Modularity of Metal-on-Metal Total Hip Arthroplasty: A Flawed Concept?

Mr. Kevin Ilo MD BSc FRCS

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School of Health Sciences

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Abstract

Modular implants have been utilised in total hip arthroplasty (THA) to replicate patient biomechanics. Metal debris and its effects are unwanted consequences. Attention has focused on modular junctions as reports of corrosion could be a source of further metal debris release. This PhD by Publication thesis presents four studies reporting analyses of retrieved modular-neck and metal-on-metal (MOM) implant and one systematic review performed recently on custom femoral stems; a better option than modular neck stems?

Study 1 reported on corrosion found on the backside of two different modular metal liners, each highlighting a different corrosion pattern, but both designs illustrate greater corrosion at the equator rather than the pole.

Study 2 reported on one design of a recalled modular metal liner, highlighting a pattern of corrosion that was as a result of anti-rotation tabs for the polyethylene liner used for the same acetabular component.

Study 3 reported on retrieval analysis of MOM implants from one manufacturer but with different modularity. There was a higher incidence of adverse local tissue reactions amongst modular implants, with low levels of bearing surface material loss but increase severity of corrosion at the neck-stem taper junction.

Study 4 reported on the effect of modularity on cobalt:chromium ratio. Implants with an additional modular junction had a significantly greater cobalt:chromium ratio.

Study 5 was a systematic review on custom femoral stems, highlighting promising implant survival and functional outcomes but a lack of direct comparative studies with standard implants and cost-effectiveness.

Although MOM and modularity have advantages, retrieval analysis shows modular neck junction susceptibility to corrosion. Mechanically assisted corrosion is likely the main contributor, but modular neck-stem junctions are susceptible to galvanic corrosion, crevice corrosion, mechanical stress, and design intolerances, making modular neck MOM implants a flawed concept. Other bearing surfaces have grown in popularity and custom-made femoral stems have been designed as a solution for modular-neck MOM implants.

Acknowledgements

I am profoundly grateful to my family, colleagues, supervisors, and mentors for their steadfast support and reassurance throughout the challenges of this journey. Special thanks to my co-authors: Harry Hothi, Robert Whittaker, Karim Aboelmagd, Prith Hallikeri, Habilan Naathan, Emma Derby, Asaad Asaad, Gordon Blunn, John Skinner, Alister Hart, Ben Van Duren, Mark Higgins, Iain McNamara and Toby Smith for their encouragement and assistance.

Their belief in me has been the bedrock of my resilience and perseverance. I owe a special debt of gratitude to my wife, Amy, whose patience and unwavering support have been my constant comfort. My son, Moses, has added a delightful dimension of chaos to my life, providing unexpected clarity amidst the busiest times.

Most importantly, I must acknowledge my parents, to whom I owe everything. Their sacrifices and unwavering belief in my potential have provided me with the foundation and determination to pursue my dreams. This achievement is as much theirs as it is mine.

Contents

Word Count… 14,670

List of Abbreviations

AL – aseptic loosening

ALTR – adverse local tissue reaction

ALVAL – aseptic lymphocyte dominated vasculitis associated lesion

AVN – avascular necrosis

BMHR – Birmingham mid head resection

CAD-CAM – computer aided design - computer aided manufacturing

CI – confidence interval

CINAHL – cumulative index for nursing and allied health literature

Co – cobalt

Coordinate measurement machines - CMM

CoCrMo – cobalt chromium molybdenum

Cr - chromium

CT – computer tomography

DDH – developmental dysplasia of the hip

EDX – energy dispersive Xray spectroscopy

GT – greater trochanter

HHS – Harris Hip Score

HA – hydroxyapatite

HO – heterotopic ossification

JBI – Joanna Briggs Institute score

KM – Kaplan-Meier

NJR – National Joint registry

MHRA – Medicines and Healthcare products Regulatory Agency

MOM – metal-on-metal

MOP – metal-on-polyethylene

MRI – magnetic resonance imaging

OA – osteoarthritis

PE - polyethylene

PMMA – polymethylmethacrylate

PROM – patient reported outcome measures

RA – rheumatoid arthritis

SEM – scanning electron microscopy

SUFE – slipped upper femoral epiphysis

THA – total hip arthroplasty

Ti – titanium

UHMWPE – ultra high molecular weight polyethylene

UK – United Kingdom

3D – three-dimension

Declarations

No material in this thesis has previously been submitted for a degree. Any joint work has been confirmed by co-authors to acknowledge my contribution.

Papers

Study 1: Corrosion of Metal Modular Cup Liners

Hothi H, Ilo K, Whittaker R, Eskelinen A, Skinner J, Hart A

Journal of Arthroplasty 2015.

The Journal of Arthroplasty is a respected journal in the field of orthopaedic surgery, specifically focusing on joint replacement. The latest impact factor of the Journal of Arthroplasty is 3.4 for the year 2023. Overall, the Journal of Arthroplasty is considered a high-quality journal with significant impact and recognition in the field of orthopaedic surgery and joint replacement research.

My involvement was in the assessment of the metal modular cup liners, collecting implant data, data analysis, preparing the draft and editing paper. The senior academic author is Prof A. Hart, and the signature declaration is R. Whittaker (co-author, researcher).

Study 2: Fretting and Corrosion Between a Metal Shell and Metal Liner May Explain the High Rate of Failure of R3 Modular Metal-on-Metal Hips

Ilo K, Derby E, Whittaker R, Blunn G, Skinner J, Hart A,

Journal of Arthroplasty 2017.

The Journal of Arthroplasty is a respected journal in the field of orthopaedic surgery, specifically focusing on joint replacement. The latest impact factor of the Journal of Arthroplasty is 3.4 for the year 2023. Overall, the Journal of Arthroplasty is considered a high-quality journal with significant impact and recognition in the field of orthopaedic surgery and joint replacement research.

My involvement was in the assessment of the metal modular cup liners, collecting implant data, data analysis, preparing the draft and editing the paper. The senior academic author is Prof A. Hart, and the signature declaration is R. Whittaker (co-author, researcher).

Study 3: Does Modularity of Metal-on-Metal Hip Implants Increase Cobalt:Chromium Ratio

Ilo K, Hothi H, Skinner J, Hart A

Hip International 2019.

The HIP International journal is a specialised publication focusing on hip-related medical research and is the official journal of the European Hip Society. The latest impact factor of HIP International is 1.8 as of 2023.

My involvement in this study was assessment of the implants, analysing blood metal ion levels, data analysis, preparing the draft and editing the paper. The senior academic author is Prof A. Hart, and the signature declaration is Dr H. Hothi (Honorary Assistant Professor).

Study 4: Metal-on-Metal total hip arthroplasty: does increasing modularity affect clinical outcome?

Ilo K, Hothi H, Skinner J, Hart A

Hip International 2020.

The HIP International journal is a specialised publication focusing on hip-related medical research and is the official journal of the European Hip Society. The latest impact factor of HIP International is 1.8 as of 2023.

My involvement in this study was assessment of the implants, analysing implant data, data analysis, preparing the draft and editing the paper. The senior academic author is Prof A. Hart, and the signature declaration is Dr H. Hothi (Honorary Assistant Professor).

Study 5: Outcomes of primary total hip arthroplasty using custom femoral stems in patients with secondary hip osteoarthritis: a systematic review

Ilo K, Hallikeri P, Naathan H, Van Duren B, Higgins M, McNamara I, Smith TO

Arthroplasty Today 2024

Arthroplasty Today is an open-access journal focusing on joint replacement of the hip and knee. The latest impact factor for Arthroplasty Today is 1.4 for the year 2023. Arthroplasty Today is a reputable journal within its field, providing high-quality, peer-reviewed research accessible to a wide audience due to its open-access format.

My involvement in this study was developing the research question, performing the review, analysis data and preparing the draft and editing the paper. The senior academic author is Prof T. Smith and the signature declaration is Mr. P Hallikeri (second author & Senior Orthopaedic Trainee),

LONDON’S GLOBAL UNIVERSITY

UCL

NHS
Royal National
Orthopaedic Hospital
NHS Trust

28th June 2024

To Whom It May Concern:

RE: Kevin Ilo

This is to confirm that Kevin was involved in the study design, data collection, analysis and manuscript writing of the two journal publications listed below. These studies have contributed to our understanding of the impact of modularity in metal-on-metal hip implants on their function in patients.

[1] Does Modularity of Metal-on-Metal Hip Implants Increase Cobalt: Chromium Ratio. **Ilo K, Hothi H, Skinner J, Hart A** - Hip International 2019

[2] Metal-on-Metal total hip arthroplasty: does increasing modularity affect clinical outcome? **Ilo K, Hothi H, Skinner J, Hart A** - Hip International 2020

Best wishes,

Harry Hothi, BEng, MSc, PhD

Implant Science Fellow at the Royal National Orthopaedic Hospital (RNOH)
Honorary Associate Professor at University College London (UCL)
Engineering Director of the London Implant Retrieval Centre (LIRC)

Robert Whittaker
2 Birch Walk
Bushey
Hertfordshire
WD23 1FW
1st July 2024

To Whom It May Concern:

RE: Kevin Ilo

I am writing to confirm that Kevin was involved and instrumental in the study design, data collection, analysis, and manuscript writing for the two journal publications listed below..

Corrosion of Metal Modular Cup Liners

Hothi H, Ilo K, Whittaker R, Eskelinen A, Skinner J, Hart A

Journal of Arthroplasty 2015.

Fretting and Corrosion Between a Metal Shell and Metal Liner May Explain the High Rate of Failure of R3 Modular Metal-on-Metal Hips

Ilo K, Derby E, Whittaker R, Blunn G, Skinner J, Hart A,

Journal of Arthroplasty 2017

Many thanks

Robert Whittaker BSc

Nottingham University Hospitals NHS
NHS Trust

City Hospital
Department of Trauma & Orthopaedic Surgery
Hucknall Road
Nottingham
NG5 1PB

2nd July 2024

To whom it may concern

Re: Kevin Ilo

I am writing to confirm that Kevin led the study design, data collection, analysis and manuscript writing for the study listed below

Outcomes of primary total hip arthroplasty using custom femoral stems in patients with secondary hip osteoarthritis: a systematic review

Ilo K, Hallikeri P, Naathan H, Van Duren B, Higgins M, McNamara I, Smith TO

Many thanks

Mr. Prith Hallikeri
MA(Cantab) MBBS FRCS

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Presentations

American Academy of Orthopaedic Surgeons, Las Vegas, USA (2015)

Corrosion of metal modular cup liners

Ilo K, Hothi H, Whittaker R, Berber R, Blunn G, Skinner J, Hart A

American Academy of Orthopaedic Surgeons, Las Vegas, USA (2015)

Metal-on-Metal Total Hip Arthroplasty: Does increasing modularity affect clinical outcome?

Ilo K, Hothi H, Whittaker R, Berber R, Blunn G, Skinner J, Hart A

Posters

American Academy of Orthopaedic Surgeons, Las Vegas, USA (2015)

Metal-on-Metal Total Hip Arthroplasty: Does increasing modularity affect clinical outcome?

Ilo K, Hothi H, Whittaker R, Berber R, Blunn G, Skinner J, Hart A

Orthopaedic Research Society, Las Vegas, USA (2015)

Modularity of Metal-on-Metal Hip Implants Increases Cobalt: Chromium Ratio (BEST OF ORS – HIP CATEGORY)

Ilo K, Aboelmagd K, Hothi H, Whittaker R, Blunn G, Skinner J, Hart A

American Academy of Orthopaedic Surgeons, Las Vegas, USA (2015)

Large diameter Metal-on-Metal Hip Arthroplasty: Modularity effects Blood Metal Ion Level Ratio

Ilo K, Asaad A, Hothi H, Whittaker R, Blunn G, Skinner J, Hart A

Chapter 1: Introduction to Thesis

1.1 Background

Total hip arthroplasty (THA), considered to be one of the most successful operative interventions, has gained popularity over the years, earning the title of “operation of the century”[1]. The most common indication worldwide is primary osteoarthritis (OA) of the hip which develops without any obvious predisposing factors, whereas secondary OA occurs due to an identifiable underlying cause or condition. THA (Figure 1.1) has been shown to be effective in improving quality of life and cost-effective in the management of OA[2, 3].

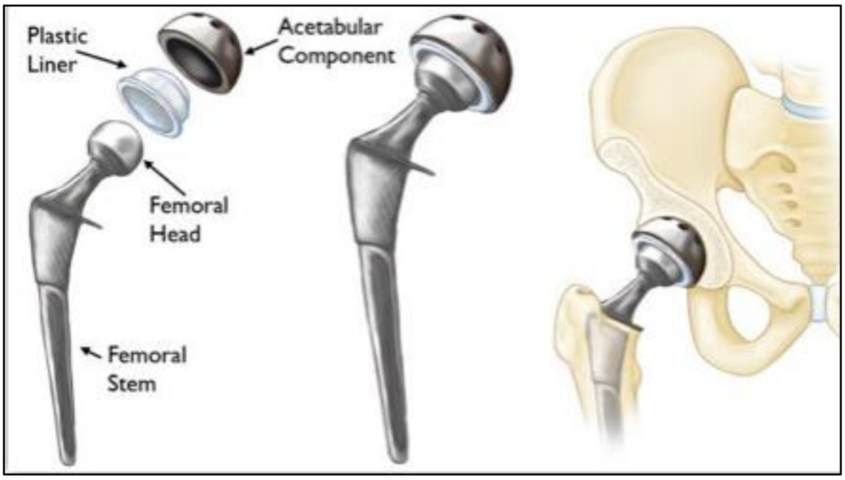

Figure 1.1: A total hip arthroplasty*

The modern THA was developed by Sir John Charnley in the 1960s. Due to its success, there is an increasing number of THAs. The UK National Joint Registry (NJR) reported that 89,716 THA procedures were performed in 2013; by 2022, this was 112,525 per year[4]. As the population ages and more THAs are performed, the burden of revision surgery will inevitably increase. Revision hip surgery is associated with increased costs to healthcare systems and significant risk to patients[5]. Accordingly, reducing failure and subsequent revision of THA is a priority for the present and future[6].

* Image taken from OrthoInfo http://orthoinfo.aaos.org

Failure of THA can be divided into patient, surgeon and implant factors. Despite the development of THA design, implant factors still contribute significantly to failure. In the early 2010s, modular-neck and metal-on-metal (MOM) designs came under scrutiny. This was highlighted by a number of implant recalls which had been attributed to metal debris concerns and higher-than-expected revision rates. Therefore, modular-neck and MOM THA implants required investigation to understand potential mechanisms of failure.

