients that present with unexplained pain that is suspicious of aseptic loosening. Radiographic criteria to diagnose aseptic loosening were originally described for cemented acetabular components, which may fail in a different mechanism from uncemented components. Additionally, the criteria were described for primary THR only, and these criteria may not be as applicable to revision THR given more complex reconstructions and pre-existing radiolucencies due to bone defects. To date there is no consistency in the literature regarding the defining optimal limits and predictive values of migration and radiolucency criteria. This study investigated the correlation between radiographic criteria and aseptic loosening following uncemented revision THR in a case-control study. This study aimed to determine the diagnostic performance of radiographic criteria to detect aseptic acetabular loosening after revision THR. Once again, for the same reasons as in the previous chapter, this study used EBRA to measure acetabular component migration after revision THR. Secondary aims were to determine the predictive values of different thresholds of migration and to determine the predictive values of radiolucency criteria.

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

Statement of Authorship

Title of Paper	The diagnostic performance of radiographic criteria to detect aseptic acetabular component loosening after revision total hip arthroplasty
Publication Status	☒ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Bone Joint J, 2017;99-B:458–64.

Principal Author

Name of Principal Author (Candidate)	John M Abrahams		
Contribution to the Paper	Ethics submission, Study design, Analysis of results, Wrote initial draft.		
Overall percentage (%)	60		
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	24/9/19.

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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■ HIP

The diagnostic performance of radiographic criteria to detect aseptic acetabular component loosening after revision total hip arthroplasty

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Aims
This study aimed to determine the diagnostic performance of radiographic criteria to detect aseptic acetabular loosening after revision total hip arthroplasty (THA). Secondary aims were to determine the predictive values of different thresholds of migration and to determine the predictive values of radiolucency criteria.

Patients and Methods
Acetabular component migration to re-revision was measured retrospectively using Ein-Bild-Rontgen-Analyse (EBRA-Cup) and manual measurements (Sutherland method) in two groups: Group A, 52 components (48 patients) found not loose at re-revision and Group B, 42 components (36 patients) found loose at re-revision between 1980 and 2015. The presence and extent of radiolucent lines was also assessed.

Results
Using EBRA, both proximal translation and sagittal rotation were excellent diagnostic tests for detecting aseptic loosening. The area under the receiver operating characteristic (ROC) curves was 0.94 and 0.93, respectively. The thresholds of 2.5 mm proximal translation or 2° sagittal rotation (EBRA) in combination with radiolucency criteria had a sensitivity of 93% and specificity of 88% to detect aseptic loosening. The sensitivity, specificity, positive predictive value and negative predictive value (NPV) of radiolucency criteria were 41%, 100%, 100% and 68% respectively. Manual measurements of both proximal translation and sagittal rotation were very good diagnostic tests. The area under the ROC curve was 0.86 and 0.92 respectively. However, manual measurements had a decreased specificity compared with EBRA. Radiolucency criteria had a poor sensitivity and NPV of 41% and 68% respectively.

Conclusion
This study shows that EBRA and manual migration measurements can be used as accurate diagnostic tools to detect aseptic loosening of cementless acetabular components used at revision THA. Radiolucency criteria should not be used in isolation to exclude loosening of cementless acetabular components used at revision THA given their poor sensitivity and NPV.

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Aseptic loosening of the acetabular component remains the most common cause for revision of primary and revision total hip arthroplasty (THA).[1] Diagnosis of aseptic loosening relies on clinical symptoms as well as radiographic criteria. Radiographic criteria currently used to identify aseptic loosening include measuring acetabular component migration relative to surrounding host bone and identifying radiolucent lines at the implant-bone interface.[2]

Radiolucency criteria to detect aseptic loosening of acetabular components were originally described for cemented components.[3] The use of the same criteria for cementless components may not be valid as the mechanism of aseptic loosening is different.[4] Radiolucency criteria may also be influenced after revision THA, where there can be decreased contact between the implant and host bone due to pre-existing bone defects, as well as residual pre-revision sclerotic bone.

Identifying migration is limited to observing obvious positional changes of the component on serial radiographs using a visual estimate. These estimates are limited due to inter-observer variation and differences in pelvic tilt or rotation that occur between radiographs. In addition, acetabular components may be loose without displaying visually obvious migration.[5]

Radiological component migration is commonly used to evaluate aseptic loosening. No consensus exists on the threshold of acetabular migration which should be used to diagnose aseptic loosening. A wide variation has been applied from > 3.0 mm of proximal translation in some studies[6,7] to > 5.0 mm or 6.0 mm in others,[8-11] while some studies refrain from describing a specific limit.[12,13] These studies report on a mixture of primary and revision acetabular component. There is also variation in the direction of translation reported (proximal, medial and 2D).[7,14] In some studies, sagittal rotation of the component is included.[15,16] Additionally, the radiographic methods used to measure migration have varying accuracy, ranging from > 4 mm for manual measurements on plain radiographs[17] to < 1 mm when using computerised techniques such as Ein-Bild-Roentgen-Analyse (EBRA-Cup)[17-19] and the current reference standard of radiostereometric analysis (RSA).[20] To the authors' knowledge, no study has used loosening status confirmed intra-operatively during re-revision surgery to establish the radiological thresholds of detection in relation to cementless acetabular components used at revision THA.

In the absence of literature defining optimal limits and predictive values of migration and radiolucency criteria, we investigated the correlation between radiographic criteria and aseptic loosening following cementless revision THA in a case-control study. This study aimed to determine the diagnostic performance of radiographic criteria to detect aseptic acetabular loosening after revision THA. Secondary aims were to determine the predictive values of different thresholds of migration and to determine the predictive values of radiolucency criteria.

Patients and Methods

We performed a retrospective case-control study of all patients who underwent re-revision THA using a cementless acetabular component in our institution between 1980 and 2015. The ethics committee of the Royal Adelaide Hospital approved this study.

The patients were allocated to one of two groups: Group A, components found not loose at re-revision, and Group B, components found loose at re-revision. Inclusion criteria for Group A were: all patients with a revision cementless acetabular component who had undergone re-revision for any cause and were found not to have a loose acetabular component at operation. Inclusion criteria for Group B were: all patients with a revision cementless acetabular component which was confirmed to be loose at the time of re-revision. Exclusion criteria for Group B were patients with an acetabular component that was re-revised for infection. Infection was not an exclusion criterion for components in Group A as the stability of acetabular component had not been compromised. Of 212 re-revision cases which were identified during the study period, after all exclusion criteria were applied, 52 acetabular components (48 patients) were included in Group A, not loose, and 42 acetabular components (36 patients) were included in Group B, loose, as detailed in Kim et al.[21]

EBRA-Cup measurements of acetabular component migration were performed using plain anteroposterior (AP) pelvic radiographs centred on the pubic symphysis as detailed in Kim et al.[21] Manual measurements of migration were performed using IMPAX software (Version 6.3, Agfa IMPAX, AGFA-Gevaert N.V, Mortsel, Belgium) using a modified Sutherland technique.[22] As the teardrop could not be adequately visualised in every radiograph, an alternative horizontal line between the ischial tuberosities was used to measure inclination and proximal translation. The centre of the acetabular component, as identified from the circle fitting tool, was used as the reference point for proximal translation. All linear measurements were calibrated using the known outer diameter of the acetabular component.

The proximal and medial translation, and change in sagittal rotation were measured for each radiograph available using EBRA-Cup. Using the manual method, change in translation and rotation was calculated only between the first radiograph available after the index revision procedure and the last radiograph prior to the re-revision procedure.

A radiolucent line was defined as a dark line of demarcation between the acetabular component and the cancellous bone. Assessment of radiolucency was performed using IMPAX software. The radiolucent zones were defined according to DeLee and Charnley.[3] The maximum thickness (mm) of each radiolucent line was recorded for each zone on the first AP radiograph available after the index revision procedure and the last radiograph prior to the re-revision procedure once again using the known dimensions of the acetabular component for calibration. A radiolucent line with a thickness ≥ 2.0 mm in any zone with the presence of a sclerotic border was considered to represent loosening. A sclerotic border was defined as condensed bright light adjacent to the surrounding cancellous bone.

Statistical analysis. The intra-observer error was calculated for migration measurements as described by Kim et al[21] using the mean and 95% confidence intervals (CI). For manual measurements, repeated analysis was performed using 33 components. There was a total of 66 radiographic measurements available for medial, proximal translation and sagittal rotation. Repeated measurements of the thickness of radiolucent lines in 179 zones on 88 radiographs were repeated by the same observer (YSK). The mean difference was 1.14 mm (95% CI 0.89 to 1.39).

Receiver operating characteristic (ROC) curves of final migration values (proximal translation and sagittal rotation) for all cases in each group were generated using GraphPad Prism 6 (GraphPad Software, La Jolla, California). Migration values of Group A were processed as the 'negative result values' and in Group B were considered as 'positive result values'. The area under the ROC curve (AUC) was used to determine the accuracy of using either translation or change in sagittal rotation to detect loosen-

Table I. Intra-observer error with 95% confidence intervals (CIs) of Ein-Bild-Rontgen-Analyse (EBRA-Cup) and manual measurements

		Medial translation (mm)	Proximal translation (mm)	Sagittal rotation (°)
EBRA-Cup	Mean	0.22	-0.08	-0.53
	95% confidence interval	0.05 to 0.39	-0.31 to 0.15	-1.02 to -0.05
Manual	Mean	1.13	2.25	1.65
	95% confidence interval	0.50 to 1.77	1.56 to 2.94	1.04 to 2.26

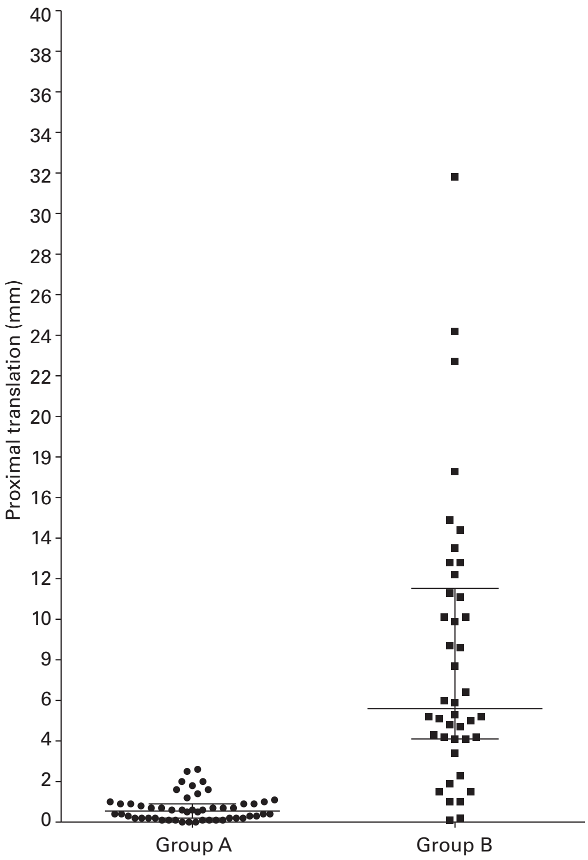

Fig. 1

Final values of proximal translation as determined using Ein-Bild-Roentgen-Analyse for Group A (not loose) and Group B (loose). The median and interquartile ranges are represented by the long and short horizontal black lines respectively.

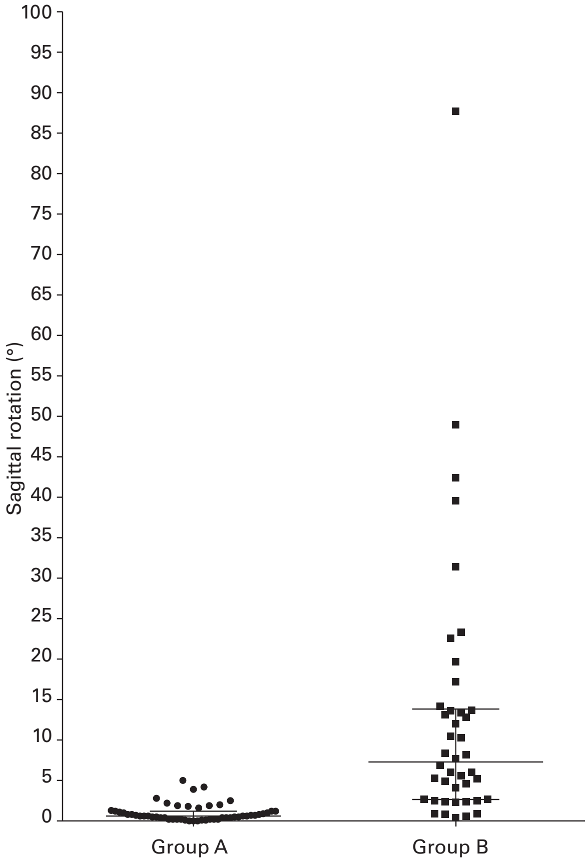

Fig. 2

Final values of sagittal rotation as determined using Ein-Bild-Roentgen-Analyse for Group A (not loose) and Group B (loose). The median and interquartile ranges are represented by the long and short horizontal black lines respectively.

ing. A test with 'very good' or 'excellent' diagnostic accuracy is defined as having an AUC of 0.8 to 0.9 or 0.9 to 1.0, respectively.[23] Sensitivity, specificity and predictive values were also generated for different combinations of thresholds for proximal translation, sagittal rotation and presence of radiolucency. The Mann-Whitney U test was used to determine if the final migration values for both Groups A and B were statistically different.