1.2 Thesis Objectives

Pre-clinical laboratory testing of modular-neck and MOM THA did not highlight any issues prior to being brought to the market for clinical use[7]. These implants became popular in the use of primary hip procedures[8, 9]. However, their clinical performance has underlined concerns. To understand the failure mechanisms for modular MOM THA, analysis of implants which have failed *in-vivo* was essential[10]. The specific objectives of this thesis are:

1) To evaluate corrosion of modular acetabular components.

2) To investigate the recall of a specific MOM modular acetabular design.

3) To compare the clinical outcomes of MOM hip implants from the same manufacturer and design but with differences in modularity.

4) To investigate whether blood metal ions are affected by modularity.

5) To review the results of custom femoral stems.

Chapter 2: The Evolution of Modular MOM Hip Arthroplasty

2.1 Development Of The Modular Acetabular Component

Sir John Charnley revolutionised the treatment for arthritis with the development of the cemented modern THA [11]. A monoblock acetabular component made of polyethylene (PE) was used. Fixation to bone was acquired by the utilisation of polymethylmethacrylate (PMMA) bone cement. Early implant designs failed due to loosening of the implant[12]. Initially this was thought to result from a reaction to the cement used to fix the implant, resulting in loosening. Therefore acetabular components which were fixed without the use of cement were developed and created[13]. These porous-coated acetabular components permitted biological fixation [14]. Modular cups also allowed the use of additional fixation, such as screws.

First-generation porous-coated acetabular cups achieved good biological fixation, but issues regarding liner dissociation from the metal shell and wear were common causes of failure[15-20]. Many first-generation modular acetabular cups had poor conformity between the liner and shell, suboptimal locking mechanisms and only a thin rim of ultra-high molecular weight polyethylene (UHMWPE) for security. Fracture and deformation of the UHMWPE at the liner-locking mechanism were associated with the dissociation of the modular components.

Second-generation modular acetabular cups retained the in-growth surface and brought in congruent contact between the liner and shell, giving the liner more support within the shell. There were ongoing concerns regarding osteolysis induced by PE wear debris that resulted in decreased bone stock and implant fixation[21-23]. Highly cross-linked UHMWPE was developed as it reduced wear of the liner[24, 25] but cross-linked UHMWPE reduced the mechanical properties of UHMWPE[26]. Simultaneously, there was a development towards larger head sizes to improve joint range of motion and reduce the risk of dislocation. The larger head size resulted in initial changes to the liner and greater thickness at the dome than at the rim. Unfortunately, if impingement occurred at the rim of the liner, which was not supported by metal, edge-loading and subsequent fractures occurred [27, 28].

Third-generation cup designs that eliminate cross-linked UHMWPE protruding above the metal rim and minimised sharp corners at the liner locking mechanism, were expected to reduce the risk of liner fracture in modular acetabular cups used with highly cross-linked UHMWPEs[29]. As cross-linked UHMWPE was more susceptible to fracture, the design modifications of the third-generation acetabular cups have reduced the risk of fracture while maintaining a large diameter femoral head and the wear properties of cross-linked UHMWPE[29]. Current modular acetabular components are suggested to offer more flexibility with bearing couple choices as different liners can be utilised[30].

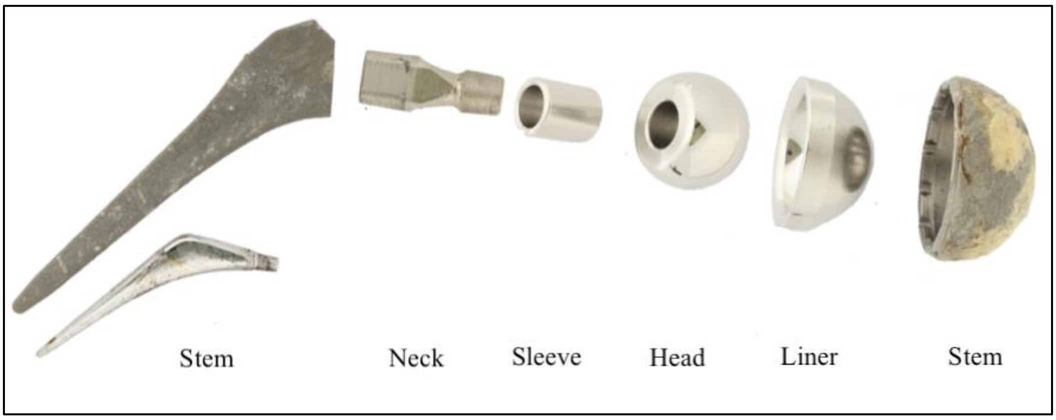

Figure 2.1: Modularity of a MOM THA.

2.2 Development of the Modular Femoral Component

Monoblock femoral components were initially designed for THA in the 1960s. These designs restricted the ability to alter offset, version, and leg length. Therefore, modular designs were introduced to solve these limitations. Modularity of femoral components can be classified as proximal, mid-stem and distal. The introduction and development of modular femoral components have played a crucial role in advancing hip replacement surgery, offering customisation and addressing many challenges inherent in earlier prosthesis designs.[31] Modularity in the femoral component allows separate elements of the prosthesis, such as the femoral head, neck and stem to be individually selected and assembled during surgery (Figure 2.1). This innovation has significantly impacted surgical flexibility, implant fit and the management of complications and revisions[32].

2.2.1 Proximal Modularity

There are many different design variations for proximal modular stem designs, which include modular heads, shoulders, necks, collars and sleeves[33]. Proximal modular designs can be a single taper junction between the head and neck. Development from monoblock femoral designs introduced the head/neck taper design. This modular junction is typically a Morse taper design that provides axial and rotational stability[34]. The Morse taper can have different angles and sizes, the smaller (12/14) taper is frequently used as it reduces impingement during the arc of motion. Modularity of the head facilitates the use of different materials for the stem and head. The modular head provides options for altering neck length, femoral head diameter and head-neck ratio. These options help to reduce impingement and increase stability[35, 36]. However this modular junction does not allow for independent adjustment of femoral offset from vertical height[37]. Modular proximal shoulders have varied designs and fixation mechanisms and can allow for variable body height and version[37].

Modular-neck designs (Figure 2.2) consist of an additional modular junction between the neck and stem, therefore there is a separate neck component. These designs allow for more customisation in terms of length and version of the neck. They have been increasingly used for primary THA as the stem can be inserted without the neck attached and is thought to better replicate an individual's biomechanics[32].

Metaphyseal modular designs contain their modular junction proximal to the femoral cut and therefore lies in the metaphysis of the femur. These implants have a proximal sleeve which was introduced to maximise implant fixation in the metaphysis. These systems allow intraoperative correction of hip biomechanics with the number of component options. The S-ROM implant is an example of this which has reported good long-term results[38].

Figure 2.2 Modular-neck THA.

2.2.2 Mid-Stem Modularity

Mid-stem modularity offers versatility in correction of sizing mismatch between proximal and distal femoral anatomy[37]. These implant designs have shown excellent results and are most commonly used in complex or revision hip surgery where there is inadequate proximal femur bone for fixation[33, 39, 40].

2.2.3 Distal Modularity

Distal modularity designs were developed to improve distal fixation and minimise thigh pain by improving load transfer. These designs have failed to gain popularity and have not shown to improve on other designs[41]. The development of modular components has many advantages. For example, with reduced inventory, there is cost-savings. Femoral components allow adjustments to 'fine tune' individual hip biomechanics and provide intraoperative flexibility. Revision of modular implants is theoretically easier as only the damaged/worn component needs exchanging. However there are concerns regarding dissociation[42], fatigue fractures[43] and corrosion[44] at modular junctions. Metal debris from corrosion at modular junctions makes it an additional source of metal ions which can cause local and systemic reactions[45].

2.3 Development of the MOM Bearing

The first THA was designed by Philip Wiles in 1938 and consisted of matched femoral heads and acetabular cups made from stainless steel. In the mid-1950s, a cobalt-chromium-molybdenum (CoCrMo) alloy, large diameter head MOM bearing was developed by McKee and Farrar in Norwich. In the decade following, comparable MOM implants were made. Peter Ring established the cementless MOM bearing, which showed good success rates[46]. However, these first-generation MOM implants produced high frictional torque due to their large heads, which caused cup loosening due to increased stress at the cup-bone interface[47]. Also, the release of metal wear debris led to adverse tissue reactions[48]. This resulted in an inevitable decline in their use.

In the 1960s, Sir John Charnley developed the ‘low friction arthroplasty’, which consisted of a thick PE cup and small metal head fixed with polymethyl-methacrylate cement. This design was further developed to include a UHMWPE cup, larger metal femoral heads and ceramic heads. However, due to PE wear, osteolysis was commonly seen and often resulted in implant failure[49]. Therefore, alternative bearing surfaces were considered to solve this issue. This led to the resurgence in MOM implants[50, 51].

The second generation of MOM implants was created by Webber. This was a high carbon cobalt chromium (CoCr) wrought forged alloy bearing[52]. The third generation of MOM implants were resurfacings. These were introduced by Derek McMinn in 1997, who developed the Birmingham Hip Resurfacing[53]. This was an attractive option as it was a bone-conserving prosthesis. It also had a larger head, which allowed for a better range of motion and better stability. This brought about the large head MOM modular THAs in the early 2000s. At the time, it was thought that MOM's superior wear properties and the large diameter head, which provided stability and a greater range of movement, were a good option for primary THA[54].

2.4 Increase in Popularity of Modular-Neck and MOM

2.4.1 MOM THA

MOM hip replacements experienced a resurgence in popularity during the late 1990s and early 2000s. This renewed interest was primarily due to their perceived benefits, including reduced wear compared to metal-on-polyethylene (MOP) bearings and the possibility of using larger femoral heads to reduce dislocation risk. These advantages were particularly appealing for younger, more active patients[55].

The peak usage of MOM hip replacements occurred in the mid to late 2000s. During this period, MOM designs were widely adopted in several countries, with significant usage noted in the United States, the UK, and Australia, among others[8, 56, 57]. The NJR data for England and Wales showed that between 2003 and 2011 there were 31,932 MOM resurfacings and 31,171 stemmed MOM THAs performed[57, 58].

2.4.2 Modular-neck THA

The concept of modularity in the femoral component of hip replacements gained popularity in the late 1980s and 1990s. The introduction of modular-neck designs offered the promise of enhanced customisation of hip biomechanics, including leg length, offset, and version, aiming to improve patient outcomes and implant longevity. Modular-neck designs saw widespread adoption in the 2000s, with their peak usage extending into the early 2010s. The flexibility offered by these designs made them popular in many countries, with up to 30,000 implanted worldwide by 2013, and significant usage in the United States, Australia and Europe[59].

2.5 Concerns of Modular-Neck and MOM THA

The first concerns about MOM hip replacements began to emerge in clinical practice as early as the 1970s. However it was not until the mid to late 2000s that the extent of the problem became more widely recognised. The initial concerns are summarised below.

2.5.1 Wear Particles

A MOM bearing has excellent wear properties[51]. The wear of MOM hip bearings has been measured as 1 mm^3/million cycle, much lower than the more widely used MOP bearings (30–100 mm^3/million cycles). There is an initial ‘run-in’ period of higher wear followed by lower, steady-state wear[60]. However, the volumetric wear and particle size of MOM bearing are less than those of MOP. The number of wear particles is 500 times greater for MOM bearings[61]. This results in a larger surface area of wear particles to release metal ions *in-vivo*[62]. The small particle size also allows for easier dissemination around the body leading to systemic effects in distant organs[45, 63, 64]. Metal ions have been reported in most organs of the body post-MOM THA[64-66].

2.5.2 Immune Response

When metal wears, particles can be engulfed by cells. Metal debris is reported to be cytotoxic and cause cell mutation [67, 68]. However, there are large studies from England, Wales and Finland that did not show an increased risk of cancer after a MOM THA[69, 70]. Nonetheless, metal wear debris causes macrophage activation and release of inflammatory cytokines to signal other inflammatory cells. These cytokines can increase osteoclastic activity resulting in osteolysis, as well as fibrosis and necrosis. Metal debris also activates the immune response resulting in a type IV delayed hypersensitivity reaction. Chronic inflammation can result in adverse local tissue reactions (ALTR), also known as an aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL) and pseudotumours[71]. Although ALTR can be asymptomatic, they can be very damaging to local tissue and bone, which can cause considerable symptoms, often resulting in revision of the MOM implant. It has been reported that patients under 40 and females are at increased risk of developing ALTR[71].

2.5.3 Trunnionosis

The modular junction between the head and neck has been reported to be an important additional source of metal ion release. It has been suggested that trunnionosis results from wear, corrosion and the subsequent release of metal ions[72-74]. Studies have reported that trunnionosis accounts for 3% of all THA revision procedures[48, 75]. There are several studies which have reported ALTR as a result of corrosion debris from trunnionosis[72, 76-79], stipulating that metal debris from modular junctions can have more clinical impact than metal debris from the bearing surface [80].

2.5.4 Modular-Neck Fractures

Early reports identified fractures in modular-neck implants resulting from design and application flaws that compromised their safety and reliability[81-87]. These fractures were primarily due to excessive mechanical stress, leading to fatigue fractures that necessitated urgent revision. Contributing factors included improper alignment or fitting of implant components, creating abnormal stress concentrations. Repeated loading could exacerbate material fatigue, leading to eventual failures[88]. Moreover, using different metals in the components could initiate corrosion, weakening the implant. More active and heavier patients may increase mechanical load accelerating this process[89]. Atwood et al.[90] reported fractures in modular titanium (Ti) alloy necks connected to Ti alloy stems, where fretting at the junction eroded the protective oxide layer, necessitating continuous repassivation. This reduced local oxygen levels, reducing local pH and enhanced corrosion, promoting crack formation[91]. In response, Ti alloy necks were replaced with CoCr necks, which have a greater modulus of elasticity and therefore stiffer. However Gilbert et al.[92] also noted cracks in these replacements, emphasising that crack propagation was influenced by corrosion rather than external stresses. These findings underscore the mechanical complications like fatigue, fracture, and loosening associated with modular-neck implants.

2.4.5 High Revision Rates

National Joint Registry data has demonstrated since the late 2000s that MOM hip implants have a significantly higher revision rate than other bearing surfaces[93]. Up to 17% of MOM hip implants have required revision within 10 years [4]. This resulted in recalls of several MOM implants. Resultantly, government authorities acted by releasing guidelines. In April 2010, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) released a medical device alert regarding the monitoring of patients with MOM hip implants[94]. Another medical device alert was released in 2012 and updated in 2017[95]. In 2011, the United States Food & Drug Administration released a mandate that required post-market monitoring of MOM implants[96]. In Canada, Health Canada released a communication to orthopaedic surgeons regarding MOM implants in May 2012[97]. In Australia, the Therapeutic Goods Administration of Australia published their safety information on MOM hip implants in September 2012; this was subsequently updated in July 2017[98].

Similarly for modular-neck components, a joint registry report from Australia showed a 12.5% revision rates for modular-neck THA at 15 years, double compared to conventional THA[99]. Failures due to stem fracture, aseptic loosening, corrosion, ALTR and osteolysis resulted in recalls of several modular-neck femoral stems[32].

2.6 Retrieval Analysis

Hip implant retrieval studies are vital for advancing understanding and improvement of orthopaedic implant technology[100]. These studies involve the detailed analysis of explanted hip implants that have been removed from patients due to failure or other clinical reasons. By examining these failed implants, researchers can gather crucial insights that significantly contribute to the field of orthopaedics. Retrieval studies provide valuable real-world data on how hip implants perform inside the human body. This can markedly differ from the conditions simulated during *in-vitro* testing. These studies reveal critical information on wear patterns, corrosion, and material degradation, helping healthcare providers and manufacturers understand how implants endure over time[101]. The degradation that implants experience due to the mechanical environment within the body, combined with biological reactions, can only be fully appreciated through such retrieval analyses.

Early reports of failure of MOM and modular-neck THA highlighted the need for a more systematic approach to understanding the issues associated with implant failure. While pre-market testing provides initial safety and efficacy data, real-world evidence from retrieved implants offers insights into how devices perform over time in diverse patient populations. Consequently, retrieval centres for failed implants emerged as a critical initiative, providing answers regarding failure mechanisms and *in-vivo* performance[101]. Earlier retrieval studies of hip implants provided insights into identifying causes of failure and improving implant design[101-105]. Similar studies were required for modular-neck and MOM designs.

2.7 What Were the Gaps in Research?

Prior to 2013, while there was growing awareness and concern over the failure rates of MOM and modular-neck THA, several gaps in knowledge existed regarding the precise mechanisms and factors contributing to these failures. The complexity of implant failure mechanisms, coupled with the variability in patient reactions, made it challenging to understand and address the issues fully.

For MOM implants, while it was known that wear particles were generated, the detailed mechanisms by-which these particles induced tissue reactions and the full range of particle sizes and types produced were not completely understood. Similarly, the specific wear mechanisms at the modular-neck junctions, including the roles of fretting and corrosion, were not fully understood. The biological responses around the hip joint and distant organs to the metal ions generated from both bearing surfaces and modular-neck junctions were an area of ongoing research. There was limited understanding of the threshold levels of metal ions in the body that would lead to adverse reactions, the systemic effects of elevated metal ion levels, and why some patients seemed more susceptible than others.

The influence of specific design features of MOM and modular-neck implants on failure rates was not fully mapped-out. This included aspects such as the optimal size and shape of components to minimise wear and the impact of surgical technique on implant longevity and performance.

Comprehensive, long-term data on the clinical outcomes of patients with these implants were lacking. While registries and clinical studies provided some information, more extensive data were needed to understand the full spectrum of complications and failure rates over time. There was also no consensus on the best practices for monitoring patients with MOM or modular-neck implants for early signs of failure. The development and validation of specific diagnostic criteria, imaging techniques, and biomarker thresholds for detecting adverse reactions were still in progress. The role of patient-specific factors (such as activity level, weight, and pre-existing conditions) in predisposing certain individuals to higher risks of implant failure and ALTR were not comprehensively understood. Finally, there was a need for further research to customise implant selection for individual patient profiles. Custom femoral stems have been developed to address abnormal proximal femoral anatomy when standard stems are not suitable. The results of these custom stems had not previously been assessed using a systematic review methodology. The following five studies present analyses performed to answer these uncertainties.

Chapter 3: Publication Abstracts

3.1 Study 1: Corrosion Of Metal Modular Cup Liners (Appendix 1)

Background

Numerous studies have highlighted corrosion issues at the modular head taper in THA but less is known about corrosion at the interface between the metal shell and liner of modular cups. This study aimed to investigate the severity and location of corrosion on the backside of metal modular cup liners, focusing on two designs: DePuy Pinnacle and Smith & Nephew R3. The primary objective was to determine if there were any differences in corrosion between these two designs.

Methods

This retrieval study analysed the first 67 CoCr alloy modular cup liners collected at our implant retrieval centre. These liners, from DePuy Pinnacle (n=35) and Smith & Nephew R3 (n=32), were coupled with Ti alloy shells and had MOM articulations. The inclusion criterion was that the metal cup liner had to be loose from the titanium (Ti) shell or could be separated without damaging the surfaces. Macroscopic and stereomicroscopic examinations were conducted independently by two observers using a microscope at up to *x40* magnification. Corrosion was scored using a scale from one (no corrosion) to four (severe corrosion), applied separately to the polar and equatorial regions of the liner. SEM (scanning electron microscopy) and EDX (energy dispersive x-ray spectroscopy) were employed to analyse the elemental composition of corrosion deposits and detailed surface characteristics.

Results

Visual inspection found evidence of corrosion in virtually all liners, with the engaging rim surface significantly more corroded than the polar regions ($p<0.001$). SEM analysis revealed considerable pitting in the vicinity of the black corrosion debris, which EDX confirmed as chromium (Cr) rich. The R3 liners exhibited significantly more corrosion than the Pinnacle liners ($p<0.001$). Corrosion scores were notably greater at the equator than the pole in both designs. One Pinnacle liner was graded as severely corroded, while 12 R3 liners had evidence of severe corrosion overall. The patterns of corrosion were consistent with the areas of engagement between the shell and liner, with the Pinnacle liners showing a uniform circumferential band of corrosion at the equator and the R3 liners displaying peaks and troughs corresponding to the modular cup shell design.

No significant associations were found between liner corrosion scores and head size (R3 only), Co/Cr ratio, or head taper corrosion for either design. Kruskal-Wallis tests indicated no significant differences in corrosion scores in relation to time to revision, patient age, Co levels, Cr levels, or Co/Cr ratios.

Conclusion

This study, the largest of its kind at the time, provides evidence of significant corrosion at the backside of modular cup liners, primarily at the equator, with design-dependent severity. The greater corrosion observed in the R3 liners may explain the higher failure rates of this design, ultimately leading to its market withdrawal. These findings suggest that fluid ingress and galvanic corrosion between dissimilar alloys contribute to the observed damage. Further research is needed to quantify material loss and understand the clinical impact of corrosion at this junction.

3.2 Study 2: Fretting And Corrosion Between A Metal Shell And Metal Liner May Explain The High Rate Of Failure Of R3 Modular Metal On Metal Hips (Appendix 2)

Background

The R3 acetabular system, particularly when used with its metal liner, has demonstrated higher revision rates compared to its ceramic and polyethylene counterparts. In June 2012, the MHRA issued an alert regarding the metal liner of the R3 acetabular system due to these higher revision rates. This study aimed to investigate the failure mechanisms of the metal liner in the R3 modular system to understand the reasons behind its higher-than-expected revision rate.

Methods

This retrospective study involved a detailed visual analysis of six retrieved R3 acetabular systems with metal liners. The implants, collected from different hospitals between July 2009 and July 2014 were visually assessed using macroscopic and microscopic techniques, SEM and EDX were performed to examine the nature and composition of corrosion products. Pre-revision imaging and blood metal ion levels were also collected.

Results

The visual analysis revealed corrosion on the backside of all metal liners. A distinct border of corrosion was observed, conforming to the anti-rotation tab insertions on the inner surface of the acetabular shell, which are designed for the PE liner. SEM indicated extensive pitting and a clear demarcation between corroded and non-corroded areas, while EDX confirmed the presence of Ti rich corrosion debris. The corrosion was primarily located circumferentially at the equator of the liners, suggesting a relationship with the design characteristics of the acetabular shell.

Clinical data indicated that five out of the six patients had elevated blood levels of cobalt (Co)and Cr ions prior to revision surgery. All pre-revision MRI scans showed adverse local tissue reactions ranging from fluid collections to soft tissue masses. The mean patient age was 63 years, and the implants were retrieved after an average of 47 months.

Conclusion

The high failure rate of the metal liner in the R3 acetabular system is likely attributed to corrosion on the backside of the liner, resulting from the geometry and design characteristics of the acetabular shell. The areas designed for the anti-rotation tabs of the polyethylene liner create intermittent contact points with the metal liner, promoting crevice corrosion. This finding is significant as it suggests that the R3 acetabular system's modular design, intended to enhance intraoperative flexibility and ease of revision surgery, may inadvertently contribute to its higher failure rate when used with a metal liner. Future designs of modular acetabular systems should consider these findings to prevent similar issues. Further research is required to quantify the extent of material loss due to corrosion and to evaluate the long-term clinical impact of this corrosion on implant performance and patient outcomes.

3.3 Study 3: Metal-On-Metal Total Hip Arthroplasty: Does Increasing Modularity Effect Clinical Outcome? (Appendix 3)

Background

Modularity of MOM implants has come under scrutiny due to concerns regarding additional sources of metal debris. This study was a retrieval analysis of implants from one manufacturer with the same MOM bearing surface. The difference between the implants was the presence or absence of modular junctions.

Methods

This study involved 31 retrieved implants from 31 patients who had received a Conserve Wright Medical MOM hip prosthesis. The 31 implants included 16 resurfacings and 15 implants with modular junctions (four conventional THAs and 11 modular-neck THAs). Implants were collected from a national retrieval centre, and patient demographics, blood metal ion levels, and imaging data were gathered. Visual assessments were conducted using macroscopic and microscopic techniques. SEM and EDX analyses were performed to examine the nature and composition of corrosion products.

Results

Pre-revision MRI scans showed evidence of ALTRs in 43% of resurfacing implants and 91% of modular implants. There was no significant difference in pre-revision blood metal ion levels or bearing surface wear between the resurfacings and modular implants. The neck-head tapers of the modular group exhibited low levels of material loss, while the neck-stem tapers showed increased severity of corrosion and material loss. This increased corrosion at the neck-stem junction may explain the higher incidence of ALTRs observed in the modular group.

Conclusion

Modular MOM hip implants are associated with a higher incidence of ALTRs, which might be attributed to increased metal debris production at modular junctions. While modularity offers potential benefits like optimised biomechanics, it also introduces risks, particularly at the neck-stem junction. This dual nature necessitates a careful evaluation of implant design and patient-specific factors in determining the suitability of modular hip implants.

3.4 Study 4: Does Modularity Of MOM Implants Increase Blood Cobalt:Chromium Ratio? (Appendix 4)

Background

This study investigated the impact of modularity on Co:Cr ratio in patients with MOM hip implants. Blood metal ion levels are commonly used for the surveillance of patients with MOM hip implants. Modular implants, which include additional junctions, have the potential to introduce more metal debris, potentially affecting the Co:Cr ratio in the blood.

Methods

This study involved 503 patients who received hip replacements from a single manufacturer (Smith & Nephew, Warwick, UK) with the same bearing surface design. The patient cohort included 54 individuals with THA, 35 with BMHR implants, and 414 with hip resurfacings. Blood samples were collected, and whole blood metal ion levels were measured. The primary focus was to analyse the Co:Cr ratios across different implant types to determine the impact of a modular junction on these levels. Statistical analysis was performed using the Mann-Whitney U-test with a significance level set at $p<0.05$.

Results

The results indicated a significant difference in Co:Cr ratios between the different implant types. The THA group exhibited the highest mean Co:Cr ratio of 2.3:1, which was significantly greater than the ratios observed in the hip resurfacing group (mean: 1.3:1; $p<0.05$) and the BMHR group (mean: 1.1:1; $p=0.11$). These findings suggest that the presence of an additional modular junction in the THA group could be contributing to the elevated Co:Cr ratio. Furthermore, revised implants displayed significantly higher Co and Cr levels compared to well-functioning implants, with revised THA implants showing a particularly higher Co:Cr ratio than revised resurfacing implants.

Conclusion

The study demonstrates that modularity in MOM hip implants, particularly in THA, is associated with a significantly elevated Co:Cr ratio. This increase is likely due to the additional metal debris generated from the modular stem-head junction. The study highlights the potential for using Co:Cr ratios as a marker to stratify implants at risk of taper failure. Future studies should also consider other factors influencing blood metal ion levels, including patient demographics, implant design variations, and different laboratory analysis methods.

3.5 Study 5: Custom Femoral Stems: A Needed Solution To Modularity (Appendix 5)

Background

This systematic review aims to evaluate the effectiveness and safety of custom femoral stems in primary THA for patients with secondary OA with abnormal hip anatomy. Custom cementless femoral stems, designed through advanced preoperative 3D imaging techniques, offer a promising solution for achieving better fit and stability, addressing the unique anatomical variations in these patients.

Methods

This systematic review adhered to the PRISMA guidelines and was registered with PROSPERO. Databases including Medline, Embase, Cochrane, and CINAHL were searched for studies published on primary THA utilising custom femoral stems. Inclusion criteria were studies on patients with secondary OA receiving custom stems, with outcomes including implant survival, revision rates, and functional scores.

Results

Out of 689 studies screened, 13 met the inclusion criteria, encompassing 806 patients and 951 custom THA procedures. The collective follow-up period averaged 11.6 years, with a mean patient age of 44.6 years. The mean reoperation and revision rates were 6.9% and 8.25%, respectively. Intraoperative fracture rates were reported at 3.23%, and the mean postoperative leg length discrepancy was 4.25 mm. Postoperative Harris Hip Scores (HHS) improved by an average of 40.32 points. Kaplan-Meier survival rates showed high stem survival with minimal revisions for aseptic loosening, demonstrating the effectiveness of custom femoral stems in achieving durable fixation and optimal patient outcomes.

Conclusion

Custom femoral stems in primary THA demonstrate promising results in terms of implant survival and functional outcomes for patients with complex hip anatomy due to secondary OA. However, the variability in study designs and methodologies, along with the lack of direct comparative studies with standard prostheses, highlights the need for further research. Future studies should focus on long-term outcomes, cost-effectiveness, and direct comparisons with off-the-shelf implants to provide more robust evidence and guide clinical practice.