Sensitivity was calculated as the proportion of cases in Group B which exceeded the given threshold. Specificity was calculated as the proportion of cases in Group A that did not exceed the threshold. A p value < 0.05 was considered significant for all statistical tests. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the final proximal translation and absolute sagittal rotation values were calculated for different thresholds in 0.5 mm and 0.5° increments. Additionally, the total percentage of all cases which were correctly identified using the specified thresholds were calculated.

Results

The intra-observer error of EBRA-Cup measurements was lower than manual migration measurements (Table I).

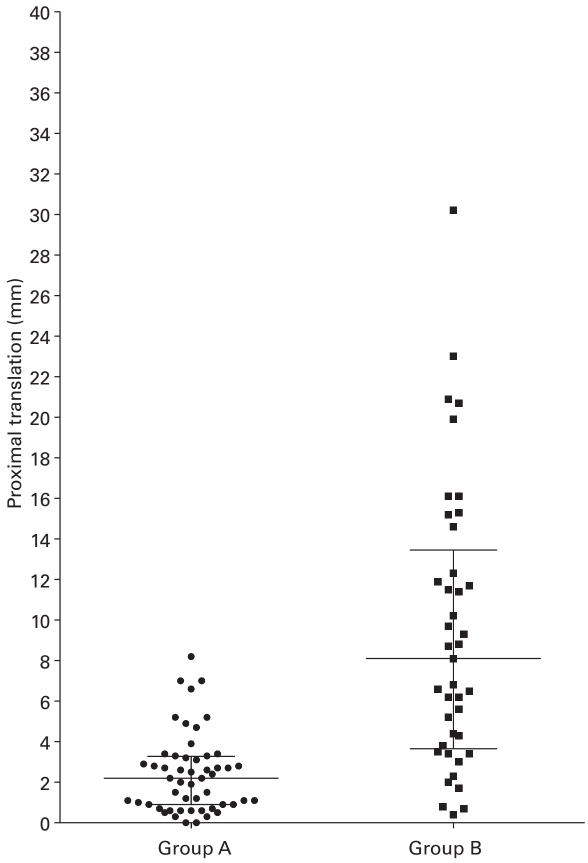

Fig. 3

Final values of proximal translation as determined using manual measurements for Group A (not loose) and Group B (loose). The median and interquartile ranges are represented by the long and short horizontal black lines respectively.

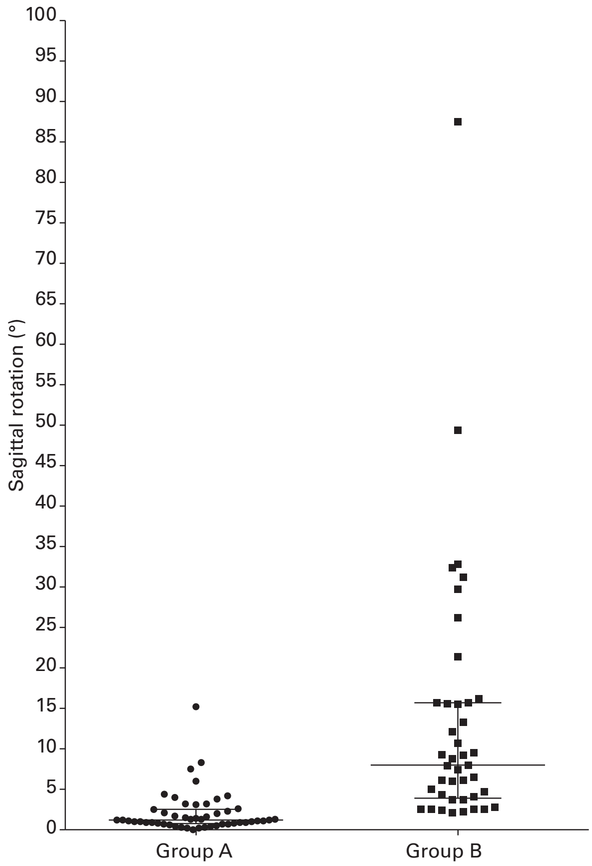

Fig. 4

Final values of sagittal rotation as determined using manual measurements for Group A (not loose) and Group B (loose). The median and interquartile ranges are represented by the long and short horizontal black lines respectively.

Final proximal translation values before re-revision as measured using EBRA-Cup and manual measurements were statistically different between Group A and B ($p < 0.001$). Using EBRA-Cup, the median proximal translation was 0.6 mm (interquartile range (IQR) 0.2 to 0.9) for Group A and 5.1 mm (IQR 4.1 to 11.53) for Group B respectively (Fig. 1). The AUC curve for proximal translation was 0.94 (standard error 0.03, 95% CI 0.89 to 0.997, $p < 0.001$), thus proximal translation was considered as a good diagnostic test to determine the outcome of loosening.

The median sagittal rotation on the final radiograph before re-revision was 0.6° (IQR 0.3° to 1.2°) for Group A compared with 7.3° (IQR 2.7° to 13.8°) for Group B ($p < 0.001$), (Fig. 2). The AUC for sagittal rotation was 0.93 (standard error 0.03, 95% CI 0.88 to 0.98, $p < 0.001$), thus sagittal rotation was considered as a good diagnostic test to determine the outcome of loosening. The AUC for medial translation measured using EBRA-Cup was 0.82 (standard error 0.04, 95 CI 0.74 to 0.91, $p < 0.001$) classifying it as a relatively poorer diagnostic test.

To determine if cases that had substantial migration influenced the difference between groups, a Mann-Whitney U test was repeated having excluded any acetabular component that translated proximally > 5 mm or rotated in the sagittal plane > 5°. The difference between Groups A and B remained significant for proximal translation ($p < 0.001$) and sagittal rotation ($p < 0.001$) using EBRA-Cup measurements.

Using manual measurements, the median proximal translation was 2.2 mm (IQR 0.9 to 3.2) for Group A and 8.1 mm (IQR 3.7 to 12.9) for Group B respectively (Fig. 3). The AUC for proximal translation was 0.86 (standard error 0.04, 95% CI 0.78 to 0.94, $p < 0.001$). The median sagittal rotation on the final radiograph before re-revision was 1.2° (IQR 0.8° to 2.5°) for Group A compared with 8.0° (IQR 4.0° to 15.7°) for Group B ($p < 0.0001$) (Fig. 4). The AUC for sagittal rotation was 0.92 (standard error 0.02, 95% CI 0.87 to 0.97, $p < 0.001$).

The combination of proximal translation > 3 mm or sagittal rotation (in any direction) > 5° using EBRA-Cup had a sensitivity, specificity, PPV and NPV of 83%, 100%, 100% and 88% respectively. This combination identified the greatest number of cases correctly (93%). For manual measurements, the optimal thresholds were > 5.5 mm of proximal translation or 4° of sagittal rotation. The sensitivity, specificity, PPV and NPV for this combination of thresholds were 90%, 82%, 80% and 91% respectively.

In Group A, on the first post-operative radiograph, 22 cases had a radiolucent line in at least one zone. Six of these cases had a radiolucent line with a thickness ≥ 2.0 mm. None of these six cases had a radiolucent line with a sclerotic border. On the final radiograph, 32 cases had a radiolucent line in at least one zone. Two of these 32 cases had a radiolucent line thickness ≥ 2.0 mm. Neither of these two cases had a radiolucent line with a sclerotic border. In Group B, on the first post-operative radiograph, 33 cases had a radiolucent line in at least one zone. A total of 13 of these 33 cases had a radiolucent line thickness ≥ 2.0 mm. Only one of these 13 cases had a radiolucent line with a sclerotic border. On the final radiograph, 38 cases had a radiolucent line in at least one zone. A total of 29 of these 38 cases had a radiolucent line thickness ≥ 2.0 mm, while 17 of those 29 cases had a radiolucent line with a sclerotic border. The sensitivity, specificity, PPV and NPV of radiolucency criteria (≥ 2.0 mm and the presence of a sclerotic border) were 41%, 100%, 100% and 68% respectively. Of the 17 cases in Group B that fulfilled the radiolucency criteria, ten cases had continuous radiolucent lines in all three DeLee and Charnley zones[3] and seven had radiolucent lines that spanned zones two and three.

A combination of thresholds of proximal translation, sagittal rotation and radiolucency criteria were assessed for both EBRA-Cup and manual measurements. The addition of radiolucency criteria (presence of a radiolucent line with ≥ 2.0 mm thickness with a sclerotic border) to proximal translation and sagittal rotation thresholds improved the sensitivity of detecting a loose acetabular component. The specificity did not decrease as radiolucency criteria had 100% specificity with no cases in Group A fulfilling radiolucency criteria. A combination of different thresholds is available in the supplementary material for EBRA-Cup and manual measurements.

Discussion

By using intra-operative confirmation of loosening to assess the validity of commonly reported radiographic criteria for loosening, we have determined the optimal limits of migration and these could be used in both clinical practice and in an academic setting. This study presents the largest cohort of cementless acetabular components used at revision THA with confirmed loosening outcomes at re-revision surgery. We found a significant difference between the final, prior to re-revision, migration values of Group A and Group B using both EBRA-Cup and manual measurements. The AUCs for proximal translation and sagittal rotation measured using EBRA-Cup were > 0.9, classifying them as excellent diagnostic tests. Manual measurements of proximal translation and sagittal rotation were found to be a good diagnostic test, although inferior to EBRA-Cup. In combination with radiolucency criteria the optimal threshold limits of migration determined using EBRA-Cup (> 2.5 mm or > 2°) were subsequently well below those using manual measurements (> 5.5 mm or > 4°). This is likely due to the higher amount of migration recorded using manual measurements compared with EBRA-Cup for both groups. The higher amount of migration may have been influenced by the higher intra-observer error of manual measurements.

The AUC for manually derived sagittal rotation was found to be better than that of manually derived proximal translation. This is likely related to the magnification error and the pelvic tilt of the patient between radiographs which may influence translation measurements more than changes in sagittal rotation.

The AUC for medial translation measured using EBRA-Cup was 0.82, (95% CI 0.74 to 0.91) classifying it as a relatively poorer diagnostic test. However, because of the limited accuracy and precision of the EBRA-Cup technique, the minimum threshold that could be used for medial translation of 1.0 mm would give a poor sensitivity of only 67% but a good specificity of 90%. This is likely due to the smaller distance that an acetabular component can potentially move in the medial direction. The better accuracy and precision of RSA may facilitate the use of medial translation as a diagnostic tool.

Patel et al[24] found that acetabular components used at primary THA may develop loosening without any radiographic signs, describing this as ‘radiographically silent loosening’. In their case-control study involving 104 hips, a total of 17 (16%) loose components did not demonstrate any features of radiographic loosening, although their method and threshold of assessing migration were not described. In our study, a threshold of proximal translation > 2.5 mm or sagittal rotation > 2°, or the presence of a radiolucent line with a sclerotic border had a sensitivity of 93%. Based on the results of our study of acetabular components used at revision THA, we suggest that radiographically silent loosening may not be as prevalent as previously reported in the revision setting.

A study of 52 primary cementless components by Udomkiat et al[2] reported a 97% sensitivity, 100% specificity, 100% PPV and 97% NPV for five criteria of radiolucency and component migration. Our study reports a lower sensitivity and specificity in the revision setting. There may be some reasons for the difference in results. First, the present study did not examine the annual progression of radiolucent lines after two years. Secondly, a large proportion of cases in our study of components used at revision THA had pre-operative bone defects and bone grafts. Finally, a threshold of > 8° of sagittal rotation was used in the study by Udomkiat et al,[2] which is relatively high and may explain their reported high specificity.

Manley et al[25] described unstable cementless acetabular components as those that had radiolucent lines in all three zones and had migrated ≥ 3 mm. This description was based on criteria originally described by Engh et al[26] in a retrieval study of femoral stems. When applied to the present study, these criteria had a very poor sensitivity of 21% although the specificity was 100%.

The present study has shown that radiolucency criteria alone have a very poor sensitivity of only 41% but a good specificity of 100%. Despite the poor sensitivity, it has been used as a sole criterion to assess the performance of acetabular components used at revision THA.[27] Carlsson and Gentz[28] in a study of cemented primary acetabular components, concluded that the absence of radiolucent lines at the bone-cement interface probably excluded the presence of clinical loosening. In the present study, radiolucency criteria had a NPV of only 68% and a PPV of 100%. The reason for this could be that cementless components may migrate within the deficiency. We suggest that radiolucency criteria alone should not be used routinely to exclude loosening of cementless acetabular components in the revision setting.

The present study has limitations. First, the study investigated many types of cementless acetabular components with different ingrowth designs which had been implanted over a long period. Several of the components investigated are no longer in clinical use. This problem will be encountered in any long-term study that spans more than 30 years. Secondly, neither EBRA-Cup nor manual migration measurements are as sensitive as RSA, but RSA can only be used prospectively. Thirdly, we used an intra-operative classification of loosening[29] that may be considered to be subjective. For example, it may be difficult to differentiate a case with fluid movement from a case that is not loose. However, there were only two cases reported to have grade 1 loosening,[29] and both had a pattern of migration like most of the other components in the loose group.

In conclusion, this study shows that EBRA-Cup and manual migration measurements can be used as a diagnostic tool to detect aseptic loosening of cementless acetabular components used at revision THA. This study has identified an optimal threshold of 2.5 mm for proximal translation or 2.0° sagittal rotation using EBRA-Cup and 5.5 mm of proximal translation or 4.0° sagittal rotation using manual measurements in combination with radiolucency criteria. EBRA-Cup requires specialised software, but can be applied retrospectively providing a series of good quality radiographs are available. The addition of radiolucency criteria improved the sensitivity without a reduction in specificity. However, radiolucency criteria alone are not recommended to exclude component loosening of cementless components used at revision THA because of the very poor sensitivity and NPV.