Chapter 4: Discussion

Section 4.1: Study 1: Corrosion of Metal Modular Cup Liners

This study investigated the corrosion at the interface between metal shells and liners of modular cups, specifically examining DePuy Pinnacle and Smith and Nephew R3 designs retrieved from 67 patients. The study used visual analysis and detailed surface assessment methods, including SEM and EDX to determine the severity and location of corrosion on the backside of metal liners. The findings revealed that virtually all liners exhibited evidence of corrosion on their back surfaces, with the engaging rim surface being significantly more corroded than the polar regions. The corrosion was identified as Cr-rich debris through EDX analysis, and SEM revealed considerable pitting in areas with black debris. Notably, R3 liners were found to be significantly more corroded than Pinnacle liners. This could help explain the higher revision rates associated with the R3 design. The study concluded that corrosion occurred in all examined liners at the engagement point between the liner and shell, likely due to galvanic corrosion from the pairing of dissimilar alloys. This corrosion at the modular cup liner interface presents an additional source of metal ions, potentially contributing to implant failure.

This 2014 retrieval study focused on the corrosion of metal modular cup liners and stands as an important publication, marking one of the first and most extensive efforts to identify and understand the degradation mechanisms affecting modular metal liners. Prior to this study, there were only two published retrieval studies on modular metal liners, with eight and 10 implants in each study[106, 107]. By analysing the largest series (n=67) of retrieved modular cups at the time, the study offered insights into the prevalence and patterns of corrosion, showing corrosion in all liners at the point of engagement between the liner and shell. This research highlighted the specific regions within the modular cup liners that were most susceptible to corrosion, notably identifying the equator of the liner as a primary site. The findings underscored the influence of design on the severity of corrosion, with a marked difference observed between the liner models, particularly highlighting the R3 liners' susceptibility.

This detailed investigation revealed galvanic corrosion as a likely mechanism behind the degradation, attributed to the interaction between dissimilar alloys used in the implant.

Galvanic corrosion was identified as a significant contributor to the corrosion process, leading to material wear and the release of metallic debris. Such comprehensive methodological analysis had not been performed in other retrieval studies at the time. The study highlighted how specific design features, such as the circumferential surface depressions in the R3 shell, contributed to a reduced area of contact and, consequently, a higher susceptibility of corrosion. This design insight was pivotal and not reported previously.

The study's findings offered clinical implications. They urged a more cautious approach to implant selection, particularly concerning metal liners. The documented evidence of corrosion led to heightened vigilance in monitoring patients with these implants, emphasising the importance of regular follow-up for signs of metal wear and potential systemic exposure to metallic debris. Blood metal ion levels, specifically their ratios in patients with MOM hip implants, was an area of clinical interest. Elevated levels of blood Co and Cr ions are considered indicators of implant wear and potential failure[108]. There were established threshold levels for Co and Cr ions to aid clinical decision-making. For example, the UK MHRA suggested specific action levels (e.g., 7 ppb for Co or Cr) above which further investigation and possibly revision surgery might be considered[109]. The more corroded R3 liners in this study, had more than double median Co:Cr ratio when compared to less corroded Pinnacle liners. To the author’s knowledge, no previous study had reported a difference in Co:Cr ratio with modular metal implants. An elevated Co:Cr ratio might suggest more active corrosion processes, particularly at modular junctions, as an earlier study had shown that Co is generally released in greater quantities during corrosive wear compared to Cr [110], although that study focused on corrosion at the modular head neck junction. Finally, at the time, this study was the largest and most comprehensive study of retrieved modular metal liners. It spurred further investigations into metal liner corrosion mechanisms and blood metal ion level ratios as a possible marker for modular junction failure.

This study stands out due to its large number of implant retrievals and for its depth of analysis, shedding light on the degradation mechanisms of these implants. By employing a multifaceted analytical approach, including visual inspection, SEM and EDX, the study offered a detailed exploration of corrosion patterns and the composition of corrosion products. Furthermore, the study's design, which involved a direct comparison between two different implant designs, provided critical insights into the impact of design factors on the risk of corrosion and also an explanation for higher-than-expected revision rates. However, limitations were evident. Firstly, the study's retrospective nature, focusing solely on implants that were revised, introduces a potential selection bias. This bias may limit the generalisability of the findings to the broader population of implants in clinical use. Future investigations could benefit from incorporating a prospective dimension, tracking implants from the time of surgery to gain a more comprehensive understanding of failure incidence and progression across a wider array of devices. Secondly, the limited sample diversity, restricted to two specific implant designs from a single retrieval centre, further constrains the study's applicability. Expanding the research to include a broader variety of implant designs and samples from multiple centres, could enhance the findings' representativeness and relevance. Thirdly, the absence of a control group of implants, either known for minimal corrosion or retrieved for reasons other than failure, limits the ability to contextualise the severity of observed corrosion patterns. Fourthly, the subjective nature of visual inspection for corrosion assessment may be considered a limitation. Despite the standardisation efforts, visual inspection remains prone to observer variability. The adoption of digital image analysis tools could complement visual assessments, offering more objective and quantifiable criteria for evaluating corrosion. Finally, the study's focus on the physical and chemical characterisation of corrosion did not extend to directly correlating these findings with clinical outcomes. Incorporating clinical data would create a more comprehensive picture of the clinical implications of modular cup liner corrosion.

This study highlighted the importance of adopting a multi-dimensional analytical framework to corrosion of orthopaedic implants. The integration of visual assessments with advanced microscopic and spectroscopic techniques allowed for an in-depth exploration of corrosion. This layered approach highlights the need for comprehensive and interdisciplinary methodologies in implant analysis, particularly for studies aimed at investigating failed retrievals. By contrasting the corrosion severity and pattern of the DePuy Pinnacle and Smith and Nephew R3 designs, it established how specific design features can affect the susceptibility of implants to corrosion. Such comparative studies are invaluable, as they not only elucidate factors contributing to or mitigating corrosion risk, but also inform the design and development of future implants with enhanced safety and performance profiles.

From a clinical perspective, the insights garnered from this study had ramifications for the continued use and management of patients with modular metal liners. This heightened emphasis on implant selection and corrosion resistance of implant materials and designs. Additionally, the study stresses the importance of meticulous post-operative monitoring for patients with MOM implants, highlighting the potential systemic implications of metal ion release due to corrosion.

Section 4.2: Study 2: Fretting and Corrosion Between a Metal Shell and Metal Liner May Explain the High Rate of Failure of R3 Modular Metal-on-Metal Hips

This study aimed to investigate the reasons behind the high revision rates observed with the R3 acetabular cup when used with its metal liner. This interest was spurred by regulatory alerts issued regarding the system, which prompted its recall[109]. The study involved a detailed analysis of six retrieved R3 acetabular systems with metal liners, focusing on visual, microscopic and chemical assessments to identify signs of fretting and corrosion. We found evidence of corrosion on the backside of all the metal liners, characterised by distinct borders that matched the anti-rotation tab insertions on the acetabular shell designed for the PE liner. SEM and EDX analysis confirmed the presence of crevice corrosion and Ti-rich corrosion debris. These findings suggested that the design and geometry of the acetabular shell, intended for PE liners with anti-rotation tabs, might not be compatible with the metal liner, leading to areas of close contact that facilitate crevice and galvanic corrosion, due to the presence of dissimilar metals.

The R3 acetabular system was introduced in 2007 as a modular implant system designed to give surgeons options in terms of liners. By 2012, there were national registry data from UK and Australia demonstrating higher than expected revision rates with use of the metal liner[109]. At the time, there were very few reports regarding the performance of the R3 metal liner[111, 112]. In mid-2014 Dramis et al.[113] reported a 24% failure rate with the use of this component. This led to a need to investigate why the metal liner option with the R3 acetabular system was prone to failure in comparison to other liner options. My 2014 study revealed the potential cause of failure in the R3 metal liner system identifying fretting and corrosion as key factors in implant failure. This provided clinicians with vital insights for evaluating the risk of failure, informing decisions regarding the need for closer monitoring or the consideration of early intervention and revision surgery.

The study's findings have validates significant regulatory actions, including the recall of the R3 metal liner and the issuance of safety alerts by healthcare regulatory bodies[109]. These actions, strengthened by the evidence generated by this research, highlight the critical importance of rigorous post-market surveillance and the responsive regulatory mechanisms necessary to safeguard patient health in the face of emerging evidence of implant-related risks. From a broader perspective, the research contributed to the growing evidence regarding use and safety of MOM hip replacements within the orthopaedic community. By detailing the specific risks associated with the R3 system's metal liner option, the study provided information to guide implant selection. In addition to its clinical implications, this study highlighted a previously underexplored mechanism of failure affecting the R3 acetabular system's metal liners. The results highlighted the unintended consequences of using specific design intentions for one type of liner material with another. This emphasises the need for further research to explore the best design features and material combinations that reduce the risk of corrosion and improve implant survival.

This study highlighted specific complications associated with modular metal lines. Through detailed examination of corrosion at the interface between the metal shell and liner, it explored how specific design elements can exacerbate the risk of implant failure. By employing a combination of visual analysis, SEM, spectroscopy, blood metal ion levels and MRI findings, it provided a comprehensive characterisation of the corrosion process, correlating it with the unique design features of the R3 system. This methodological approach, focused on retrieved implants, presented direct evidence of *in-vivo* performance issues, offering valuable insights into the real-world implications of design and material selection in orthopaedic implants. However, the research has limitations. The relatively small sample size of retrieved implants may limit the generalisability of the findings, potentially obscuring the full spectrum of variability in implant performance and failure mechanisms. Future research could benefit from a broader collection of samples, possibly through multicentre studies, to offer a more comprehensive picture of these issues. Additionally, the absence of a control group meant that the findings regarding fretting and corrosion are not as conclusively linked to the specific design features of the R3 system as they could be. Future studies incorporating control groups, including implants with lower reported failure rates or different material compositions, could provide a clearer comparative analysis, strengthening the causal links between design choices, material compatibility and corrosion risk. The study's reliance on visual analysis, despite its standardisation, introduces subjectivity to the assessment of corrosion. This subjective component could influence the reproducibility of the findings and may benefit from augmentation with more objective, quantitative measures of corrosion. Digital imaging and analysis software could offer a more precise and quantifiable assessment of corrosion[114].

Furthermore, the study's focus on the physical evidence of corrosion did not extend to a direct examination of clinical outcomes. Incorporating clinical data into future research could provide a more holistic view of the implications of corrosion on implant performance and patient health, offering clearer guidance for clinical practice. Finally, while the research effectively highlights design-related factors contributing to corrosion, it does not fully explore other potential influences, such as patient activity levels, surgical techniques, or the dynamics of micromotion at the implant interface. Analyses considering these additional factors could offer a deeper understanding of how various elements interact to influence corrosion and implant failure, informing both implant design and surgical practice.

A critical lesson from this study was the impact of design and material compatibility on implant performance. The study detailed how specific design elements intended for PE liners inadvertently contributed to corrosion when used with metal liners. This linkage between design features, such as the anti-rotation tabs and the corrosion patterns observed, clearly illustrates how minor design considerations can have significant implications for implant integrity and patient safety. The findings serve as a reminder for implant designers and manufacturers about the importance of comprehensive design evaluation, particularly concerning how different materials interact within an implant system.

From a clinical perspective, the study's findings regarding the specific causes of failure in the R3 metal liner system have a direct bearing on clinical decision-making, informing surgeons about the potential risks associated with modular metal liners. Prior to this study, there were limited studies that had investigated the R3 acetabular system. This study was the first to identify a potential cause of increased failure rates[113, 115, 116]. In addition, the regulatory actions and safety alerts supported by this study's findings underscore the importance of post-market surveillance in orthopaedic implants. The recall of the R3 metal liner, reinforced by evidence of increased fretting and corrosion, illustrates research's vital role in safeguarding patients.

Section 4.3: Study 3: Metal-on-metal total hip arthroplasty: does increasing modularity affect clinical outcome

This study retrospectively analysed 31 retrieved MOM implants from a single manufacturer with the aim of determining whether the addition of modular junctions influenced clinical outcomes in patients. By comparing 16 resurfacing implants against 15 modular THA implants, which include conventional and modular-neck THAs, the study offered a perspective on the implications of modularity in hip prostheses. One of the study's pivotal findings was the significant difference in the incidence of ALTR between the two groups, with a notably higher prevalence observed among patients with modular implants. This correlation between modularity and an increased risk of ALTR highlights a critical area of concern, as these tissue reactions can lead to severe complications such as extensive soft tissue damage and the need for revision surgery. A key aspect of the study's findings pertains to the corrosion observed at the modular junctions, particularly the neck-stem junction, which exhibited a higher severity of corrosion and material loss compared to the neck-head tapers. The higher incidence of ALTR in the modular implant group, as revealed through pre-revision MRI scans, further corroborates the link between modular junction degradation and negative clinical outcomes.

At the time of this study and currently, there is no accurate method of determining material loss from the neck-stem taper junction as the unworn shape of the taper surfaces cannot be accurately measured. To estimate the material loss of the neck-stem taper, we used the Talyrond 365, taking a series of 14 vertical straightness profiles along the axis of the neck-stem taper surfaces. These traces were used to estimate the maximum linear deviation (equal to the maximum depth of material loss) on each surface. To the author's knowledge, this had not previously been reported to measure material loss from this modular junction. Straightness traces of the 11 male, neck-stem taper demonstrated surface damage with areas of material deposition and material loss with a maximum depth of 58.17 microns. The increased severity of corrosion and material loss at this modular junction might contribute to the observed disparities in clinical outcomes.

A critical aspect of the study was its focus on the stem-neck taper junctions of modular-neck THAs, which were found to exhibit more severe corrosion when compared to the head-neck taper junctions. This observation was particularly concerning, as nearly all investigated stem-neck taper junctions showed moderate to severe corrosion, underlining a potentially inherent risk in the design of dual-modular implants. This finding was significant, highlighting the susceptibility of these junctions to mechanically-assisted crevice corrosion, a process exacerbated by micromotion and the presence of gaps due to manufacturing tolerances, which can further facilitate corrosion through crevice formation and galvanic interactions between dissimilar metals. Altogether, this retrieval study showed that the material loss at this junction is greater than originally thought. This was not highlighted during pre-clinical testing. In this study, one modular-neck stem component was sectioned to visualise the stem trunnion. This showed severe damage, contradicting the advantages of leaving a well-fixed stem in place.

This study added to the existing knowledge that while the modularity in MOM hip prostheses offers surgical flexibility and potential for personalised biomechanical optimisation, it also poses significant risks. The presence of modular junctions increases the probability of corrosion, which can lead to the release of metal ions and particles. These degradation products are responsible for the development of ALTR and other systemic responses that can negatively affect patient health. In this study, 91% of the modular implants had MRI evidence of ALTR compared to 43% of the resurfacing implants. The modular implant group also showed a higher Co:Cr ratio. It is believed that Co is the more clinically relevant metal responsible for adverse tissue reactions, which might explain these results[117]. It also adds to the evidence that the Co:Cr ratio may be utilised as a tool to identify trunnionosis or failure of modular junctions. The quantitative analysis of material loss and the characterisation of corrosion at modular junctions presented in this study underscored the importance of material compatibility and meticulous design in the development of hip implants. Despite the absence of significant differences in wear rates between resurfacing and modular implants, the incidence of ALTR was markedly higher in the modular group. This correlation points to the critical impact of modular junctions on clinical outcomes, suggesting the benefits of modularity must be carefully weighed against the potential increase in corrosion and subsequent risk of ALTR.