Take home message:

- EBRA-Cup and manual migration measurements can be used as sensitive diagnostic tools to detect aseptic loosening of cementless acetabular components used at revision THA.
- By using intra-operative confirmation of loosening to assess the validity of commonly reported radiographic criteria for loosening, we have determined the optimal limits of migration and these could be used in both clinical practice and in an academic setting.
-This study presents the largest cohort of cementless acetabular components used at revision THA with confirmed intra-operative loosening outcomes at re-revision surgery.

Supplementary material

Two tables showing the sensitivity, specificity, PPV, NPV and percentage of correctly identified cases for different thresholds of proximal translation and sagittal rotation determined using EBRA-Cup and manual measurements, combined with radiolucency criteria are available alongside the online version of this article at www.bjj.boneandjoint.org.uk

Author contributions:

J. M. Abrahams: Ethics submission, Study design, Analysis of results, Wrote initial draft.
Y. S. Kim: Data collection, Analysis of results, Edited manuscript to publication.
S. A. Callary: Planned the study, Analysis of results, Edited manuscript through to publication.
C. De Ieso: Data collection, Analysis of results, Critical review of manuscript.
K. Costi: Assisted with data collection, Critical review of manuscript.
D. W. Howie: Planned the study, Interpretation of results, Critical review of manuscript.
L. B. Solomon: Planned the study, Ethics submission, Interpretation of results, Edited manuscript through to publication.

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Table i. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and percentage of correctly identified cases for different thresholds of proximal translation and sagittal rotation, combined with radiolucency criteria as measured using manual measurements

Proximal translation (mm)	Sagittal rotation (°)	Sensitivity (%)	Specificity (%)	PPV	NPV	% Correctly identified
1	1	100	18	50	100	51
1.5	1	100	22	51	100	53
2	1	100	26	53	100	55
2.5	1	100	30	54	100	57
3	1	100	38	57	100	62
3.5	1	100	40	58	100	63
4	1	100	40	58	100	63
4.5	1	100	40	58	100	63
5	1	100	40	58	100	63
5.5	1	100	40	58	100	63
6	1	100	40	58	100	63
6.5	1	100	40	58	100	63
1	1.5	100	20	51	100	52
1.5	1.5	100	28	53	100	56
2	1.5	100	36	56	100	61
2.5	1.5	100	40	58	100	63
3	1.5	100	52	63	100	70
3.5	1.5	100	58	66	100	73
4	1.5	100	60	67	100	74
4.5	1.5	100	60	67	100	74
5	1.5	100	62	68	100	75
5.5	1.5	100	62	68	100	75
6	1.5	100	62	68	100	75
1	2	100	22	51	100	53
1.5	2	100	30	54	100	57
2	2	100	38	57	100	62
2.5	2	100	44	59	100	65
3	2	100	56	65	100	72
3.5	2	100	62	68	100	75
4	2	100	64	69	100	76
4.5	2	100	64	69	100	76
5	2	100	66	71	100	77
5.5	2	100	66	71	100	77
6	2	100	66	71	100	77
1	2.5	98	24	51	92	53
1.5	2.5	98	32	54	94	58
2	2.5	95	40	57	91	61
2.5	2.5	95	46	59	92	64
3	2.5	95	60	66	94	72
3.5	2.5	95	68	71	94	76
4	2.5	95	70	72	95	77
4.5	2.5	95	70	72	95	77
5	2.5	95	72	74	95	79
6	2.5	95	72	74	95	79
1	3	98	24	51	92	53
1.5	3	98	32	54	94	58
2	3	95	40	57	91	61
2.5	3	93	46	58	88	63
3	3	93	60	66	91	71
3.5	3	93	70	72	92	76
4	3	93	72	73	92	78
4.5	3	93	72	73	92	78
5	3	93	74	75	93	79
5.5	3	93	74	75	93	79
6	3	93	74	75	93	79
1	3.5	98	26	52	93	54
1.5	3.5	98	34	55	94	59
2	3.5	95	42	57	91	62
2.5	3.5	93	48	59	89	64
3	3.5	93	62	67	91	72
3.5	3.5	93	74	75	93	79
4	3.5	93	76	76	93	80
4.5	3.5	93	76	76	93	80
5	3.5	93	78	78	93	81
5.5	3.5	93	78	78	93	81
6	3.5	93	78	78	93	81
1	4	98	28	53	93	55
1.5	4	98	36	56	95	60
2	4	95	44	58	92	63
2.5	4	93	50	60	89	65
3	4	93	64	68	91	73
3.5	4	93	76	76	93	80
4	4	93	78	78	93	81
4.5	4	93	78	78	93	81
5	4	93	80	79	93	82
5.5	4	93	82	81	93	83
6	4	93	82	81	93	83
1	4.5	98	28	53	93	55
1.5	4.5	98	36	56	95	60
2	4.5	95	44	58	92	63
2.5	4.5	93	52	61	90	67
3	4.5	93	68	70	92	75
3.5	4.5	93	80	79	93	82
4	4.5	93	82	81	93	83
4.5	4.5	93	82	81	93	83
5	4.5	93	84	83	93	84
5.5	4.5	93	86	84	93	85
6	4.5	93	86	84	93	85
1	5	98	28	53	93	55
1.5	5	98	36	56	95	60
2	5	95	44	58	92	63
2.5	5	93	52	61	90	67
3	5	93	68	70	92	75
3.5	5	93	80	79	93	82
4	5	93	82	81	93	83
4.5	5	90	82	80	91	82
5	5	90	84	82	91	83
5.5	5	90	86	84	91	84
6	5	90	86	84	91	84
1	5.5	98	28	53	93	55
1.5	5.5	98	36	56	95	60
2	5.5	95	44	58	92	63
2.5	5.5	93	52	61	90	67
3	5.5	93	68	70	92	75
3.5	5.5	93	80	79	93	82
4	5.5	93	82	81	93	83
4.5	5.5	90	82	80	91	82
5	5.5	90	84	82	91	83
5.5	5.5	90	86	84	91	84
6	5.5	90	86	84	91	84
1	6	95	28	52	88	54
1.5	6	95	36	55	90	59
2	6	93	44	58	88	62
2.5	6	90	52	61	87	66
3	6	90	68	70	89	74
3.5	6	90	80	79	91	81
4	6	90	82	80	91	82
4.5	6	88	82	80	89	81
5	6	88	84	82	89	82
5.5	6	88	86	84	90	83
6	6	88	86	84	90	83

Table ii. Sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV) and percentage of correctly identified cases for different thresholds of proximal translation and sagittal rotation, combined with radiolucency criteria as measured using Ein-Bild-Rontgen-Analyse

Proximal translation (mm)	Sagittal rotation (°)	Sensitivity (%)	Specificity (%)	PPV	NPV	% Correctly identified
1	1	95	62	67	94	77
1.5	1	93	65	68	92	78
2	1	93	69	71	92	80
2.5	1	93	69	71	92	80
3	1	93	69	71	92	80
3.5	1	93	69	71	92	80
4	1	93	69	71	92	80
4.5	1	93	69	71	92	80
5	1	93	69	71	92	80
5.5	1	93	69	71	92	80
6	1	93	69	71	92	80
1	1.5	95	67	70	95	80
1.5	1.5	93	73	74	93	82
2	1.5	93	79	78	93	85
2.5	1.5	93	79	78	93	85
3	1.5	93	79	78	93	85
3.5	1.5	93	79	78	93	85
4	1.5	93	79	78	93	85
4.5	1.5	93	79	78	93	85
5	1.5	93	79	78	93	85
5.5	1.5	93	79	78	93	85
6	1.5	93	79	78	93	85
1	2	95	73	74	95	83
1.5	2	93	79	78	93	85
2	2	93	87	85	94	89
2.5	2	93	88	87	94	90
3	2	93	88	87	94	90
3.5	2	93	88	87	94	90
4	2	93	88	87	94	90
4.5	2	93	88	87	94	90
5	2	93	88	87	94	90
5.5	2	93	88	87	94	90
6	2	93	88	87	94	90
1	2.5	93	77	76	93	84
1.5	2.5	88	83	80	90	85
2	2.5	86	90	88	89	88
2.5	2.5	86	92	90	89	89
3	2.5	86	92	90	89	89
3.5	2.5	86	92	90	89	89
4	2.5	86	92	90	89	89
4.5	2.5	86	92	90	89	89
5	2.5	86	92	90	89	89
5.5	2.5	83	92	90	87	88
6	2.5	83	92	90	87	88
1	3	93	79	78	93	85
1.5	3	88	85	82	90	86
2	3	86	92	90	89	89
2.5	3	86	94	92	89	90
3	3	86	94	92	89	90
3.5	3	86	94	92	89	90
4	3	86	94	92	89	90
4.5	3	86	94	92	89	90
5	3	86	94	92	89	90
5.5	3	83	94	92	88	89
6	3	83	94	92	88	89
1	3.5	93	79	78	93	85
1.5	3.5	88	85	82	90	86
2	3.5	86	92	90	89	89
2.5	3.5	86	94	92	89	90
3	3.5	86	94	92	89	90
3.5	3.5	86	94	92	89	90
4	3.5	86	94	92	89	90
4.5	3.5	86	94	92	89	90
5	3.5	86	94	92	89	90
5.5	3.5	83	94	92	88	89
6	3.5	83	94	92	88	89
1	4	93	79	78	93	85
1.5	4	88	85	82	90	86
2	4	86	92	90	89	89
2.5	4	86	94	92	89	90
3	4	86	96	95	89	91
3.5	4	86	96	95	89	91
4	4	86	96	95	89	91
4.5	4	86	96	95	89	91
5	4	86	96	95	89	91
5.5	4	83	96	95	88	90
6	4	83	96	95	88	90
1	4.5	93	79	78	93	85
1.5	4.5	88	85	82	90	86
2	4.5	86	94	92	89	90
2.5	4.5	86	96	95	89	91
3	4.5	86	98	97	89	93
3.5	4.5	86	98	97	89	93
4	4.5	86	98	97	89	93
4.5	4.5	86	98	97	89	93
5	4.5	86	98	97	89	93
5.5	4.5	83	98	97	88	91
6	4.5	83	98	97	88	91
1	5	93	81	80	93	86
1.5	5	88	87	84	90	87
2	5	86	96	95	89	91
2.5	5	86	98	97	89	93
3	5	86	100	100	90	94
3.5	5	86	100	100	90	94
4	5	86	100	100	90	94
4.5	5	86	100	100	90	94
5	5	86	100	100	90	94
5.5	5	83	100	100	88	93
6	5	83	100	100	88	93
1	5.5	93	81	80	93	86
1.5	5.5	88	87	84	90	87
2	5.5	86	96	95	89	91
2.5	5.5	86	98	97	89	93
3	5.5	86	100	100	90	94
3.5	5.5	86	100	100	90	94
4	5.5	86	100	100	90	94
4.5	5.5	86	100	100	90	94
5	5.5	86	100	100	90	94
5.5	5.5	83	100	100	88	93
6	5.5	83	100	100	88	93
1	6	93	81	80	93	86
1.5	6	88	87	84	90	87
2	6	86	96	95	89	91
2.5	6	86	98	97	89	93
3	6	86	100	100	90	94
3.5	6	86	100	100	90	94
4	6	86	100	100	90	94
4.5	6	83	100	100	88	93
5	6	83	100	100	88	93
5.5	6	81	100	100	87	91
6	6	81	100	100	87	91

CHAPTER FIVE

Accuracy of EBRA-Cup measurements after reconstruction of severe acetabular defects at revision THR.

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The only validated thresholds of early and late acetabular component migration following revision THR have been performed using EBRA-Cup. However, RSA is the most sensitive technique to measure implant migration in vivo and it allows measurement irrespective of whether the radiographs at different time points have different pelvic tilt and rotation, a major limitation of EBRA-Cup. Whilst the levels of agreement and error between these two techniques have been previously established in studies of cemented acetabular components used at primary THR, these are not established for hips that have complex acetabular reconstructions with uncemented acetabular components following revision THR. In revision THR routine bony landmarks may not be visible. In the presence of a pelvic discontinuity, where the inferior portion of the pelvis can move independently of the superior portion, can also lead to measurement error with the EBRA-Cup technique. Therefore, the primary aim was to determine the accuracy of EBRA-Cup measurements of uncemented acetabular component migration. The secondary aim was to compare the number of cases identified above and below migration thresholds from both EBRA-Cup and RSA measurements.

Statement of Authorship

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Contribution to the Paper	Ethics submission, Study design, Analysis of results, Wrote initial draft.		
Overall percentage (%)	60		
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	24/9/19

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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Accuracy of EBRA-Cup Measurements after Reconstruction of Severe Acetabular Defects at Revision THR

Running Head: Accuracy of EBRA Migration Measurements

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ABSTRACT

Radiostereometric Analysis (RSA) is the most accurate method of measuring component migration using radiographs but is restricted to use in prospective studies. EBRA-Cup can be used retrospectively, but its accuracy to measure component migration following revision is unknown. This study aimed to determine the accuracy of EBRA-Cup measurements of uncemented acetabular component migration after revision THR. The secondary aim was to compare the number of cases identified using EBRA-Cup and RSA as having proximally migrated above and below 1mm at 2 years post-operatively. EBRA-Cup measurements were performed on plain antero-posterior (AP) pelvic radiographs taken at the same time as RSA radiographs in a prospective cohort of 53 hips undergoing acetabular revision. At 2 years, the mean difference between the RSA and EBRA-Cup measurements for 17 components used to treat pelvic discontinuity was 0.90mm, significantly greater than the mean difference of 0.28mm for 36 components without discontinuity (p=0.0001). The mean difference between the RSA and EBRA-Cup measurements at 2 years for hips that were reconstructed with an acetabular component alone, 0.28mm, was significantly lower than hips that were reconstructed with an acetabular component in combination with an augment and/or cage, 0.74mm (p=0.0005). In conclusion, EBRA-Cup can accurately measure migration of uncemented acetabular components used at revision THR. The presence of pelvic discontinuity, and addition of augments and cages, significantly influenced the accuracy of EBRA-Cup measurements. EBRA-Cup and RSA had good agreement on classification of components that migrated proximally above or below 1mm at 2 years, with 100% sensitivity and 87% specificity.

INTRODUCTION

Early migration has been shown to predict later loosening of acetabular components used at both primary[1,2] and revision total hip replacement (THR).[3] The survival of acetabular components used in first-time revision THR is only 75% at 10 years, excluding re-revision for infection, with acetabular component loosening being the most common reason for failure.[4] Survivorship of the acetabular component used in hips with a history of more than one prior revision is worse than that of a first-time revision.[5] The majority of clinical studies that examine cohorts of acetabular components used at revision THR[6] used non-computerised methods to assess migration on radiographs. These methods are associated with an error of ±5mm[7-10] and may not be able to adequately detect early acetabular component migration.

A recent systematic review identified acetabular migration measured by Radiostereometric Analysis (RSA) and Ein-Bild-Roentgen-Analyse (EBRA-Cup) as the only two validated surrogate markers of long-term primary THR outcome.[2] RSA is considered the 'Gold Standard' in vivo measurement method because of its superior accuracy of 0.007mm (SD 0.04).[11] However, RSA can only be used in prospective clinical studies due to the requirement for intraoperative bead insertion and subsequent dual radiographs taken over a specialised calibration cage. EBRA-Cup measurements are made from anteroposterior (AP) pelvic radiographs taken routinely as part of clinical review and allow analysis of large retrospective cohorts.[12] EBRA-Cup is more accurate than other methods that use AP pelvic radiographs[13] because radiographs with incompatible pelvic tilt and rotation are excluded.

The accuracy of EBRA-Cup to measure cemented acetabular component migration following primary THR is 0.39mm (SD 0.32).[12,14] The EBRA-Cup measurement accuracy when assessing uncemented acetabular components used at revision THR is not known. In an optimal setting, accuracy would be determined using a phantom model.[15,16] However, the variation in pelvic tilt and subsequent identification of pelvic bone landmarks in AP radiographs after revision THR are not able to be replicated in a phantom study. Therefore, the measurement error of EBRA-Cup should be established by comparison to in vivo RSA measurements.

Determining the amount of early migration that is clinically acceptable following revision THR is difficult due to the different implants and surgical treatment methods used to treat varying bone defects. The mean migration of cohorts has been used to predict the long term results of acetabular components used at primary THR.[17,18] Excessive amounts of migration are more likely to occur in acetabular components following revision THR than following primary THR which disproportionately affects the reported mean of the cohort. Thresholds of individual acetabular component migration are therefore used to determine the percentage of components in a cohort with an unacceptable amount of early migration following revision THR.[19-21] Using RSA measurements, Klerken et al[19] determined that every millimetre of proximal migration two years postoperatively increased the risk of aseptic loosening by 37%. Recently Kim et al[20] determined that, using EBRA-Cup, the threshold of >1mm proximal migration two years postoperatively of uncemented acetabular components used at revision THR has a 64% sensitivity and 94% specificity for aseptic loosening at re-revision surgery. It would be advantageous for future studies to know how accurately EBRA-Cup can detect acetabular components that migrate >1mm.

Therefore, this study aims to determine the accuracy of EBRA-Cup to measure migration of uncemented acetabular components used to reconstruct Paprosky II and

III acetabular defects. Secondary aims were to determine if other patient or surgical treatment factors affected the accuracy of EBRA-Cup measurements, and if the number of hips identified above and below published acceptable early migration thresholds differs between EBRA-Cup and RSA measurements.

METHODS

Diagnostic Study, Level I Evidence.

This study was approved by the ethics review board of our institution. This study examined a single-centre prospective cohort of acetabular revisions that involved the use of an uncemented porous tantalum acetabular component (Trabecular Metal Acetabular Revision System, Zimmer Pty Ltd, Indiana, USA) to treat a Paprosky II or III defect by two surgeons (D.W.H. and L.B.S.) since these implants were made available at our institution, the Royal Adelaide Hospital, Adelaide, Australia in 2003. All hips that had an RSA follow-up of two or more years were included. Exclusion criteria for the study were (1) if EBRA-Cup could not include the baseline AP pelvic radiograph taken four days post-surgery in the analysis, (2) if there were less than four AP radiographs available for EBRA-Cup analysis, (3) if EBRA-Cup excluded the 2 year migration radiograph and it was not possible to interpolate the amount of migration from surrounding time points.

Acetabular defects[22,23] and pelvic discontinuity were diagnosed on preoperative radiographs and confirmed intraoperatively (Table 1).

At surgery, the acetabulum was reamed and trialled with sequentially larger components to maximinse the amount of contact with the host bone. Acetabular bone defects were filled with allograft or tantalum augments that were screwed into host bone. In selective cases, a cage was used as a ‘cup-cage construct’ with or without an augment. To investigate the influence of additional fixation on EBRA-Cup measurement error, we divided the cohort into two groups, namely hips that were reconstructed with an acetabular component alone and hips that were reconstructed with an acetabular component in combination with an augment and/or cage (Table 1). Between four and six tantalum beads (RSA Biomedical, Umeå, Sweden) were inserted into both the ilium and ischium around the acetabular component, to allow for RSA analysis. Plain anterior-posterior (AP), lateral and specific RSA radiographs of the hip and pelvis were performed within four days post-surgery and at 6 weeks, 3, 6, 12 and 24 months follow-up. The RSA radiographs were taken using a uniplanar RSA setup with two radiographic tubes. A room-mounted unit (Siemens Ysio Digital System; Siemens AG, Berlin, Germany) and a mobile radiographic unit (Shimadzu Art analog mobile machine; Shimadzu Medical Systems Ltd, Tokyo, Japan) were positioned with a 40-degree angle between the tubes. The calibration cage (Cage 43; RSA Biomedical) contained two 35 x 43cm high-resolution digital radiographic cassettes (Agfa CR General Plates; Agfa Healthcare, Mortsel, Belgium) with a focal length to the film of 1.6m for each. The radiographic tubes were exposed simultaneously at 110 kV and 16 mAs. The exposures were digitized with an AGFA Centricity CR SP1001 processor (AGFA Healthcare). Radiographs were analysed using UmRSA software (Version 6.0; RSA Biomedical). Proximal migration of the acetabular component was determined in reference to markers that were inserted within an intact segment of the ilium. The limits used with the UmRSA software were 0.3 for the mean error of each rigid body and less than 250 for the condition number.

EBRA-Cup analysis was performed on AP pelvic radiographs that were taken at the same radiographic appointment as the RSA radiographs. Radiographs were retrieved from the hospital PACS (Agfa IMPAX, AGFA-Gevaert N.V, Mortesl, Belgium) at the highest quality setting and were analysed with EBRA-Cup (Universität Innsbruck, Innsbruck, Austria). The standard reference lines used within EBRA-Cup were the ischial tuberosities, the inferior obturator line, the ilio-ischial line and a horizontal line between the roof of the sciatic notches or the superior border of the sacral foramina. If EBRA-Cup excluded a radiograph after the baseline radiograph because of incompatible pelvic tilt or rotation, results that used the initial post-operative radiograph as the baseline were included. Any results that did not use the initial AP pelvic post-operative radiograph as a reference were excluded. A 3mm limit of comparison within the EBRA-Graf software was used. EBRA-Cup measurements included proximal and medial translation.

Statistical analysis

In this study, the term accuracy was defined as the closeness of agreement between EBRA-Cup and the accepted reference value (RSA).[24] Hence, EBRA-Cup and RSA measurements were collated as matched pairs for every available time point in GraphPad Prism. RSA measurements were considered the 'Gold Standard' in all analyses. Error was calculated as the mean difference of the paired observations (proximal and medial migration measurements) and also presented as the root mean square error (RMSE). Intra-observer error was defined as mean difference in EBRA-Cup measurements of 36 radiographs when repeated by the same observer (JMA).

To determine if a difference between sub-cohorts existed, a Mann-Whitney U test was performed on proximal migration values at two years. P values of <0.05 were considered statistically significant. If two-year migration results were not available using EBRA-Cup, the result was interpolated from the migration data available before and after the two-year time point. A Bland-Altman plot was used to determine if an increased measurement error between the two different techniques was observed with larger migration measurements. Sensitivity with respect to the 1mm threshold at two years was calculated as the number of acetabular components that EBRA-Cup and RSA both identified as migrating >1mm divided by the number of acetabular components identified by RSA as migrating >1mm. Specificity was calculated as the number of acetabular components that EBRA-Cup identified as migrating <1mm divided by the number of acetabular components identified by RSA as migrating <1mm, whereby the acetabular components identified are the same.

RESULTS

During the study period, 76 hips with Paprosky II or III defects were treated with porous tantalum acetabular components and had at least two-years of RSA follow-up. Of these 76 hips, 23 were excluded for the following reasons: (1) 15 hips - EBRA-Cup software excluded the baseline AP pelvic radiograph due to the pelvic tilt being incompatible with the remaining radiographs or the bone landmarks could not be identified on the initial baseline radiograph due to poor image quality; (2) 2 hips - insufficient radiographs available for analysis with EBRA-Cup; (3) 3 hips - had only two year follow-up, and the final radiograph was excluded by EBRA-Cup due to pelvic tilt incompatibility; (4) 3 hips- two-year results could not be interpolated from surrounding data. Therefore, 53 hips were included in the final study cohort. The mean age of the study cohort was 69 years (Table 1). Pelvic discontinuity was present in 17 hips. For 28 hips, the procedure was the first revision. The total number of EBRA-Cup and RSA measurements available for comparison was 240. Of the 53 patients who had proximal migration EBRA-Cup results, 43 also had medial migration results.

Intra-observer error of EBRA measurements

The mean difference of proximal migration measurements in 26 radiographs was 0.00mm (median 0.04, SD 0.14, 95%CI -0.06 to 0.07, RMSE 0.14). The mean difference of medial migration measurements in 34 radiographs was 0.04mm (median -0.04mm, SD 0.20mm, 95%CI -0.03mm to 0.12mm, RMSE 0.20).

Comparison of EBRA-Cup and RSA measurements of acetabular component migration

The mean difference between EBRA-Cup and RSA proximal migration measurements across all time points was 0.20mm (median 0.14, SD 2.08; 95%CI -0.07 to 0.46; RMSE 2.01, Figure 1). The proximal migration curve for all 53 acetabular components measured by EBRA-Cup is illustrated in Figure 2. The mean difference between EBRA-Cup and RSA measurements at two years was 0.51mm (median 0.20, SD 1.53; 95%CI 0.08 to 0.93; RMSE 1.60). There was no apparent trend of increasing difference in measurements when compared to the average size of the measurements. However, it was observed that the difference between EBRA and RSA measurements was larger for measurements greater than 10mm (Figure 3).

The mean difference between EBRA-Cup and RSA medial migration measurements was 0.01mm, (median -0.01, SD 1.82; 95% CI -0.29 to 0.27; RMSE 1.81). Using a Bland-Altman plot, there was an apparent increase in the difference between the two methods as the average of the measurements increased (Figure 4).

Accuracy of EBRA-Cup to measure migration of acetabular components used to treat hips according to pre-operative bone defect and presence of pelvic discontinuity.

The mean difference between EBRA-Cup and RSA proximal migration measurements at 2 years for the seven hips with a Paprosky II defect was 0.26mm (median 0.31, SD

0.28, 95%CI -0.04 to 0.55). This was lower than that for the 46 hips with Paprosky III defects of 0.54mm (median 0.20, SD 1.61, 95%CI 0.07 to 1.00). There was no difference in the EBRA-Cup measurement error between hips with Paprosky II defects when compared to those with a Paprosky III defect without a pelvic discontinuity. There was no difference for hips with a Paprosky IIIA defect when compared to those with a Paprosky IIIB defect. The mean difference between the RSA and EBRA-Cup proximal measurements at 2 years for the 36 hips without pelvic discontinuity was 0.28mm (median 0.17, SD 0.77; 95%CI 0.01 to 0.54; RMSE 0.81) was significantly lower than the 17 hips with pelvic discontinuity, 0.90mm (median 0.36, SD 2.34; 95%CI -0.22 to 2.03; RMSE 2.45mm; $p<0.0001$).

Accuracy of EBRA-Cup to measure migration of acetabular components used to treat hips reconstructed with an acetabular component alone compared with other constructs

For the hips that were reconstructed with an acetabular component alone, the mean difference between the RSA and EBRA-Cup proximal migration measurements at 2 years was 0.28mm (median 0.26, SD 0.85; 95%CI -0.05 to 0.62) which was significantly lower than hips that were reconstructed with an acetabular component in combination with an augment and/or cage, 0.74mm (median 0.19, SD 2.00; 95%CI -0.06 to 1.56; $p=0.0005$).

Sensitivity and Specificity of EBRA-Cup to identify proximal migration >1mm at 2 years

RSA measurements detected that six acetabular components had migrated >1mm. The sensitivity of EBRA-Cup measurements was 100%, finding the same six acetabular components to have also migrated >1mm (Figures 5 and 6).