The study emphasised a need for rigorous implant surveillance and the development of more sophisticated monitoring protocols for patients with MOM hip prostheses. Furthermore, the study's findings had broader implications for regulatory bodies, implant manufacturers, and the informed consent process. By providing empirical evidence of the increased risks associated with modular MOM implants, the research contributed to the dialogue on implant safety and efficacy, potentially influencing regulatory guidelines and prompting manufacturers to pursue innovations in implant design and material science. The methodological strengths of this study are underscored by its approach to data collection and analysis. The utilisation of retrieved implants as the basis for examination allows for a direct assessment of the implants' condition post-use, providing a tangible evidence base for evaluating the extent of wear and corrosion.

Despite these strengths, the study presented with limitations that could impact the interpretability and generalisability of its conclusions. The relatively small sample size poses a challenge to the statistical robustness of the findings, potentially limiting their applicability to the broader population of patients with MOM hip prostheses. To address these methodological weaknesses, future research could aim to expand the cohort of studied implants. Prospective cohort studies, monitoring patients from the time of implantation, could offer a more robust approach to assess the long-term impact of modularity on clinical outcomes, minimising selection biases. Furthermore, further research is required to investigate what factors contribute to the higher prevalence of ALTR in this population and whether patient factors increase susceptible. Finally, ALTR are variable and can range in severity, so classifying this could be useful[118].

The study's approach to estimating material loss at the neck-stem taper, while innovative, acknowledges the challenges in accurately determining this due to the complexities of the implant's geometry. Advances in imaging techniques and computational modelling could offer more precise methodologies for assessing wear patterns, particularly at complex junctions such as the neck-stem taper. Additionally, the reliance on visual scoring systems for evaluating corrosion and fretting introduces an element of subjectivity into the analysis. From a methodological standpoint, the study's reliance on retrieved implants for analysis is both a strength and a limitation. While this approach offers direct evidence of wear, corrosion, and failure mechanisms, providing invaluable insights into the *in-vivo* performance of these devices, it also highlights the challenges associated with retrospective studies, such as the potential for selection bias and the limited ability to draw definitive causal inferences.

The finding of increased corrosion susceptibility at modular junctions, particularly the neck-stem junction, is a pivotal, with broad implications for implant design and usage. It not only identifies a specific target for improvement but also underscores the critical need for advancements in material science to address these vulnerabilities. Clinically, this study has implications for the management of patients with MOM hip prostheses. The documented increase in ALTR among patients with modular implants confirms the strategic approach to patient monitoring, emphasising the importance of regular clinical evaluations and the potential for early intervention.

Section 4.4: Study 4: Does modularity of metal-on-metal hip implants increase cobalt: chromium ratio?

This study investigated the impact of modularity in MOM hip implants on Co:Cr ratio. This retrospective study analysed 503 patients with hip replacements by a single manufacturer and the same bearing surface, categorised into three groups: 54 with THAs, 35 with BMHRs, and 414 with hip resurfacings. The study's objective was to determine if the presence of a modular junction in these implants leads to a significant difference in Co and Cr levels and their ratio. Prior to this study, there were few studies that investigated the effect of modularity on Co:Cr ratio[119-122]. However, this study contained the largest number of patients at the time. The study influenced the understanding and surveillance of MOM hip implants. Central to the study's findings is the observation that modularity in MOM implants may contribute to an increased blood Co:Cr ratio. This finding is important, as it acknowledges the potential for identifying modular junction failure, thereby necessitating a more vigilant approach to implant surveillance. The study's emphasis on the importance of closely monitoring blood metal ion levels in patients with modular MOM implants is a direct consequence of these findings, highlighting the need for healthcare providers to adopt surveillance protocols to detect and address early potential complications. Furthermore, this study introduced the principle that the Co:Cr ratio was an important marker for evaluating the performance and wear of modular MOM hip implants. By establishing a potential link between modularity and elevated Co levels compared to Cr levels, this study paved the way for future research aimed at exploring the specific mechanisms through-which modular junctions contribute to increased metal wear and corrosion. Additionally, the study contributed to a re-evaluation of clinical guidelines and surveillance protocols for patients with MOM hip implants. The suggestion that the Co:Cr ratio could be used to risk stratify implants susceptible to taper failure introduced a new dimension to patient monitoring, advocating for an alteration in the reporting of clinical reference levels. The current threshold set by regulatory bodies, such as the MHRA, which stands at 7ppb for Co and Cr levels, may require revision to account for the unique challenges posed by modular implants.

A notable strength of the study is its sample size with 503 implants. This dataset not only provides assurances on statistical power but also offers a broad perspective on the variability of patient responses to different MOM hip implants, enhancing study validity. Furthermore, the study's methodological approach in comparing different types of hip implants manufactured by the same company isolates the factor of modularity. This comparison is instrumental in delineating the specific influence of modular components on metal ion release, providing a robust foundation for the study's conclusions pertaining to the impact of modularity. Central to the study's methodology is the utilisation of blood metal ion levels as a metric for assessing metal debris release from the implants. By focusing on the concentrations of blood Co and Cr ions, the study concentrates on a direct biomarker of implant wear and corrosion, offering an objective measure to gauge systemic exposure to metal ions.

Despite these methodological strengths, the study is not without its limitations. The retrospective design, while offering valuable insights from existing data, inherently limits the capacity to control confounding variables that might influence metal ion levels, such as patient activity, component position and excretion. This design choice also confines the research to the data available in medical records, potentially introducing selection bias. Future research could benefit from a prospective cohort study design, allowing for a more standardised data collection process and the ability to monitor metal ion levels longitudinally, thus offering a clearer inference between modularity and increased Co:Cr ratios. Moreover, the study's focus on metal ion levels, while crucial, does not extend to the direct correlation of these levels with specific clinical outcomes or symptoms, leaving uncertainty in understanding of the clinical significance of elevated Co:Cr ratios. Integrating comprehensive clinical assessments and patient follow-up data could offer a more holistic view of how increased metal ion release impacts on patient health and implant success over the long term. Additionally, the inclusion of both revised and unrevised implants within the study cohort, along with the variability in the duration of implantation, introduces another factor that could distort the interpretation. A more stratified analysis, considering the status of the implant (revised versus unrevised) and adjusting for the duration of implantation, might provide a clearer insight into the effects of modularity. Lastly, the potential variability in laboratory techniques for measuring blood metal ion levels across different sites could introduce measurement inconsistencies, affecting the comparability and accuracy of the ion level data. Greater standardisation in blood sample collection and analysis process, either by centralising laboratory assessments or ensuring uniform protocols across sites, would significantly enhance the reliability of the metal ion measurements.

Clinically, the study has implications for the monitoring and management of patients with MOM hip implants. The potential for modular implants to contribute to increased metal ion release, specifically Co, necessitates as an additional aspect to patient surveillance, advocating for more frequent monitoring of blood metal ion levels in patients with these types of implants and assessment of blood metal ion ratios rather than just individual values. This enhanced surveillance protocol could facilitate early detection of metal-related complications, enabling timely clinical interventions that may mitigate the adverse effects associated with increased metal debris exposure. The broader implications of this research extend to the design and regulation of MOM hip implants. The findings could influence regulatory standards and guidelines, promoting a more stringent evaluation of implant safety and efficacy, particularly concerning modularity and its impact on metal ion release.

Section 4.5: Study 5: Custom femoral stems: A needed solution to modularity

Modular neck implants were designed to better replicate patient biomechanics, but their high failure rates and additional metal debris concerns necessitated a better solution. In the context of my research, which critically examines outcomes and complications associated with modular MOM hip arthroplasty, the decision to include a systematic review on custom femoral stems was significantly influenced by my clinical experiences during my training year as a joint arthroplasty fellow. This pivotal year not only introduced me to the advanced technology behind custom femoral stems but also allowed me to gain hands-on experience with this patient-specific solutions. As an aspiring hip surgeon, I was intrigued by the potential of these custom-designed stems to optimize fixation, stability, and individual biomechanics without the need for additional modular junctions.

A primary motivation for focusing on custom femoral stems results from the complications associated with modular designs. Modular hip prostheses, particularly those featuring a modular neck, have historically been plagued by high failure rates due to mechanical and biochemical interactions at the modular junctions. Corrosion, wear and subsequent metal debris release lead to biological responses, resulting in systemic and localised adverse reactions. As detailed throughout the thesis, modular neck designs have shown susceptibility to fretting and crevice corrosion, which not only compromises implant integrity but also patient safety and implant longevity.

Custom femoral stems, designed through precise preoperative planning and tailored to the individual's unique anatomical requirements, present a promising alternative. By eliminating the need for additional junctions in the proximal part of the femur, custom stems reduce the risks associated with modularity, such as junctional corrosion and mechanical failure. This systematic review of custom femoral stems aimed to critically evaluate their clinical effectiveness and safety, assess their performance in terms of implant survival and functional outcomes, and compare these with the results from standard, off-the-shelf prosthetic designs.

This systematic review is integral to this thesis as it contributes directly to a broader understanding of how custom femoral stems can mitigate the identified risks of modular designs while potentially enhancing patient-specific outcomes. The review illuminates the potential benefits of customisation in surgical practice by examining a body of literature that focuses on the application of custom femoral stems, particularly in patients with unusual proximal femoral anatomy. Moreover, the review supports the thesis' overarching narrative that advancements in hip arthroplasty should not only focus on enhancing material properties and engineering designs, but also on adopting a more patient-centred approach in implant selection. Custom femoral stems represent a shift towards personalised orthopaedic solutions, offering significant implications for clinical outcomes by addressing the specific biomechanical and anatomical needs of each patient.

Custom femoral stems have emerged as a potential alternative, offering the ability to fine-tune and recreate individual biomechanics without an additional modular junction. Furthermore, custom stems can optimise metaphyseal fit, improving stability and fixation[123]. This systematic review provided a comprehensive evaluation of the effectiveness and safety of custom femoral stems in THA for patients with secondary OA due to abnormal hip anatomy. This review, adhering to PRISMA guidelines[124], systematically searched for studies published on primary THA utilising custom femoral stems. Inclusion criteria were studies including patients with secondary OA receiving custom stems, with outcomes including implant survival, revision rates, and functional scores. Data were extracted from eligible studies, with a focus on overall and cause-specific revision rates. Thirteen studies met the inclusion criteria including 806 patients and 951 THA procedures using custom femoral stems. The review's findings propose custom femoral stems as a viable and effective option for patients with complex hip anatomy due to secondary OA, citing their promising implant survival and functional outcomes. It advocates for further research to explore long-term outcomes and direct comparisons with standard prostheses, potentially guiding future clinical practice and the design of hip implants tailored to meet the unique anatomical requirements of this patient group. This research amalgamates data from various studies to critically evaluate the effectiveness and safety of employing custom femoral stems for patients challenged by secondary OA due to abnormal hip anatomy. This review not only bridges a gap in the existing literature but also highlights a shift toward a more individualised approach in orthopaedic care, particularly for those with congenital or developmental deformities that complicate primary THA procedures. The introduction of custom femoral stems, tailored to fit the unique anatomical nuances of each patient, emerges from this review as a promising innovation in the management of complex hip deformities. By synthesising outcomes related to implant survival, functional improvement post-surgery, and the incidence of revision surgeries and complications, the review supports enhancing patient care through customisation. This not only underscores the viability of custom femoral stems in achieving excellent patient outcomes, but also highlights the low incidence of complications associated with their use.

The review identifies the need for further studies, especially randomised controlled trials and longitudinal studies, to draw more definitive comparisons between custom and standard prostheses. This call for further research emphasises the necessity of substantiating the long-term efficacy and cost-effectiveness of custom femoral stems, ensuring that these innovative solutions can be confidently recommended in clinical practice. Furthermore, the review adheres to the PRISMA guidelines[124], ensuring a rigorous, transparent, and reproducible approach to systematic review reporting. This method enhances the reliability of the review's findings. Moreover, the positive outcomes associated with the use of custom femoral stems, as highlighted in this review, advocates for the adoption of personalised orthopaedic solutions, marking a departure from the traditional, one-size-fits-all approach to THA. This shift toward personalisation has the capability of enhancing surgical outcomes and patient satisfaction but also encourages innovation in preoperative planning, imaging techniques, and manufacturing processes, potentially making custom solutions more accessible and cost-effective.

The systematic review critically examines the utility and effectiveness of custom femoral stems in addressing the unique challenges presented by secondary OA, a condition often characterised by complex anatomical variations due to prior disease, developmental anomalies, or previous interventions. This review collates and analyses data across a spectrum of studies, including patients with various pathologies, to offer a comprehensive evaluation of the role that custom femoral stems play in optimising surgical outcomes for this challenging patient cohort. These patients tend to develop arthritis younger and there are concerns regarding durability, fixation and high expectations. This systematic review is notable for its strict adherence to established methodological standards, particularly the PRISMA guidelines[124]. The review employed a thorough literature search, using a well-defined and robust search strategy across multiple databases. This approach ensured that all relevant studies were examined, minimising the risk of overlooking critical data. Additionally, the review's methodological rigor is supported by a precise delineation of inclusion criteria and a systematic approach to study selection. As a result, the review presents a focused and relevant synthesis of evidence that directly addressed the research question.

Despite these methodological strengths, the review has limitations. The inherent heterogeneity among the included studies, with variations in design, patient demographics, and surgical techniques, introduces some study heterogeneity that may impede the direct comparability of outcomes. To address this, future studies could benefit from conducting subgroup or sensitivity analyses that allow for a more nuanced examination of data within more homogenised patient groups or surgical categories. Another notable omission is the analysis of cost-effectiveness, an increasingly important consideration in healthcare decision-making. The inclusion of economic evaluations or a dedicated cost-effectiveness analysis could significantly enhance the review's utility, providing insights into the financial implications of employing custom femoral stems versus standard options for both healthcare and societal costs. This dimension is particularly pertinent given the personalised nature of custom implants and the associated costs. Despite their clinical benefits, custom femoral stems face limitations primarily due to these higher costs and the detailed planning required, including the use of advanced imaging. Furthermore, the dependency on specific manufacturing processes tailored to individual patients can limit their broader application. The current lack of extensive cost-related data poses a challenge to fully understanding the economic impact of employing custom stems in primary THA. The investment in custom femoral stems should be weighed against the potential for long-term cost-effectiveness. The proposed premise here is that the decreased likelihood of revision surgeries, especially those stemming from complications such as leg length discrepancy, aseptic loosening, periprosthetic fracture, and dislocation, may compensate for the initial higher investment. Further longer-term clinical and cost-effective analyses are recommended to examine these hypotheses.