RSA measurements detected that 47 of 53 acetabular components migrated <1mm. The specificity of EBRA-Cup measurements was 87%, with 41 of these 47 components correctly identified as migrating <1mm. The remaining six acetabular components were incorrectly identified as having migrated >1mm; three of these had a pelvic discontinuity and were treated with a cup-cage construct, one had an anterior column fracture and was treated with an acetabular component alone and two did not have a discontinuity and were treated with an acetabular component alone.

Discussion

Acetabular components used at revision THR have larger amounts of migration than those used at primary THR[25] and have a higher rate of revision THR within 10 years.[4,26] Measuring early migration of revision acetabular components accurately is important to establish if new surgical techniques and implant designs are likely to have good long term outcomes.[27] While RSA and EBRA-Cup remain predominantly used as research tools, some recent studies have identified individual thresholds that could be applied in a clinical setting.[2,21] Despite measuring proximal migration of complex reconstructions in the presence of large acetabular defects, the mean difference between EBRA-Cup and RSA was 0.20mm which is similar to that previously reported 0.39mm (SD 0.36)[12] and 0.31mm (95% CI 0.24 to 0.43)[9].

The accuracy of EBRA-Cup measurements is influenced by the difficulty of consistently identifying bone landmarks and the varying rotation and tilt of the pelvis in consecutive AP radiographs. Some landmarks, such as the ischial tuberosity, are prone to developing osteophytes and change in morphology over time. Other landmarks such as the teardrop may be obscured or not even present following revision THR. Landmarks such as the inferior margin of the obturator foramen can vary in shape depending on the degree of pelvic tilt, and therefore finding a consistent reference line may be subject to a degree of error. Drawing matching parallel horizontal lines across multiple landmarks, required by EBRA-Cup is often difficult and do not match up. For example, a line that crosses the inferior margin of the sacral foramina is not always parallel to a line that crosses the inferior margin of the obturator foramen or the ischial tuberosity following revision or complex THR. RSA methodology by comparison uses small spherical beads to represent the acetabular bone reference segment that can be reliably identified.

The mean intra-observer error for proximal migration of 0.00mm (95%CI -0.06 to 0.07) was very similar to the -0.08mm (95%CI -0.31 to 0.15) error described previously by Kim et al.[20] The observer error needs to be considered when interpreting whether an acetabular component is likely to be above or below the two-year proximal migration threshold of 1mm and in some cases further radiographic follow-up may be required.

Although there was a large standard deviation in our results, the larger differences observed between EBRA-Cup and RSA proximal migration measurements occurred in three acetabular components that migrated >10mm. For example, one component was measured to have migrated 14mm by EBRA-Cup compared to 7mm by RSA. Despite the difference being large, it is clinically not significant as both results are diagnostic of loosening.[21] The sensitivity of EBRA-Cup measurements was 100% to detect acetabular component migration >1mm according to RSA measurements and specificity was 87%. Four of the six hips that were incorrectly determined by EBRA-Cup as having migrated >1mm had pelvic discontinuity or an anterior column fracture which significantly affects the measurement accuracy.

The accuracy of measuring migration was significantly worse for acetabular components used to treat pelvic discontinuity and/or complex reconstructions with additional metalwork (augments and cages). There are several reasons for this. First, the larger errors observed in the hips treating pelvic discontinuity are in part due to the different reference point used by EBRA-Cup and RSA methods. RSA measurements were performed with reference to tantalum markers in the ilium only, whereas EBRA-Cup uses the second most distal horizontal line that is commonly placed on the pubis or ischium.[12] Therefore, the amount of migration measured may be different if an acetabular component is well fixed to the ilium but not to the ischium. Unfortunately, there are not sufficient landmarks in the bony pelvis that would allow consistent horizontal lines above the level of the acetabular component for use in EBRA-Cup software. Secondly, in the presence of pelvic discontinuity, the distal ischial segment may migrate independently to the proximal region of the pelvis and lead to a change in the spacing between horizontal lines and subsequent inappropriate inclusion or exclusion of radiographs in EBRA-Cup. In this relatively small cohort of patients with discontinuity, there were too few patients with adequate ischial beads visible in RSA radiographs to enable measurement of the movement between the ischium and ilium. Future RSA studies should investigate the amount of movement across the discontinuity over time. Thirdly, in the presence of augments and/or cages, it may be difficult to correctly mark the ellipse of the acetabular component using EBRA-Cup, while tantalum beads within the liner may be used to represent the acetabular component in RSA measurements.

Although one of the strengths of the EBRA-Cup software is comparing radiographs with similar pelvic tilt, in our study this led to the exclusion of 30% of hips in the original cohort. Pelvic tilt may vary significantly depending on patient clothing, ability to lie flat on the examination table, changes in spinal morphology or other pathology in the pelvis such as a contralateral hip replacement or development of a fixed flexion deformity. The relatively large number of incompatible radiographs confirms that change in pelvic tilt between AP radiographs is often underappreciated in routine clinical practice. It is not possible using eyesight alone to determine subtle acetabular component migration that could indicate loosening. Improved protocols to aid in the standardisation of radiographs are required to improve compatibility. Due to the potentially large number of hips that are likely to be excluded when using EBRA-Cup measurements, we recommend that RSA measurements be used in future studies.

There are several limitations to this study. First, our study did not determine the accuracy of the EBRA-Cup measurements against known movements of a phantom model. Radiographs of a phantom could not be replicate the random variation of pelvic tilt; image quality; radiographic beam centring; skeletal movement across cases with discontinuity; and exclusion of bone landmarks often observed in routine clinical radiographs after revision THR. However, RSA measurements were used as the gold standard, which allowed our study to investigate the true application of EBRA-Cup on clinically relevant pelvic radiographs. Secondly, there were a varying number of radiographs and duration of follow-up for each hip. This may have influenced the two-year EBRA-Cup results due the smoothing function within the software. Thirdly, the EBRA-Cup technique uses the horizontal line that may be labelled on the pubic symphysis or the ischial foramen as the reference segment for proximal translation, while assuming that the pelvis is in continuity and is a single reference segment. In this study RSA used the ilium as the reference for acetabular component migration.

In conclusion, EBRA-Cup can accurately measure migration of uncemented acetabular components used at revision THR. While the presence of pelvic discontinuity, and the addition of augments and cages, significantly influenced the accuracy of EBRA-Cup migration measurements, EBRA-Cup and RSA measurements had good agreement on classification of components above and below 1mm at 2 years with a sensitivity and specificity of 100% and 87% respectively.

Acknowledgements

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Figure Legends:

Figure 1: The proximal migration (mm) of each acetabular component at all time points measured by RSA (y-axis) and EBRA-Cup (x-axis).

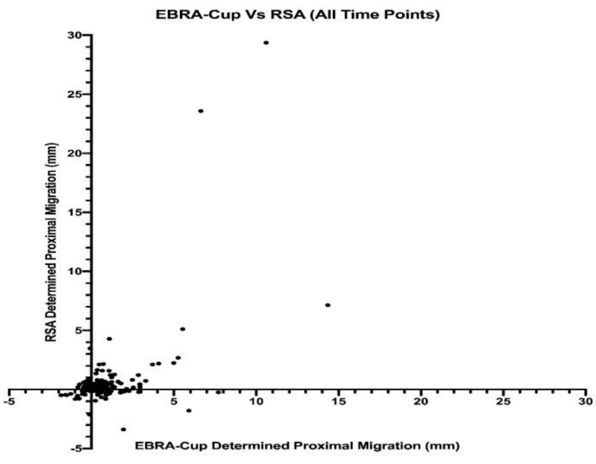


Figure 2: The proximal migration (mm) of 53 components over time measured with EBRA-Cup.

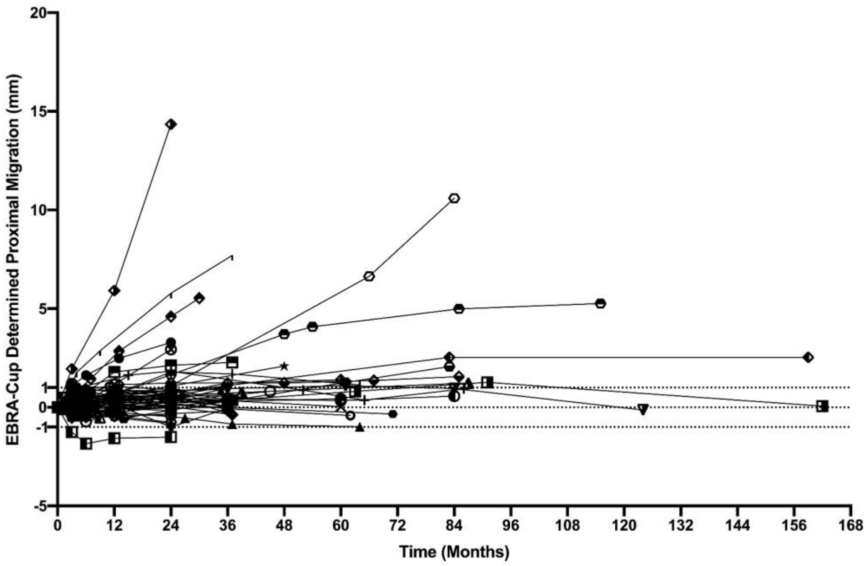


Figure 3: The Bland-Altman plot for all measurements of proximal migration (mm) of each acetabular component at all time points. The absolute difference (mm) between EBRA-Cup and RSA measurements is plotted against the absolute average (mm) of each measurement.

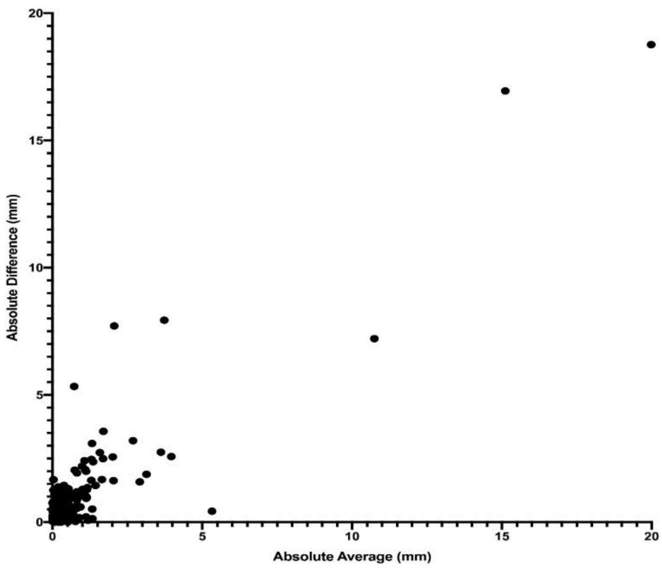


Figure 4: The Bland-Altman plot for all measurements of medial migration (mm) of each acetabular component at all time points measured. The absolute difference (mm) between EBRA-Cup and RSA measurements is plotted against the absolute average (mm) of each measurement.

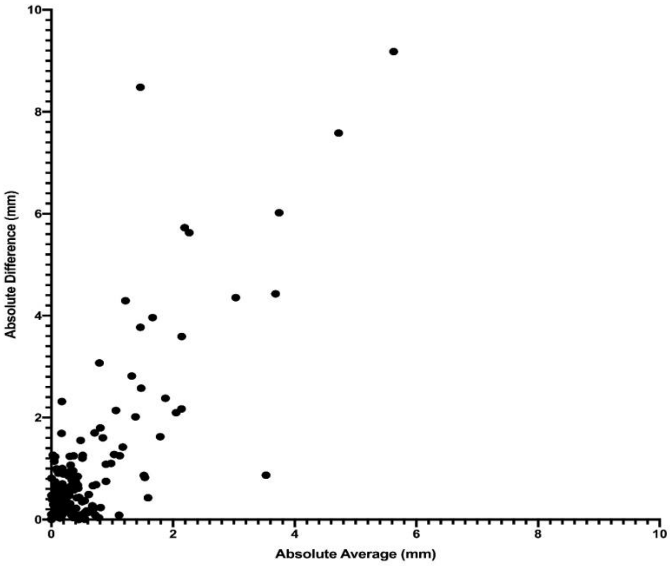


Figure 5: The proximal migration (mm) of each acetabular component at 2 years without pelvic discontinuity as measured by RSA (y-axis) and EBRA-Cup (x-axis). Dotted lines represent threshold of 1mm at two years.

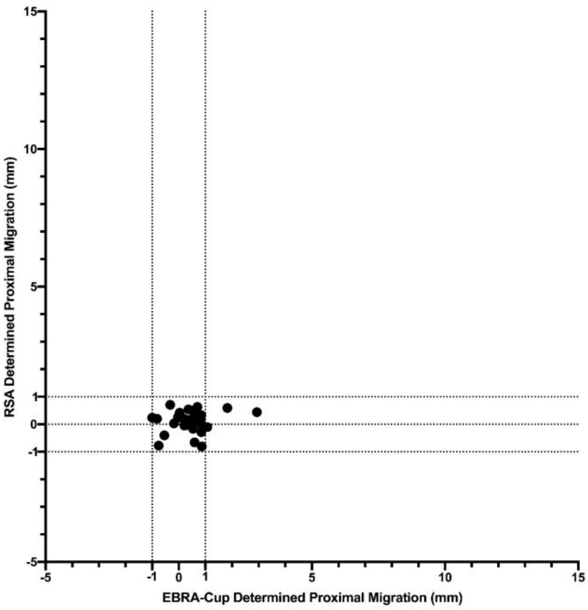
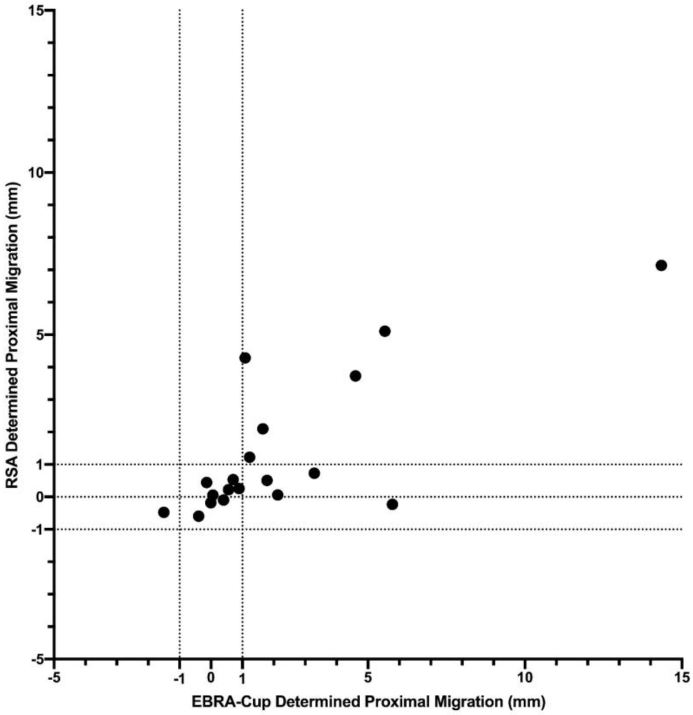


Figure 6: The proximal migration (mm) of each component at two years with pelvic discontinuity as measured by RSA (y-axis) and EBRA (x-axis). Dotted lines represent threshold of 1mm at two years.



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Tables:

Hips	53
Mean Age (years) (median; range)	69 (67.5; 35 to 89)
Side (Right:Left)	32:21
Gender (Female:Male)	32:21
Paprosky Grade (IIb:IIc:IIIa:IIIb)	4:3:28:18
Hips with Discontinuity	17
No of previous acetabular implants (0:1:2:3:4:5:6:7)	28:10:5:7:2:0:0:1
Mean Acetabular Component Size (median; range)	65(64; 50 to 80)
Construct Cup alone: Cup + Augment: Cup Cage: Cup Cage + Augment	28:13:9:3

Table 1: Cohort demographics for all patients included in the study.

CHAPTER SIX

The Stability of the Porous Tantalum Components Used in Revision THR to Treat Severe Acetabular Defects

As published in The Journal of Bone and Joint Surgery, November 2018

A recent systematic review of clinical outcomes of different reconstruction techniques used to treat severe acetabular defects at revision THR[84] showed that the trabecular metal acetabular revision system (TMARS) had the most promising early to mid-results. The migration of the TMARS as determined with RSA or EBRA has not been reported previously in the literature, which is the best predictor of long term outcomes. Additionally, after assessing the initial results it was hypothesised that the use of inferior screw fixation could improve the early stability of these reconstructions. Therefore, the objectives of the present study were to use RSA to compare the migration of the porous tantalum acetabular components used to treat severe bone defects with an established proximal translation threshold that was previously shown to be predictive of subsequent loosening, and to determine the effect that the addition of inferior screws through the acetabular component into the ischium or pubis had on migration.

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

Statement of Authorship

Title of Paper	The Stability of the Porous Tantalum Components Used in Revision THA to Treat Severe Acetabular Defects: A Radiostereometric Analysis Study
Publication Status	[X] Published [ ] Accepted for Publication [ ] Submitted for Publication [ ] Unpublished and Unsubmitted work written in manuscript style
Publication Details	J Bone Joint Surg Am. 2018;100:1926-33. http://dx.doi.org/10.2106/JBJS.18.00127

Principal Author

Name of Principal Author (Candidate)	John M Abrahams		
Contribution to the Paper	Conceptualization; Formal analysis; Validation; Writing – original draft		
Overall percentage (%)	60		
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	24/9/19.

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	S. A. Callary		
Contribution to the Paper	Formal analysis; Funding acquisition; Methodology; Project administration; Software; Writing – review & editing		
Signature		Date	24/9/2019.

Name of Co-Author	D. W. Howie		
Contribution to the Paper	Conceptualization; Funding acquisition; Methodology; Supervision; Writing – review & editing		
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Contribution to the Paper	Conceptualization; Formal analysis; Funding acquisition; Methodology; Project administration; Supervision; Writing – review & editing)		
Signature		Date	24/9/19

The Stability of the Porous Tantalum Components Used in Revision THA to Treat Severe Acetabular Defects

A Radiostereometric Analysis Study

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Background: The acetabular components used in revision total hip arthroplasty (THA) to treat severe acetabular bone defects have high rates of re-revision at mid to long-term follow-up. Early translation of acetabular components used in revision THA is a good predictor of later loosening, and radiostereometric analysis (RSA) is the most sensitive method to measure migration. The objectives of the present study were to use RSA to compare the migration of the porous tantalum acetabular components used to treat severe bone defects with the previously established acceptable proximal translation threshold of ≤1 mm within 2 years, and to determine the effect on migration of the addition of inferior screws through the component into the ischium or pubis.

Methods: RSA was utilized to measure the migration of 55 porous tantalum components used to treat severe acetabular defects (28 Paprosky IIIA, 27 Paprosky IIIB; 21 hips with pelvic discontinuity) at a mean follow-up of 4 years (range, 2 to 12 years).

Results: Forty-eight of the 55 components migrated less than the threshold that predicts later loosening (>1 mm) and 50 had not been re-revised at the time of the latest follow-up. Seven components, none of which had inferior screw fixation, exceeded the translation threshold. Of these, 6 were implanted to treat pelvic discontinuity. Of those 6 components, 5 were re-revised for loosening related to patient symptoms. At 2 years, the absolute median proximal translation of components with inferior screw fixation was |0.3| mm (range, |0.1| to |0.9| mm), compared with |0.4| mm (range, |0.03| to |16.4| mm) for those without inferior screws (p = 0.04).

Conclusions: As measured with use of RSA, the majority of porous tantalum acetabular components used in a revision THA to treat severe acetabular defects had acceptable early migration. This predicts good long-term survivorship of these components. The use of inferior screws further improved acetabular component fixation.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

One of the most important factors affecting the initial stability of the acetabular components used in revision total hip arthroplasty (THA) is the severity of bone loss[1]. The worst survivorship is reported in cases with severe bone loss[2]. Early stability of acetabular components is a predictor of survivorship for loosening[3,4]. Loosening is the most common reason for revision THA[5,6], and the risk of failure because of loosening increases with each subsequent re-revision[7].

The most common revision techniques used to treat severe acetabular defects have poor component survivorship at mid-term to long-term follow-up[8-10]. In recent years, specialized revision acetabular components have been developed to treat severe bone loss[11-15]. A systematic review of current

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Fig. 1
Anteroposterior radiographs showing hips reconstructed without inferior (ischial and pubic) screw fixation. **Fig. 1-A** Hip reconstructed with a cup-cage construct. **Fig. 1-B** Hip reconstructed with a cup-cage and 2 additional augments. **Fig. 1-C** Hip reconstructed with use of a buttress-type augment.

reconstruction techniques concluded that porous tantalum components have the most promising early to mid-term results with respect to re-revision rates and radiographic loosening[16]. Nonetheless, the reported survivorship when utilizing these implants varies, and the early stability of these components has not been measured with use of sensitive methods. For example, 1 study reported 85% survivorship for loosening at 7 years in patients with pelvic discontinuity[15]. However, an additional 11% of components in the study were not considered loose despite migrating a large amount of "up to 1 cm," which would be indicative of loosening in other clinical studies[16].

Initial stability of uncemented acetabular components has been shown to be a predictor of long-term survivorship[3,4], and measurement of early migration is recommended as part of the stepwise introduction of new prostheses[17-19]. Radiostereometric analysis (RSA) is the most sensitive radiographic method of measuring migration of acetabular components. The accuracy and precision of RSA allow the use of smaller patient cohorts to determine the migration patterns of components among different reconstruction techniques[20-22]. A systematic review of RSA studies showed that the acetabular components utilized in primary THAs that had a mean proximal translation of >1 mm at 2 years had an unacceptable risk of aseptic loosening, defined as exceeding 10% at 10-year follow-up, with every additional millimeter of translation increasing this risk by 10%[4]. For revision THA, a study utilizing RSA reported that every millimeter of proximal translation at 2 years increased the risk of subsequent aseptic loosening by 37%[23]. In a case-control study, Kim et al. assessed the relationship between early migration of the acetabular components used in revision THA and whether or not the components were loose at the time of re-revision[24]. In that study, an individual proximal translation of >1 mm within 2 years had a positive predictive value for re-revision for aseptic loosening of 90%.

To our knowledge, no study has assessed the migration of porous tantalum components in revision THA, as measured with use of sensitive techniques. The objectives of the present study were to use RSA to compare the migration of the porous tantalum acetabular components used to treat severe bone defects with an established proximal translation threshold that was previously shown to be predictive of subsequent loosening, and to determine the effect that the addition of inferior screws

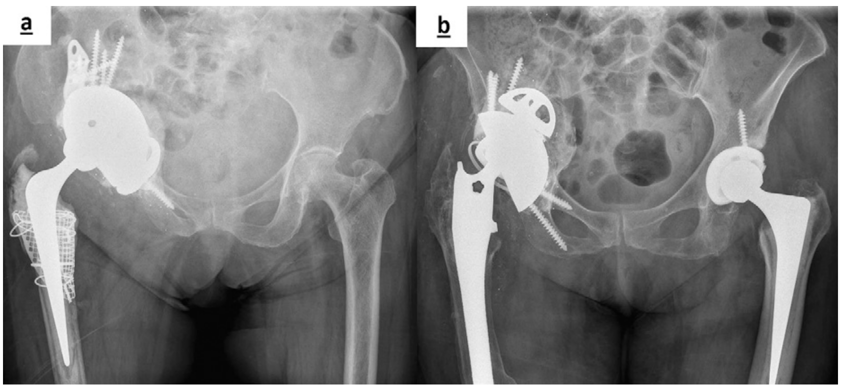

Fig. 2
Anteroposterior radiographs showing hips reconstructed with inferior (ischial and pubic) screw fixation. **Fig. 2-A** Hip reconstructed with a cup-cage construct and an augment with an additional ischial screw. **Fig. 2-B** Hip reconstructed with a cup and an augment with additional ischial and pubic screws.

TABLE I Characteristics of Hips

Hips	55
Age *(yr)*	
Mean	69
Median	68
Range	35–89
Side*	
Right	30 (55%)
Left	25 (45%)
Paprosky grade*	
IIIA	28 (51%)
IIIB	27 (49%)
Screw fixation*	
Ilium	41 (75%)
Ilium + ischium or pubis	14 (25%)
Hips with discontinuity	21 (38%)
No. of previous acetabular implants*	
1	27 (49%)
2	11 (20%)
3	6 (11%)
4	9 (16%)
5	2 (4%)
Cup size *(mm)*	
Mean	65
Median	64
Range	50–80
Head size*	
28 mm	6 (11%)
32 mm	25 (45%)
36 mm	22 (40%)
40 mm	2 (4%)
Constrained liner*	5 (9%)
RSA follow-up *(yr)*	
Mean	4
Median	3
Range	2–12

*Data are presented as the number of hips with the percentage in parentheses.

through the acetabular component into the ischium or pubis had on migration.

Materials and Methods

This was a single-center prospective cohort study of all acetabular revisions that involved the use of a porous tantalum acetabular component (Trabecular Metal Acetabular Revision System, Zimmer) to treat a Paprosky III defect[25,26]. All procedures were performed by 2 surgeons (D.W.H. and L.B.S.) at Royal Adelaide Hospital. All Paprosky III acetabular defects were treated with use of these implants from the time that they became available at our institution in 2003. At the time of revision, all patients had 12 tantalum beads (1.0-mm diameter; RSA Biomedical) inserted into the surrounding pelvic bone in order to enable RSA of acetabular component migration. Pelvic discontinuity was diagnosed or suspected with use of preoperative radiographs and was confirmed intraoperatively. Exclusion criteria for the study were (1) hips with <2 years RSA follow-up because of patient death, patient frailty, or long-distance travel required to have RSA radiographs taken; (2) acetabular component re-revision for any reason other than loosening; and (3) inadequate visualization of tantalum markers on radiographs.

Surgical Technique

All surgical procedures were performed with a posterior approach, with the majority through an extensile posterior approach[27-29]. After removing the acetabular component and membrane, the acetabulum was reamed and trialed with sequentially larger components to maximize the amount of host-bone contact. In all cases with pelvic discontinuity, the hip bone was expanded with use of an oversized cup or with a combination of cup and augment. Any defects that caused the trial implant to not be in contact with host bone were filled with allograft and/or tantalum augments screwed into the host bone. The revision tantalum component was cemented to any augment used, and the fixation was supplemented with screws. In selective cases, an ilio-ischial cage was utilized in a cup-cage construct. Initially, screws were inserted into the ilium only (Fig. 1); however, in 2012, after reviewing the RSA results of the acetabular components that were re-revised for loosening, inferior (ischial or pubic) screws were used in all cases in which adequate press-fit and acetabular component stability could not be achieved intraoperatively before fixation was supplemented with screws (Fig. 2). To enable longer screws to be inserted into the ischium in cases that were reconstructed with a cup-cage, the ischial flange of the cage was removed with use of a metal-cutting burr on the back table prior to insertion. All patients were mobilized without weight-bearing restrictions from day 1.