A significant gap in existing research is the lack of direct comparative studies between custom-made and standard femoral stems in complex THA cases. This limits our understanding of the relative benefits (or harms) of custom designs in these specialised scenarios. However, patient reported outcome measures (PROMs) were promising, showing significant improvements. This aspect is particularly vital and encouraging, considering that the patient population for these procedures is generally younger, with higher physical demands and expectations. The review highlights a potential need for personalised approaches in hip surgery. It stresses the importance of continuous innovation in preoperative imaging, computational modelling, and prosthetic manufacturing to improve the precision and effectiveness of custom implants. Additionally, it highlights the lack of long-term data on the performance and durability of custom femoral stems, indicating a need for rigorous research to compare custom and standard implants and to evaluate the cost-effectiveness of personalised implant solutions.

Clinically, the results of this systematic review have implications for surgical practice. This evidence-based endorsement of custom implants as a viable and often preferable option for patients with secondary OA and abnormal hip anatomy enhances surgical planning and decision-making processes. It may aid patient counselling, enabling practitioners to offer a better understanding of the benefits and potential risks associated with custom femoral stems. Furthermore, the positive outcomes associated with custom femoral stems highlighted in the review stimulate further technological advancements in the field. The demand for precise, patient-specific prosthetic solutions drives innovation in 3D imaging, digital fabrication techniques, and materials science, heralding a new era of custom hip implants that promise greater compatibility, durability and overall patient satisfaction.

For surgeons navigating the intricacies of complex primary THA, the decision to opt for a custom femoral stem is a pivotal one. This choice necessitates an in-depth comprehension of the patient's unique anatomical structure, an awareness of the constraints posed by standard implants, and a keen insight into the distinct advantages and potential obstacles associated with custom-designed solutions. Surgeons confronted with the challenges of performing THA on patients with complex hip anatomies now have a substantial option to consider in custom femoral stems. These stems, meticulously designed to conform to the individual's specific anatomical requirements, have the potential to reduce the incidence of complications markedly. Furthermore, they may substantially lower the likelihood of needing revision surgeries, thereby enhancing the overall long-term success of the procedure[125]. This tailored approach not only aligns with the surgical objectives but also aligns with the evolving standards of patient-centred care in orthopaedics, emphasising the importance of personalised treatment plans for optimal patient outcomes.

Chapter 5: Conclusions

This thesis concludes my research that began in 2008 focusing on MOM hip implant retrievals[126-130]. My initial research explored retrieved hip resurfacings and bearing surface wear, a topical subject when MOM hip resurfacings were widely implanted, and initial concerns about MOM surfaced. This research laid the groundwork for the comprehensive retrieval analyses presented in this thesis.

Currently, metal debris from MOM hip replacements remains and will always be a significant concern in orthopaedics[45, 80, 131, 132]. Microscopic metal particles, released due to wear and corrosion at the bearing surfaces and modular junctions of implants, can cause various local and systemic health issues. Understanding these complications is critical for managing patient outcomes and guiding the future use of metal implants. Notably, the neck-stem junction of modular-neck implants shows a higher susceptibility to corrosion than the neck-head junction. The design and geometry of these junctions, while facilitating ease of assembly and disengagement, fail to mitigate motion and subsequent corrosion effectively[133].

Modular junctions in hip implants, especially the neck-stem junction, is particularly susceptible to corrosion and wear. Mechanically-assisted crevice corrosion exacerbates the release of metal ions and particles, contributing to local tissue damage and implant failure[133]. The complexity of these junctions often leads to a higher incidence of corrosion-related complications, emphasising the need for better materials and designs to mitigate these issues.

It is now well-known that systemic dissemination of metal ions from hip implants poses several health risks. Elevated levels of Co and Cr ions in the bloodstream can have various systemic effects. Cardiovascular complications, including cardiotoxicity, arrhythmias, and cardiomyopathy, are particularly concerning with elevated Co levels[134, 135]. Neurological effects are also associated with high systemic metal ion levels. Patients may experience cognitive decline, headaches, and sensory disturbances, which can affect their daily functioning and quality of life[136-138]. These neurological symptoms are particularly troubling as they can be progressive and challenging to treat. Another significant systemic effect is thyroid dysfunction[139]. Metal ions can alter thyroid function, leading to conditions such as hypothyroidism[136]. This can have widespread effects on the body’s metabolism, energy levels, and overall health. Hypersensitivity or allergic reactions to metal ions are another systemic issue[140, 141]. Some patients may develop dermatitis, rashes, and other allergic responses, which can be severe. Renal impairment is also a concern due to the kidneys' role in filtering metal ions from the blood. Prolonged exposure to high levels of metal ions can lead to renal dysfunction, which can complicate the patient's overall health management.

The potential carcinogenic effects of long-term exposure to elevated metal ion levels are an ongoing concern[142, 143]. While the evidence is still inconclusive, some studies suggest an increased risk of cancer, necessitating further research to understand the long-term risks associated with MOM implants. Elevated metal ion levels can also impact haematological health. Changes in blood cell counts and haemoglobin levels can lead to conditions such as anaemia and other blood disorders, further complicating the patient's health status.

It is still challenging to accurately determine the volume of metal debris and wear from modular-neck-stem junctions and modular metal liners in hip replacements[144]. These difficulties arise from the complexity of implant design, the limitations of current measurement techniques, and the inherent variability in wear patterns. Addressing these challenges is essential for improving measurement accuracy and developing more reliable and durable hip implants. One of the primary challenges stems from the shape of the modular junction in hip implants. The dual-taper design of modular neck-stem junctions and the interfaces between metal liners and acetabular shells involve intricate shapes that are difficult to assess using standard measurement tools. These components have precise contours and varying angles that require advanced measurement techniques to capture the complete wear profile accurately. Furthermore, many wear and corrosion issues occur on surfaces that are not easily accessible or visible, such as the internal taper surfaces of modular components. Inspecting and measuring these hidden areas often requires disassembling the implant, which can alter the wear patterns and compromise the accuracy of the measurements. The limitations of current measurement techniques further complicate the assessment of wear and material loss. The gravimetric approach, measures the weight of components before and after use to estimate material loss[145]. However, this method also faces challenges. Accurate initial weight measurements are crucial for the gravimetric method to be effective, and any errors in the initial weighing can lead to incorrect estimates of material loss. Additionally, the material loss from implants may be only a few milligrams, making it difficult to detect such small changes accurately. The gravimetric method provides a total value for material loss but lacks information about the distribution of damage or the specific contact conditions that led to wear, which limits the ability to understand wear mechanisms fully[146, 147]. Coordinate measurement machines (CMMs) offer high precision in measuring material loss but present their own set of challenges when applied to modular-neck-stem junctions and metal liners. CMMs use a spherical ruby touch-probe stylus to measure surfaces, but the size of the probe and its resolution can limit the ability to capture fine details of the worn surfaces, particularly in complex geometries[148]. The unique design of modular junctions requires a computational approach to reverse engineer the as-manufactured geometry, a process that can be complex and time-consuming. Inaccuracies in the reverse engineering process can also affect measurement results.

Joint registry data has shown a significant decrease in the use of MOM bearing surfaces in THA[4]. Modular-neck implants have also seen a decline in their use due to higher rates of failure and issues regarding ALTR. Recent studies have identified factors contributing to the failure of modular-neck junctions, such as male sex, longer lever arm, high BMI, young age, longer time since implantation, and an active lifestyle[133]. However, there are still reports of good survivorship and clinical outcomes at long-term follow-up[149-154]. Further research is needed to understand why there are satisfactory results with MOM and modular-neck components, focusing on surgical technique, patient factors, and implant factors. Despite well-documented complications associated with MOM hip implants, MOM resurfacings continue to be utilised in specific patient populations due to several compelling advantages. These include the preservation of more femoral bone compared to traditional THA, larger femoral heads for greater stability and reduced risk of dislocation, and a more natural distribution of biomechanical forces across the hip joint[155, 156]. For younger, more active individuals, MOM resurfacings can offer a durable solution capable of withstanding higher demands[157]. The success of MOM resurfacings largely depends on careful patient selection and precise surgical technique. Patients who are most likely to benefit from MOM resurfacing are typically young, active, and have good bone quality. Surgeons specialising in MOM resurfacing have developed refined techniques to minimise the risk of complications, including accurate positioning of the implant components and optimising the surgical approach to preserve as much bone as possible. Experienced surgeons are able to achieve better outcomes with this procedure, which was likely a factor in the initially high failure rate of MOM hip resurfacings[158].

Future directions

One of the primary benefits of retrieval studies is the identification of specific mechanisms that lead to implant failure. This includes understanding the types of wear, the locations of wear, and the role of corrosion. By ‘pin-pointing’ these failure mechanisms, more durable implants can be developed. For example, findings from retrieval studies can lead to the creation of new alloys, coatings, and design modifications that significantly enhance implant longevity[101]. Retrieval studies offer essential feedback to surgeons about how their techniques might influence implant performance. For example, improper alignment or fixation can lead to early implant failure[129, 159]. Understanding these factors enables surgeons to refine their techniques, thereby improving patient outcomes and reducing the incidence of implant failures. The insights gained from retrieval studies also contribute to the development of industry standards and clinical guidelines. Regulatory bodies and professional organisations use retrieval data to establish best practices for implant design, testing, and clinical use[160]. These guidelines help ensure that new implants are safe, effective, and meet the highest quality standards. Moreover, retrieval studies are crucial for evaluating implant technologies. Innovations such as modular designs or novel bearing surfaces can be assessed in real-world conditions through these studies. This feedback is critical for validating the performance and safety of innovative implants before they are widely adopted in clinical practice[161]. Ensuring patient safety is a critical aspect of retrieval studies. By identifying and addressing potential problems with implants, these studies help regulatory agencies, make informed decisions regarding the approval of new implants and the issuance of recalls or safety warnings when necessary[100, 101, 161]. Altogether, the understanding of why implants fail can lead to the development of more durable implants, ultimately reducing the need for revision surgeries. This not only improves the quality of life for patients but also lowers healthcare costs associated with treating failed implants[5].

The use of MOM bearing surfaces and modular-neck implants is becoming increasingly rare and unlikely to make a resurgence in the future. In the realm of bearing surfaces, ceramics have revolutionised the field by offering superior wear rates and eliminating the need for monitoring blood metal ion levels[162, 163]. Ceramic-on-ceramic and ceramic-on-polyethylene bearing surfaces have demonstrated exceptional performance, as evidenced by extensive studies and joint registry data[164-166]. The success and low complications of ceramic bearing surfaces makes it highly improbable that MOM bearings will ever regain popularity again, even though

MOM resurfacing has shown good functionality and high survivorship in specific patient groups. There are also emerging developments in ceramic resurfacing technologies, highlighting the continuous innovation in this area[167, 168].

Similarly, the likelihood of modular-neck implants making a comeback is low. The advent of monoblock designs, particularly custom-made femoral stems, addresses the issues associated with the modular-neck junction. These custom femoral components are tailored to individual patients, potentially enhancing biomechanics and longevity. Future research should focus on the material science aspects of implant design, investigating new alloys and surface treatments that reduce metal ion release while optimising biomechanical compatibility and durability. Additionally, economic evaluations are crucial to determine the cost-effectiveness of custom femoral stems, ensuring that the advantages of personalised implants are both accessible and justifiable within the broader healthcare system. Overall, the advancements in bearing surfaces and custom femoral stem designs signify a significant shift away from the flawed concept of MOM modular-neck implants, paving the way for more effective and patient-specific orthopaedic solutions.

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Appendix

Appendix 1: Corrosion of Modular Cup Liners

Hothi HS, Ilo K, Whittaker RK, Eskelinen A, Skinner JA, Hart AJ. *Corrosion of Metal Modular Cup Liners*. J Arthroplasty. 2015 Sep;30(9):1652-6. doi: 10.1016/j.arth.2015.03.022. Epub 2015 Mar 31. PMID: 25890504.

Abstract

Numerous studies have reported on corrosion at the modular head taper, however less is known about the inter- face between the metal shell and liner of modular cups. This study examined the backside of a series of metal modular cup liners of two designs (DePuy Pinnacle and Smith & Nephew R3), retrieved from 67 patients. Visual inspection found evidence of corrosion in virtually all liners, with the engaging rim surface significantly more corroded than the polar regions (P b0.001). EDX confirmed that black surface deposits were chromium rich corrosion debris, while SEM analysis revealed considerable pitting in the vicinity of the black debris. The R3 liners were significantly more corroded that the Pinnacles (P b0.001); this may help to explain the higher revision rates of this design.

Introduction

Modern total hip replacements (THRs) with metal-on-metal (MOM) bearing surfaces have consisted of implants with varying degrees of modularity, offering the surgeon greater flexibility during surgery. For example, the use of modular neck components allows for patient-specific adjustments to be made to features such as leg length and horizontal or vertical femoral offsets [1]. Approximately 50% of all stemmed MOM hips implanted in the UK have involved a modular acetabular cup, usually consisting of a titanium outer shell and a cobalt-chromium articulating liner [2]. Cup modularity is advantageous as it enables optimal component positioning to be achieved and also allows for a well-fixed shell to be retained during revision surgery [3,4].

Whilst the clinical advantages of increased modularity are clear, recent studies have reported evidence of considerable corrosion at component junctions, in particular in that of the femoral head taper [5–7]. Corrosion has been shown to be correlated with material loss at this taper surface [8] and the associated metal ion release is reported to result in local tissue reactions [9]. However the extent of corrosion damage at the interface between the liner and shell of metal modular cups and the clinical significance of this are currently less clear. Higgs et al. [4] reported evidence of scratching and discolouration at rim of the backside of the CoCr liner in a series of 18 cups; considerable pitting and black corrosive debris were also observed at the rim by Gascoyne et al. [10] in approximately 25% of their series of retrievals.

The aim of this study was: (1) to determine, using visual analysis and detailed surface assessment methods, the severity and location of corrosion on the backside of metal liners in a consecutive series of retrieved hips with two different cup designs: DePuy Pinnacle and Smith & Nephew R3 and (2) determine if there were any differences in corrosion between the two designs.