Radiographic Analysis

Following revision THA, RSA and plain anteroposterior and lateral radiographs were made at 3 days, 3 and 6 months, and 1, 2, and 3 years postoperatively, and then biennially thereafter. A uniplanar RSA set-up with 2 radiographic tubes was used, as described by Howie et al.[30]. Radiographs were analyzed with use of UmRSA software (version 6.0; RSA Biomedical). Acetabular component migration was defined as the change in position of the outer ellipse of the acetabular component relative to the beads placed in the ilium. The precision of the RSA measurements was determined by performing double examinations at day 3 in 24 of the 55 cases. A radiolucent line was defined as a dark line of demarcation between the acetabular component and the cancellous bone (measurements made by J.M.A. and S.A.C., both blinded to the clinical data).

The acceptable threshold of early translation was defined as a proximal translation of ≤1 mm within 2 years[4,24].

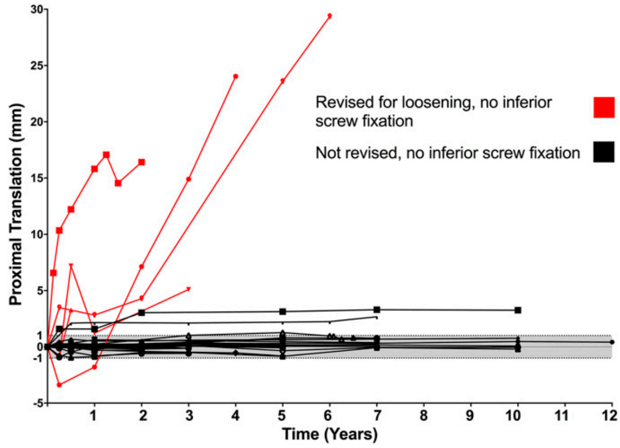

Fig. 3-A

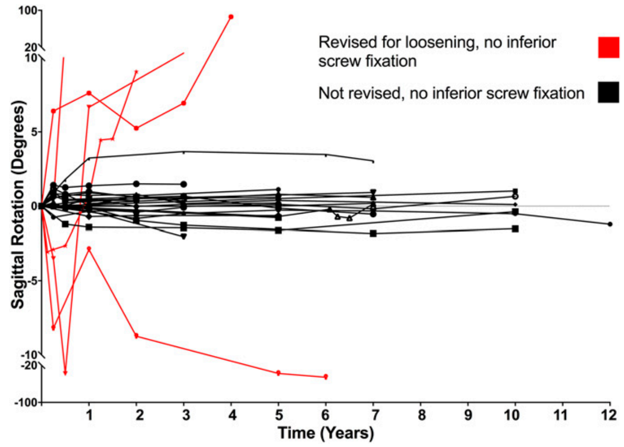

Fig. 3-B

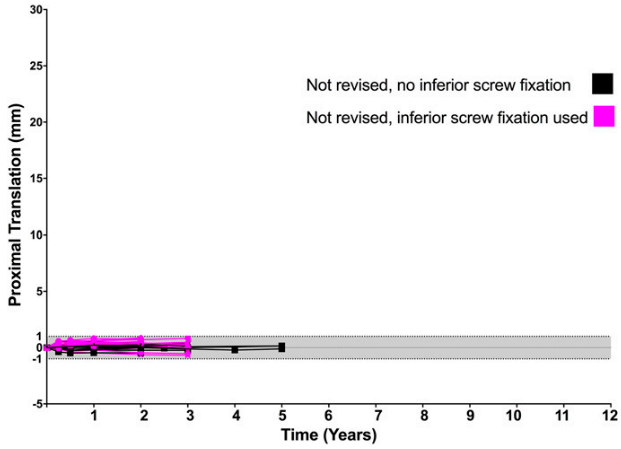

Fig. 3-C

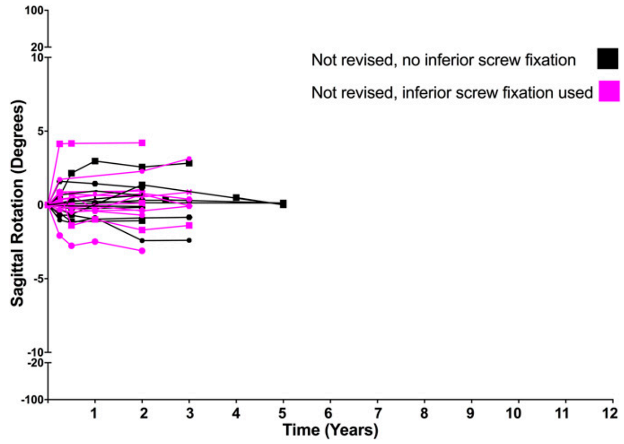

Fig. 3-D

Figs. 3-A through 3-D Graphs showing the migration of the acetabular components. **Fig. 3-A** Proximal translation for the 29 components implanted prior to the introduction of inferior (ischial and pubic) screw fixation. Lines in red denote hips that were re-revised for loosening. Lines in black denote hips that had not been re-revised. The shaded band denotes the acceptable threshold of early translation, ≤1 mm. Note that all revised components migrated >1 mm at 2 years. **Fig. 3-B** Sagittal rotation for the 29 components implanted prior to the introduction of inferior (ischial and pubic) screw fixation. Lines in red denote hips that were re-revised for loosening. Lines in black denote hips that had not been re-revised. **Fig. 3-C** Proximal translation for the 26 components implanted after the introduction of inferior screw fixation. Lines in pink denote components augmented with inferior screw fixation. Lines in black denote components without inferior screw fixation. The shaded band denotes the acceptable threshold of early translation, ≤1 mm. Note that no component migrated >1 mm at 2 years. **Fig. 3-D** Sagittal rotation for the 26 components implanted after the introduction of inferior screw fixation. Lines in pink denote components augmented with inferior screw fixation. Lines in black denote components without inferior screw fixation.

Components identified as having >3 mm of proximal translation or >5° of sagittal rotation, or those that developed a complete continuous radiolucent line, at the time of the latest follow-up were considered to be radiographically loose[31].

Statistical Analysis

The migration results in this study were reported as a median because the cohort is not normally distributed and has a large number of outliers. The mean was also presented because previous studies have referred to the mean of a cohort to allow comparison with other such studies.

Statistical tests were performed on GraphPad Prism (version 7.0b; GraphPad Software). The effects of changes in surgical technique at 2 years were analyzed with use of the Mann-Whitney U test. A p value of <0.05 was considered significant.

Results

Since the introduction of porous tantalum acetabular components in our department, 81 consecutive hips with Paprosky III acetabular defects in 78 patients were treated with reconstructions involving porous tantalum components by the 2 study surgeons (D.W.H. and L.B.S.). Of these, 26 hips

TABLE II Two-Year Proximal Translation and Number of Hips Re-Revised for Loosening, by Defect and Type of Screw Fixation

	No. of Hips	Proximal Translation at 2 Years				Proximal Translation of >1 mm within 2 Years*	Re-Revision for Loosening*
		Median	P Value†	Mean	Range		
All components	55	0.3		0.9	0.03–16.4	7 (13%)	5 (9%)
Paprosky grade			0.09				
IIIA	28	0.3		0.4	0.03-3.3	1 (4%)	1 (4%)
IIIB	27	0.5		1.6	0.04–16.4	6 (22%)	4 (15%)
Pelvic discontinuity			0.31				
No	34	0.3		0.4	0.03–3.0	1 (3%)	0 (0%)
Yes	21	0.4		1.9	0.04–16.4	6 (29%)	5 (24%)
Inferior screws			0.04				
No	41	0.4		1.2	0.03–16.4	7 (17%)	5 (12%)
Yes	14	0.3		0.5	0.1–0.9	0 (0%)	0 (0%)

*Data are presented as the number of hips with the percentage of the total number of hips for each row in parentheses. †As determined with use of the Mann-Whitney U test for median.

(26 patients) were excluded for the following reasons: 20 hips had <2 years of RSA follow-up because of patient death (5) or frailty or long-distance travel required (15), 1 hip was re-revised within 2 years for infection, and 5 hips had an inadequate number of tantalum markers visible to allow RSA. This left a study cohort of 55 hips (52 patients). The demographics of study patients are summarized in Table I. Twenty-eight (51%) of the 55 hips had Paprosky IIIA defects. Twenty-one hips (38%) had pelvic discontinuity. The mean RSA follow-up for the entire cohort was 4 years (range, 2 to 12 years). The mean time between the primary THA and the revision THA was 9 years (range, 6 to 14 years) for hips treated prior to the introduction of inferior screw fixation at our institution, and was 4 years (range, 2 to 6 years) for those treated afterward.

Acetabular Component Re-Revision

Five acetabular components in 3 patients were re-revised for loosening. Two of those patients underwent 2 re-revisions of the same hip, with 1 undergoing re-revision at 12 and 32 months and the other undergoing re-revision at 24 and 65 months. The third patient was re-revised at 8 years. All 3 patients had pelvic discontinuity at the time of each revision and none had reconstructions with inferior screws. All 5 acetabular components were identified on RSA as having >1 mm proximal translation within 2 years, and all were

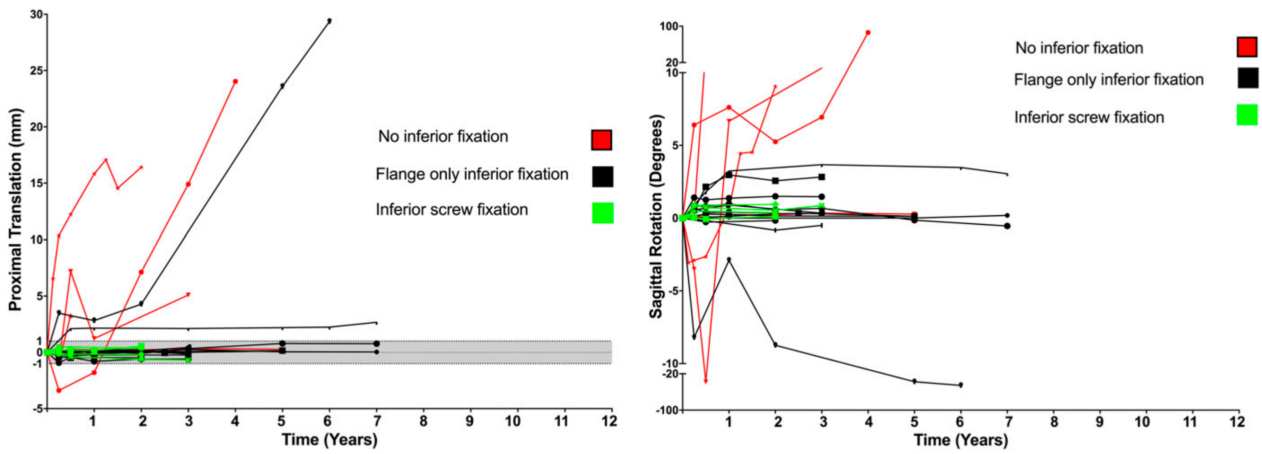

Fig. 4-A Fig. 4-B

Figs. 4-A and 4-B Graphs showing the migration of the acetabular components, stratified according to the use of additional inferior fixation. **Fig. 4-A** Proximal translation. Hips with no inferior fixation are represented by red lines. Hips with flange-only inferior fixation are represented by black lines. Hips with inferior screw fixation are represented by green lines. **Fig. 4-B** Sagittal rotation of components. Hips with no inferior fixation are represented by red lines. Hips with flange-only inferior fixation are represented by black lines. Hips with inferior screw fixation are represented by green lines.

subsequently confirmed as loose at the time of the re-revision procedure. There was no osseous ingrowth in any of the retrieved components.

Other Re-Revisions

Three hips developed recurrent dislocation and needed a liner exchange to a semi-constrained or constrained liner that was cemented within the same acetabular component. A fourth hip developed an acute infection 7 years postoperatively that was treated with debridement and head exchange. The acetabular component was retained.

Clinical Outcomes of the 26 Exclusions

The outcomes of the 26 excluded hips are known up to either patient death or the completion of the study. Radiographical assessment of these hips did not show any change in component position. Excluding the re-revision for infection described above, only 1 other hip underwent re-revision. The hip needed revision for recurrent dislocation, which was treated by changing the liner to a constrained liner that was cemented within the same acetabular component.

RSA Results

Using 24 double examinations, the mean difference in RSA measurements of proximal translation was 0.02 mm (95% confidence interval [CI], -0.06 to 0.10), and that of sagittal rotation was 0.0° (95% CI, –0.12° to 0.23°). The proximal translation and sagittal rotation of all components is illustrated in Figures 3-A through 3-D. The 5 acetabular components that were subsequently re-revised for loosening had large proximal translations and sagittal rotations that increased over time until re-revision.

Proximal Translation at 2 Years as a Predictor of Future Loosening

The median absolute proximal translation of all components at 2 years was |0.3| mm (Table II). Seven components were identified as having >1 mm of proximal translation within 2 years. Of these, 5 were associated with substantial pain and were re-revised as described above. The other 2 components migrated 2.1 and 3.0 mm within the first 2 years, but the translation of these 2 components remained relatively unchanged through the time of the latest follow-up at 7 and 10 years, respectively (Fig. 3).

There was a trend for the absolute proximal translation at 2 years to be lower for hips with Paprosky IIIA defects compared with those with Paprosky IIIB defects (p = 0.09) and for hips with no pelvic discontinuity compared with those with discontinuity (p = 0.31) (Table II). The absolute proximal translation was significantly lower for hips with inferior screws compared with those without (p = 0.04). None of the hips that were treated with inferior screws had component migration of >1 mm.

Twenty-one components were utilized to treat pelvic discontinuity with either inferior screw fixation, flange-only ischial fixation, or without any ischial or pubic fixation (Fig. 4). The median absolute proximal translation was |0.4| mm (range, |0.1| to |0.6| mm) for the 4 components with inferior screw fixation, |0.5| mm (range, |0.04| to |4.3| mm) for the 12 components with flange-only ischial fixation, and |3.3| mm (range, |0.1| to |16.4| mm) for the 5 components without any ischial or pubic fixation. Translation of >1 mm was identified in 0, 2, and 4 of the components in these groups, respectively.

Sagittal Rotation of Hips with Pelvic Discontinuity

There was a large amount of sagittal rotation in the 5 hips that were re-revised for loosening (Fig. 3). Except for the aforementioned 5 hips, no other hip had rotated the 5° or more that would have been diagnostic of loosening. Of the 21 components utilized to treat pelvic discontinuity, the median absolute sagittal rotation at 2 years was |0.4°| (range, |0.1°| to |0.9°|) for the 4 components with inferior screw fixation, |0.6°| (range, |0.01°| to |8.7°|) for the 12 components with flange-only ischial fixation, and |9.1°| (range, |0.6°| to |11.7°|) for the 5 components without any ischial or pubic fixation (Fig. 4).

Radiographic Identification of Potentially Loose Implants

Other than the 5 components that were re-revised for loosening, only 1 component had migrated >3 mm proximally at the time of the latest follow-up. That hip remained asymptomatic and was not re-revised. In 1 other component, the ischial flange of the cup-cage construct fractured before the 3-year follow-up; this same acetabular component developed a complete continuous radiolucent line around it between 5 and 7 years of follow-up, suggesting the component was likely to be loose[31]. No other acetabular component developed a continuous radiolucent line.

Discussion

We used RSA to measure the migration of porous tantalum components used in revision THA to treat severe acetabular bone defects, and analyzed the results according to defect classification and whether inferior screw fixation was utilized. The proximal translation of the components at 2 years was compared with the threshold of >1 mm proximal translation within 2 years that has previously been identified as having a 90% positive predictive value for subsequent loosening[24]. In the present study, 7 of 55 acetabular components exceeded this threshold and, of these, 5 were re-revised for loosening. Although migration of the 2 unrevised components stabilized, both fulfilled the criteria for radiographic loosening, which no other unrevised component in the study fulfilled[31]. Furthermore, of the components that did not exceed the threshold for translation at 2 years, none have been subsequently re-revised for loosening to date.

The majority of the proximal translation and sagittal rotation occurred within the first 6 weeks. The amount of proximal translation at 2 years of components with inferior screw fixation was significantly lower than that of those without inferior screw fixation (p = 0.04). Inferior screw fixation was introduced after RSA migration data were analyzed for the initial 29 components. The 5 components that were re-revised had larger than expected sagittal rotation around the axis of the iliac screws, and it was suspected that this was because of poor inferior fixation. Considering that bones with these defects often do not have an intact rim, it is reasonable to believe that the initial stability of these components would have been improved by a 3-point fixation, which is difficult to achieve with screws in the ilium alone, or even with an inferior flange not screwed to the ischium. Therefore, we tried to improve the ischial and pubic fixation of the component by inserting ischial and/or pubic screws. The use of long intramedullary screws into the ischium and pubis could potentially provide better fixation by ensuring that the acetabular component is compressed to these segments of host bone.

Five (17%) of the 29 hips that were operated on prior to the introduction of inferior screw fixation subsequently underwent re-revision for loosening 1 to 8 years after the index revision. Two additional components of these first 29 were radiographically loose but had not undergone re-revision at the time of the latest follow-up. None of the 26 hips that were operated on after the introduction of inferior screw fixation had undergone re-revision, migrated >1 mm, or were considered to be radiographically loose at a mean of 4 years since the time of surgery (range, 2 to 6 years). The results of this study have directly impacted the treatment of hips with large acetabular defects, particularly those with pelvic discontinuity, at our institution. This study has shown the benefit of closely monitoring new implants with a sensitive technique to measure migration.

The strength of the present study is the accurate measurement of component migration. This study highlights that the prospective follow-up of patients and accurate analysis of early results can lead to a positive change in clinical practice. This study had several limitations. First, there were a relatively large number of exclusions; however, exclusions other than those relating to insufficient RSA marker visualization were unavoidable. Secondly, although only Paprosky III cases have been included, the degree of bone loss treated in each hip varied, as did the number of prior revisions. Finally, although hips with inferior screw fixation and those without were similar in that they all had severe Paprosky III bone defects, there may have been other variables that influenced the results. Future studies are needed to investigate the role of these variables in implant stability.

In conclusion, as measured with sensitive RSA, the majority of porous tantalum acetabular components used in a revision THA to treat severe acetabular defects had minimal early migration. These results predict good long-term survivorship of the components. The use of inferior screws where indicated further improved acetabular component fixation. ■

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CHAPTER SEVEN

Thesis Conclusions

7.1 Major Findings

7.1.1 – Scoping Review (Chapter Two)

A systematic search of the literature showed that there are insufficient studies to perform any review of studies that report EBRA migration of acetabular component migration after revision THR. The same search identified more studies reporting on RSA migration of acetabular cup migration, but the reported results were insufficient and inadequate for a systematic review or meta-analysis. Therefore, a scoping review was used to compare all RSA studies in the literature that have measured acetabular component migration following revision THR. This review identified a number of trends. First, no cohort had a mean or median proximal migration of <0.2mm at two years, this threshold having previously been considered "acceptable" according to Pijls et al[72]. Secondly, cemented reconstructions were identified as having a higher level of migration at two years than uncemented reconstructions. Thirdly, reconstruction of larger defects was associated with greater migration.

The manner in which the amount of migration was reported varied between studies with some studies reporting means and some reporting medians. Furthermore, the values of migration were reported as absolute and in other studies they were reported as signed values from negative to positive. Clearly, this made comparison across studies difficult. The scoping review made six recommendations for enhanced reporting in future studies, the most important of these being that migration should be reported according to the defect type treated and that individual migration curves for each hip should be presented. The scoping review also identified that, because of the poor and inconsistent methods of reporting migration across studies, it was not possible to perform a meta-analysis to examine migration for specific types of acetabular components. Furthermore, migration should be reported for individual cases to allow for better comparison across studies.

7.1.2 – Establishing early migration thresholds (Chapter Three)

A study of revision THR patients that underwent a re-revision procedure has determined that early proximal migration and sagittal rotation are excellent predictors of later acetabular component loosening. This was the first study to examine a cohort of patients that underwent uncemented revision THR, with known intraoperative outcomes at re-revision surgery. Despite the use of EBRA rather than RSA, EBRA exhibited acceptable precision the threshold of migration exceeding 1mm within 2 years to predict failure was able to be validated. There was a substantial difference in the migration pattern from time of implantation between acetabular components determined to be loose or not loose acetabular components at the time of re-revision surgery. This confirms that early stability of acetabular components is critical to long term outcomes, rather than primarily being due to late term complications. Despite Klerken et al[86] quantifying the relative risk of each millimetre of migration at two years for re-revision, the present work was the first to confirm the threshold using intraoperative outcomes and using a cohort of patients with more severe defects that were managed exclusively with uncemented reconstructions.

7.1.3 – Diagnostic performance of migration to detect aseptic loosening (Chapter Four)

Using the same cohort of patients as the previous chapter, it was possible to determine that a migration greater than 2.5mm or 2.0° rotation at any time point can accurately diagnose aseptic loosening. The presence of radiolucencies following uncemented revision THR were deemed as being very inaccurate predictors of loosening when used as the only criteria. This is most likely related to the complexities of reconstructions and the presence of pre-existing defects, which affect the radiographic projection of the implant bone interface, and subtle changes may be difficult to appreciate on different radiographs with different pelvic tilt and rotation. A comparison of EBRA measurements with manual measurements of acetabular component migration, found that although manual measurements can be used to determine the presence of acetabular component loosening, these measurements are less accurate, and require different thresholds for migration and furthermore have poorer positive and negative predictive values.

7.1.4 – Accuracy of EBRA-Cup measurements of acetabular component migration following revision THR (Chapter Five)

Despite results of prior studies that have compared EBRA measurements with RSA measurements, this thesis was the first to determine the agreement of these two measurement techniques for measuring migration of uncemented porous tantalum acetabular components used in the reconstruction of hips with severe, namely Paprosky II and III, acetabular defects. The accuracy of EBRA to measure acetabular component migration after revision THR was determined to be good, and a key finding was the agreement of categorisation of patients according to the thresholds established in Chapter 2. This study confirmed for the first time that EBRA has less accuracy when measuring migration of acetabular components in hips with pelvic discontinuity or additional metal work such as augments and/or ilio-ischial cages than in hips with no pelvic discontinuity or additional metalwork.

7.1.5 – Measuring migration of porous tantalum components used to reconstruct severe acetabular defects (Chapter Six)

Seven of 55 acetabular components were identified as having migrated more than 1 mm at two years, namely the previously identified threshold for later loosening, and, of these, five had been re-revised for loosening at the time of the latest follow-up. All cases that migrated in excess of the threshold were operated on during the first part of the study, prompting a change in the surgical technique aimed to improve acetabular component fixation. This consisted of enhancing the inferior fixation of the components with the addition of ischial and/or pubic screws. At 2 years, the absolute median proximal translation of components with enhanced inferior fixation was significantly lower, |0.3| mm (range, |0.1| to |0.9| mm), compared with |0.4| mm (range, |0.0| to |16.4| mm) for those without enhanced inferior fixation ($p = 0.04$).

7.2 – Limitations

With regards to the scoping review, the major limitation of this work was the absence of homogenous cohorts that could be used for a meta-analysis, and the differences in the manner in which the statistics were reported. This led to limited conclusions and an inability to make relevant comparisons between cohort studies. As future studies improve both design and reporting methodology, the ability to perform a full meta-analysis may be possible. Although all publications reported on the bone defects of the study cohort, only three of the 17 publications in the review attempted to correlate bone defect severity with early migration. A significant limitation was that 15 of the 17 publications in the review used a classification system to report bone defects which is subject to significant variability in interpretation and observer error and is not used to guide treatment. Therefore, it was very difficult to make meaningful comparisons between the different reconstruction techniques used.

With regards to the studies of predicative and diagnostic performance of acetabular component migration, one major limitation of this retrospective work was the use of a number of acetabular components that are no longer in use. Another limitation was the use of EBRA to measure migration, a technique which is affected by the quality of the x-rays, this being further exacerbated by the relatively long study period that included the use of hard copy radiographs that were subsequently digitised. Because the EBRA technique requires comparable pelvic tilt, a number of hips were excluded that may have otherwise been included had migration analysis been possible with RSA. However, due to the long follow-up nature of the study that spanned 35 years, it was not possible to use current components or to use RSA, which was not available for many patients at the time of index surgery. Given these restrictions EBRA was the most sensitive and accurate measurement technique to perform the studies.

With regards to the determination of the accuracy of EBRA-Cup measurements of acetabular components used at revision THR, the major limitation of this work was the relatively large number of radiographs, and therefore hips, that were excluded from analysis using EBRA. This may have potentially skewed the level of agreement between EBRA and RSA. The use of landmarks with EBRA may not have been consistent between patients because of the large variation in bone defects and of the acetabulum and the variable use of additional metalwork, thereby affecting the accuracy of the technique. The EBRA technique may be more subjective than RSA, and therefore replication of this study with operators of different experience may yield different results. Furthermore, the significant variation across the cohort in number of radiographs and duration of follow-up for each hip may have influenced the two-year EBRA-Cup results due the smoothing function within the software. Furthermore, the EBRA-Cup technique uses the horizontal line that may be labelled on the pubic symphysis or the ischial foramen as the reference segment for proximal translation, while assuming that the pelvis is in continuity and is a single reference segment. In this study RSA used the ilium as the reference for acetabular component migration.

With regards to the study of porous tantalum acetabular components used to reconstruct severe acetabular defects, the major limitation of this study was the relatively large number of exclusions and the variability of bone loss patterns among cases. Despite this, this study represented the largest series of severe acetabular defects to be followed with RSA.

7.3 Future Studies

7.3.1 - Improve EBRA using Tantalum beads

Although RSA is recognised as the most accurate in vivo method to measure migration, one of the limiting factors of RSA that affects both recruitment and follow-up is the need for specialised radiographs taken above a calibration cage, thereby potentially excluding patients that may move away from the institution or are unable to attend follow-up for various reasons. Potentially, the use of tantalum markers would improve consistency in identifying and labelling reference landmarks in EBRA and may improve the accuracy and precision of this technique. This would have the additional benefit of enabling the use of sensitive radiographic measurement in significantly more patients and in centres that do not undertake RSA.

While this technique would not be able to report on acetabular component migration in all planes of movement, which RSA does, the most reliable predictor of loosening is proximal migration, which can be measured using the modified EBRA technique.

7.3.2 - Analysis of pelvic segment migration in hips with pelvic discontinuity

In Chapter 5 it was identified that measuring acetabular component migration using EBRA in hips with pelvic discontinuity was less accurate than in hips without pelvic discontinuity. This might be explained by movement of the proximal bone segment, the ilium, relative to the distal bone segment, the ischium and pubis at the site of the discontinuity. In Chapter 6, acetabular components secured with distal screws into the ischium and/or pubis had lower amounts of migration when compared to those that had fixation with the flange of the ilio-ischial cage alone. Further studies are required to determine the amount of movement between the bone segments after fixation and whether there is movement between the acetabular component and the distal segment, the ischium and pubis.

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