Methods

This was a retrieval study of the first 67 cobalt-chromium (CoCr) alloy modular cup liners collected at our implant retrieval centre that met our inclusion criteria. The liners were from two different manufacturers and all had been coupled with titanium (Ti) alloy shells. All of the hips had a metal-on-metal articulation and we required that the metal cup liner was loose from the titanium shell (or could be separated with- out damaging the surfaces) so that its backside could be assessed. The retrieved hips consisted of the DePuy Pinnacle cup (n = 35) and the Smith & Nephew R3 cup (n = 32).

The Pinnacles were retrieved from 17 male and 18 female patients with a median age of 61 years (37–77) at primary surgery and a median time to revision of 59 months (10–102). The median head size was 36 mm (36–40) and the median pre-revision whole blood cobalt and chromium levels were 6.22 ppb (0.6–130) and 4.65 ppb (0.6–42.4) respectively. The median Co/Cr ratio was 1.32 (0.27–5.21). The reason for revision for these implants, as defined by the revising surgeon, was unexplained pain (n = 33) and infection (n = 2).

The R3s were retrieved from 13 male and 19 female patients with a median age of 63 years (47–72) at primary surgery and a median time to revision of 56 months (28–72). The median head size was 44 mm (38–50) and the median pre-revision whole blood cobalt and chromium levels were 13.7 ppb (1.5–116) and 4.8 ppb (1.5–45.5) respectively. The median Co/Cr ratio was 2.74 (0.64–6.83). The reason for revision for these implants, as defined by the revision surgeon, was unexplained pain (n = 31) and femoral loosening (n = 1).

Table 1 summarises the key patient and implant data. The study design of the current work is summarised in **Figure 1**.

	Pinnacle cups	R3 cups	P value	Significant Difference
Gender (male: female)	17:18)	13:19	0.625	No
Age at primary surgery	61 (35-77)	63 (47-72)	0.061	No
Time to revision	59 (10-102)	56 (28-72)	0.362	No
Head size	26 (36-40)	44 (38-50)	<0.001	Yes
Whole blood Co (ppb)	6.22 (0.6-130)	13.7 (1.5-116)	0.003	Yes
Whole blood Cr (ppb)	4.65 (0.6-42.4)	4.8 (1.5-45.5)	0.439	No
Co/Cr ratio	1.32 (0.27-5.21)	2.74 (0.64-6.83)	0.001	Yes

Table 1: Implant and patient data showing median (range) values with p-values indicating the significance of differences between the parameters.

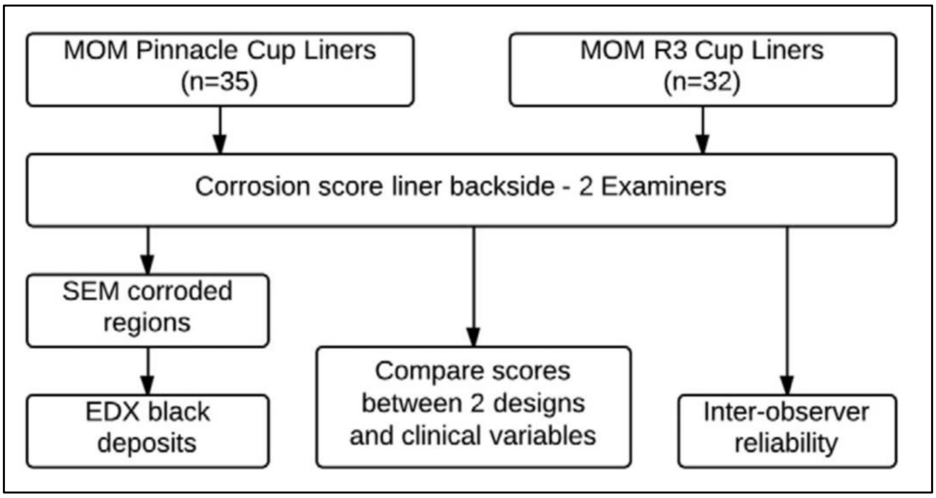

Figure 1: Summary of study design

Visual Assessment of Corrosion

Macroscopic and stereomicroscopic examinations of the backside of all 67 metal liners were performed independently by two experienced observers (A and B) to assess the presence and severity of surface corrosion. A scoring scale of 1 (no corrosion) to 4 (severe corrosion), as defined by Goldberg et al. [11], was used to quantify corrosion, which was identified as discoloured or dull regions or areas with evidence of pitting, etching or black debris. This scoring method was originally developed for the inspection of femoral head tapers however the grading criteria are applicable for the cup liner backside. Scores were assigned separately to the polar and equatorial regions of the liner, Fig. 2, and overall scores were determined following assessment of the surface as a whole. A Leica M50 microscope [Leica Microsystems, Germany] at up to ×40 magnification was used to assist in examinations.

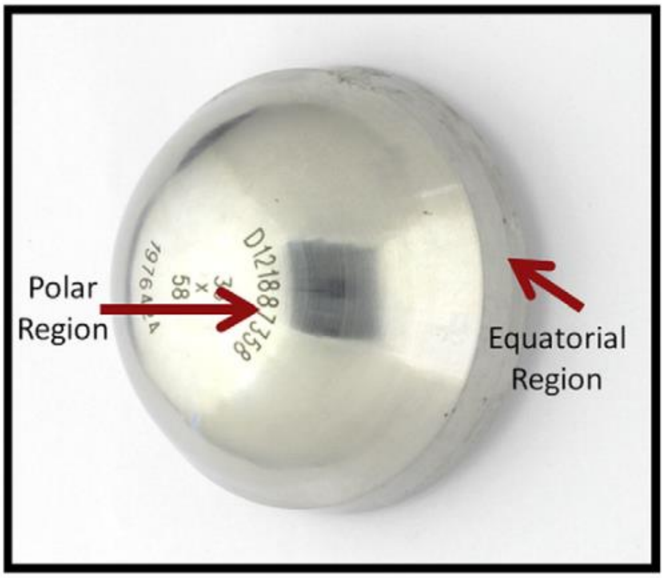

Figure 2: Polar and equatorial/rim regions of the backside of the cup liner

The severity of corrosion at the taper surfaces of the corresponding femoral heads was also determined by a single examiner using the method defined by Goldberg et al. [11].

Scanning Electron Microscopy

The liners were viewed in a JEOL JSM (Tokyo, Japan) scanning electron microscope (SEM) using secondary electron detection at an accelerating voltage of 20 KV. This was used to further examine corroded regions identified macroscopically and microscopically and compare with visually pristine areas on the liners. The elemental composition of corrosion deposits visually identified as black debris was then analysed using energy-dispersive X-ray spectroscopy (EDX) within the SEM system.

Statistical Analysis

Cohen's weighted Kappa statistic (κ) was used to assess the inter-observer reproducibility of the corrosion scores as determined by the two independent examiners, where $\kappa \leq 0$ = poor, 0.01–0.20 = slight, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = substantial, 0.81–1 = almost perfect [12].

The Mann–Whitney U test was used to determine if there was a significant difference between the corrosion scores of: (1) the polar and equatorial regions of both liner designs and (2) the overall corrosion scores for the two designs.

Non-parametric Spearman correlation tests were used to determine the significance of any associations between the liner corrosion scores and (1) femoral head size (R3 only), (2) Co/Cr ratio and (3) head taper corrosion score. Associations with head size for the Pinnacle hips were not considered as virtually all heads were 36 mm.

Kruskal–Wallis non-parametric ANOVA tests were used to determine the presence of any statistically significant differences between the overall corrosion scores of the two designs (separately) in relation to (1) time to revision, (2) patient age at primary surgery, (3) Co and Cr blood metal ion levels, (4) Co/Cr ratios. Post-hoc analysis was then performed using Mann–Whitney tests to identify which particular differences were significant.

Results

The inter-observer reproducibility of the corrosion scores determined by the two examiners was found to be almost perfect ($\kappa = 0.856$) indicating that this is a reliable method of visual inspection.

Visual Assessment of Corrosion

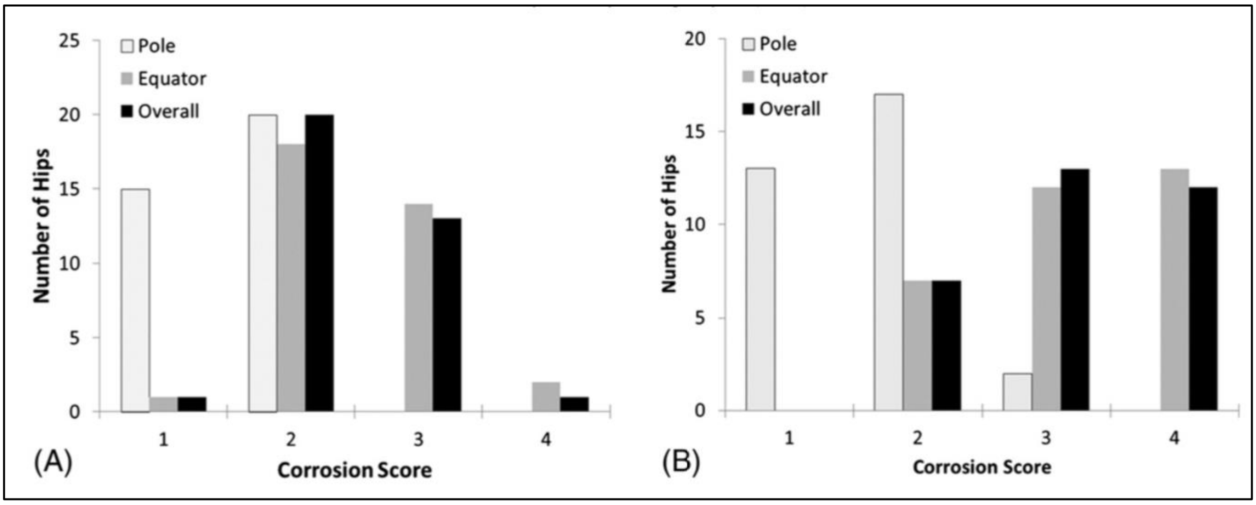

Figure 3: (A) Corrosion scores of for the Pinnacle cup. (B) Corrosion scores for the R3 cup

Corrosion scores by examiner A for the Pinnacle and R3 cup liners are illustrated in **Figure 3**. The majority of the Pinnacle liners showed mild to moderate corrosion overall. Mild or no corrosion was seen at the polar regions, however at the equatorial region 46% (n=16) of the Pinnacle liners showed evidence of moderate to severe corrosion. Conversely, 94% (n=30) of the R3 liners exhibited mild or no corrosion at the pole whereas 79% (n=25) of liners were moderately or severely corroded at the equator. The corrosion scores overall of the R3 liners were significantly greater than of the Pinnacle liners (P<0.001). With both designs there was significantly greater corrosion scores at the equator that at the pole (p<0.001). Examples of the different corrosion scores observed at the equator of liners is illustrated in **Figure 4**.

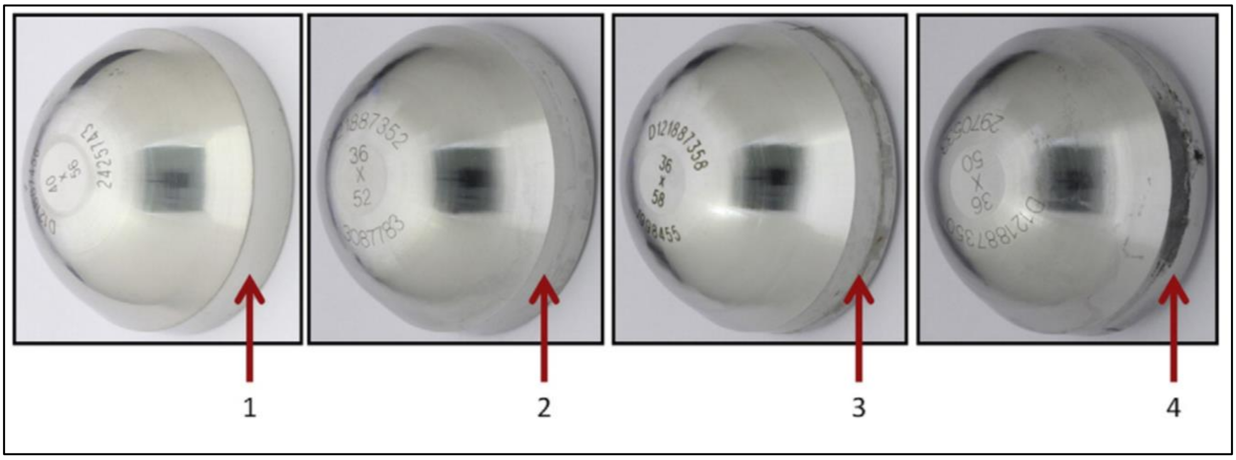

Figure 4: Examples of the four corrosion scores observed at the liner rim

There were distinct differences between the corrosion patterns between the Pinnacle and the R3 liners (**Figure 5**).

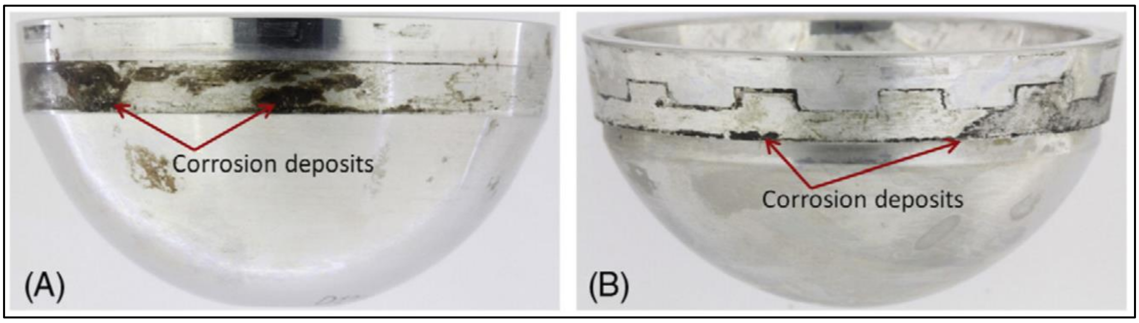

Figure 5: Differences in corrosion patterns observed between the (A) Pinnacle & (B) R3 Liners

The Pinnacle liners exhibited a clear band of corrosion running circumferentially close to the rim. Whereas the R3 liners consisted of a similar band with a pattern of peaks and troughs. This was consistent with the design on the inner surface of the modular shell.

There was no correlation between the corrosion scores of the liner and head size (R3 only, p =0.735). There was also no correlation between corrosion scores and Co/Cr for the two designs (Pinnacle p=0,934 and R3 p=0.251), head taper corrosion for the two designs (Pinnacle p=0.360 and R3 p=0.314). There was also no significant difference between the corrosion scores of the R3 liners in relation to time to revision (p=0.969), patient age (p=0.869), Co levels (p=0.188), Cr levels (p=0.081), and Co/Cr ratios (p=0.761). Regarding the Pinnacle liners, there was an insufficient number of hips (n=1) in two of the corrosion score categories (score 1 and 4). Therefore, a Kruskal-Wallis test was not possible to be performed. Hence, the Pinnacle liners scores were separated into two groups: (1) no and mild corrosion (scores 1 and 2) and [193] moderate and severe corrosion (scores 3 & 4). The Mann-Whitney tests were used and no significant difference between the corrosion scores of the Pinnacle liner and time to revision (P = 0.418), patient age (P = 0.978), Co levels (P = 0.989), Cr levels (P = 0.801) and Co/Cr ratios (P = 0.269).

Scanning Electron Microscopy (SEM)

Further inspection with SEM illustrated that both designs exhibited evidence of third-body scratching, orientated circumferentially at the polar regions of both designs (**Figure 6A**). There was a distinct margin between the corroded regions of the equator and the uncorroded regions.

The corroded areas illustrated substantial black debris and pitting (**Figure 6B**). The black deposits were shown to be Cr rich corrosion debris on EDX analysis (**Figure 7**).

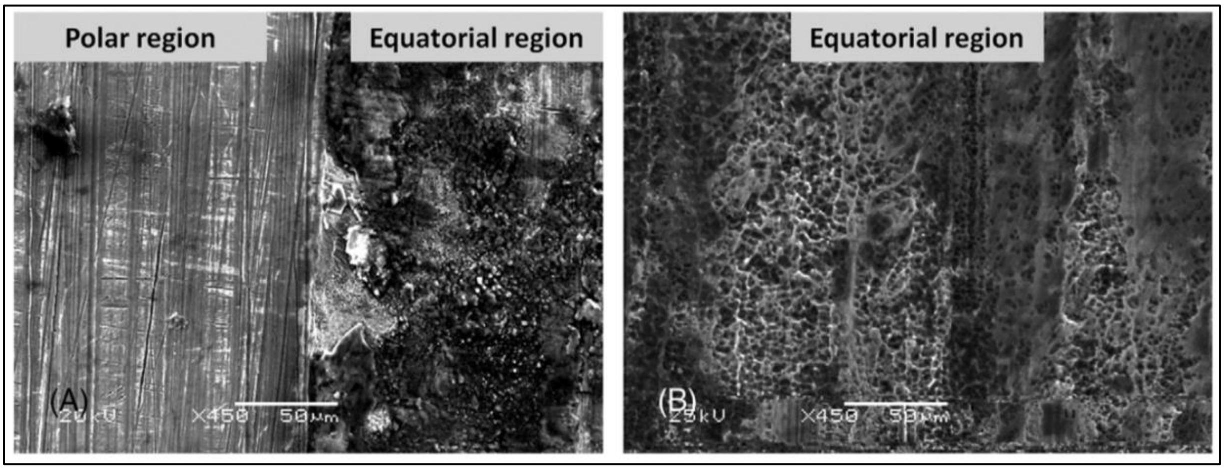

Figure 6: SEM images illustrating (A) third body scratching at the polar region of a liner (B) substantial pitting observed in the corroded regions

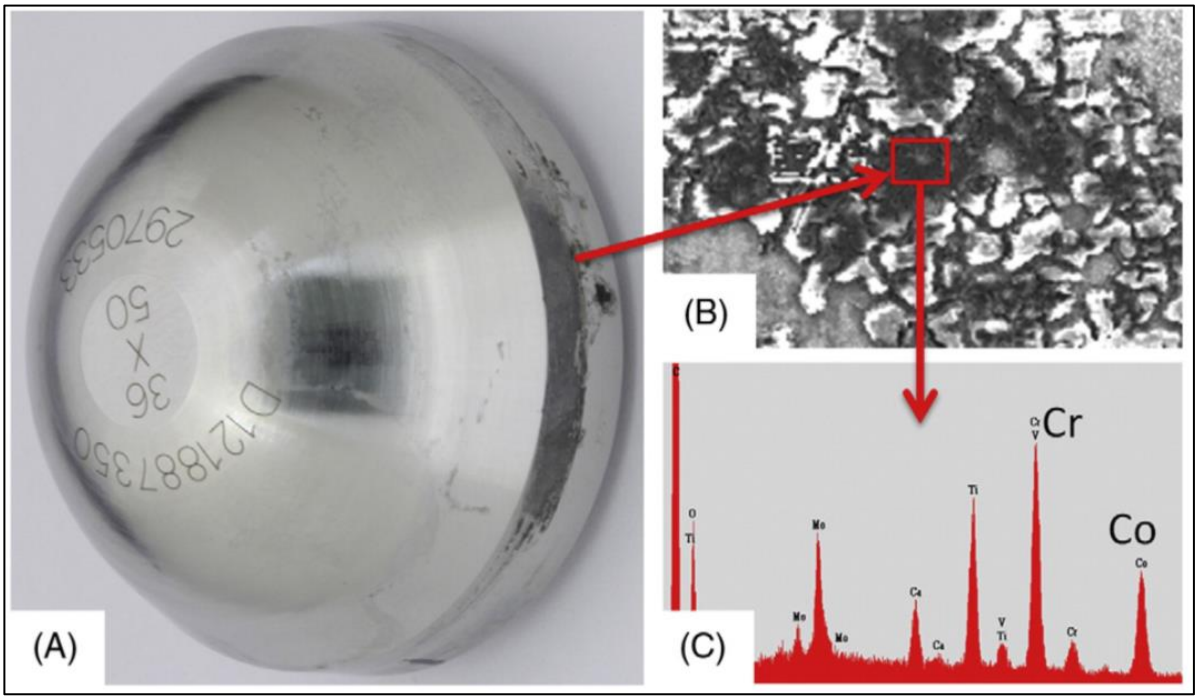

Figure 7: EDX analysis revealing corrosion deposits as being rich in Cr

Discussion

A number of previous clinical and retrieval studies have presented clear evidence implicating corrosion as mechanism of material loss at the surfaces of metal hip implants. However, the size of the clinical impact of corrosion in relation to implant failure is unclear. Visual evidence of corrosion has been observed at the stem-cement interface of cemented stems [13,14], the modular neck-stem junction [9,15], the modular stem-head junction [7,11] and the interface between the shell and liner of modular cups. The current study reports retrieval findings of the backside of the modular cup liner in the largest series of retrieved modular cups to date; we found very high agreement between the visual grading of components by two independent examiners, suggesting this is a reliable method of assessment.

We have shown that corrosion to some extent occurred in all liners at the point of engagement between the liner and shell and was likely due to a mechanism of galvanic corrosion as a result of the pairing of dis- similar alloys (CoCr and Ti). We observed considerable pitting in regions that were macroscopically identified as being corroded and black sur- face deposits were confirmed as being rich in Cr ions with comparatively less evidence of Co. The R3 liners were significantly more corroded than the Pinnacle liners; this may help explain why the median Co/Cr ratio of the R3 hips (2.74) was over twice that of the Pinnacles (1.32); it is acknowledged however that other sources of corrosion such as the femoral head taper junction may contribute to this also. The bands of corrosion observed are consistent with the surface areas of engagement between the shell and liner. The Pinnacle liner and shell have a contact region that is uniformly circumferential and the resulting area of engagement is larger than that which occurs between the liner and shell of the R3. The R3 shell has a series of surface depressions that run circumferentially across the inside of the component; these have been designed to be fitted with a polyethylene liner which has a series of corresponding tabs to prevent rotational movement of the component. The metal liner of the R3 does not have these tabs but the metal shell retains the surface depressions, resulting in a reduced area of contact between the shell and liner, leading to greater corrosion. Furthermore, the space between the shell and the liner depressions creates an environment for fluid ingress (originating from the rim of the cup and also the opening of the screw holes), potentially leading to crevice corrosion and therefore accelerating the corrosion process. The influence of surface area on corrosion at the shell-liner junction is synonymous with the findings re- ported for the femoral stem-head junctions; it has previously been shown that short and rough stem trunnions, which have a lower surface contact area with the head taper than long, smooth trunnions, lead to greater corrosion and material loss at this junction [16,17].

The polar regions of the liner backside of both designs are not intended to be engaged with the shells however our SEM analysis revealed evidence of third body scratching in this region. This suggests that third body material is likely to have entered this interface via the screw holes in the shells, which we found had not been covered during implantation of the components. It is speculated that this passage of material entry will have contributed to the corrosion processes therefore we suggest that screw holes that are not utilised are covered during surgery.

Our finding of considerable corrosion at the engaged region of the backside of these liners presents evidence of an additional source of metal ions that may contribute to implant failure; the clinical impact of debris from this junction is however not clear. Our observations are in agreement with those reported by Gascoyne et al. [10], who examined 8 cases, revealing clear evidence of corrosion at the shell-liner junction. The significantly greater corrosion observed on the surfaces of the R3 liners than the Pinnacles may help explain the high revision rates that were observed in this design, ultimately leading to its recall; the Pinnacle implants have a reported failure rate of 8.45% at 7 years [18], whilst a recent study has reported failure rates of 24% for R3 MOM bearings at their centre [19].

Limitations

As with all retrieval work, this study included only hips that had failed and consequently required revision. We are not able to compare our retrieval findings with the surface changes that occur in the modular cup of well-functioning hips.

Future Work

Future work may involve quantifying the volume of material lost from the backside of the liner and determining to what extent this may have been due to a mechanism of corrosion. This may aid in under- standing the clinical impact of surface damage at this junction. Previous studies [20,21] have highlighted the susceptibility of thin titanium outer shells to deforming during implantation; the effect of this deformation on the integrity of the shell-liner junction is unclear and warrants future investigation.

Conclusion

We have used the largest number of retrieved modular cups to date to present evidence of corrosion at the backside of the cup liner. We have shown that corrosion occurs primarily at the equator of the liner and the severity of corrosion appears to be design dependent; the evidence of significantly greater corrosion of the R3 liners may suggest a potential reason for the high failure rates, ultimately leading to the withdrawal of this device from the market.

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Appendix 2: Fretting And Corrosion Between A Metal Shell And Metal Liner May Explain The High Rate Of Failure Of R3 Modular Metal On Metal Hips

Ilo KC, Derby EJ, Whittaker RK, Blunn GW, Skinner JA, Hart AJ. Fretting and *Corrosion Between a Metal Shell and Metal Liner May Explain the High Rate of Failure of R3 Modular Metal-on-Metal Hips*. J Arthroplasty. 2017 May;32(5):1679-1683. doi: 10.1016/j.arth.2016.12.024. Epub 2016 Dec 22. PMID: 28159422.

Abstract

Background: The R3 acetabular system used with its metal liner has higher revision rates when compared to its ceramic and polyethylene liner. In June 2012, the medical and healthcare products regulatory agency issued an alert regarding the metal liner of the R3 acetabular system.

Methods: Six retrieved R3 acetabular systems with metal liners underwent detailed visual analysis using macroscopic and microscopic techniques.

Results: Visual analysis discovered corrosion on the backside of the metal liners. There was a distinct border to the areas of corrosion that conformed to antirotation tab insertions on the inner surface of the acetabular shell, which are for the polyethylene liner. Scanning electron microscopy indicated evidence of crevice corrosion, and energy-dispersive X-ray analysis confirmed corrosion debris rich in titanium.

Conclusion: The high failure rate of the metal liner option of the R3 acetabular system may be attributed to corrosion on the backside of the liner which appear to result from geometry and design characteristics of the acetabular shell.

Introduction

Modularity of total hip arthroplasty (THA) was developed to give more flexibility to the surgeon intraoperatively to better accommodate patient geometry as well as potentially allowing easier revision surgery in the future. Modular acetabular components have allowed the use of a metallic shell that can be coupled with different liner materials. This has permitted further choice dependent on cases and functional requirement [1].

The R3 acetabular system (Smith and Nephew, Memphis, TN) contains an uncemented modular hemispherical titanium shell, which was first released in Europe and Australia in 2007.

For primary fixation, it uses a porous coating with the option of 3-hole shell for adjuvant screw fixation. The R3 acetabular system initially was available with three different liner options: polyethylene, metal, and ceramic. The metal option for the R3 is high carbide cobalt-chromium in the as-cast microstructural condition. However, the metal liner was subsequently recalled on June 1, 2012, by Smith and Nephew, and on June 25, 2012, the medical and healthcare products regulatory agency issued a medical device alert regarding the metal liner component of the R3 acetabular system, advising to stop its use and increase surveillance of these implants.

In this study, we aim at understanding the failure mechanisms of the R3 modular acetabular system with its metal liner through analysis of retrievals.

Methods

This was a retrospective study performed at a national implant retrieval centre. We investigated all failed R3 modular acetabular systems, which consisted of a metal liner collected from July 2009 to July 2014. Six implants from different hospitals were collected. Pre-revision cobalt and chromium blood ion levels were collected alongside relevant patient demographic and radiographic data.

Before analysis, the implants were cleaned in a cleaning solution consisting of 10% Decon 90 and deionized water. The implants were then placed in an ultrasound-cleaning machine for a period of 15 minutes, then rinsed with deionized water to remove loose debris, and then left to dry. The components of each implant were then visually analysed macroscopically and microscopically. A Leica M50 Stereomicroscope at 40 magnification was used to examine all areas of the acetabular shell and metal liner to identify any changes that may have occurred on their surfaces. Changes to the surface of hip implants have previously been described by Mckellop et al. [2]. Evidence of corrosion and fretting was noted and their location described in relation to their proximity to its pole or equator. Severity of corrosion was not assessed due to the subjectivity of its qualitative measurement.

For further detailed analysis, a scanning electron microscope (SEM, Joel, JSM 5500, Tokyo, Japan) was used to perform detailed microscopic analysis of areas of interest highlighted from the microscopic inspection, thus enabling identification of microscopic changes such as pitting and fretting scars. Energy-dispersive X-ray spectroscopy was used to chemically characterize any evidence of corrosive debris.

Results

Clinical data for the retrieved R3 acetabular systems are shown in **Table 1**. Pre-revision magnetic resonance imaging (MRI) scans were performed for five implants. All showed evidence of adverse reactions ranging from fluid collections to soft tissue masses. The mean patient age was 63 (range 56-67) at time of implantation and they were retrieved after a mean of 47 months (range 28-67). All except one patient had both raised Co (median 9, range 5.66 – 27.7) and Cr (median 8.1, range 5.6 – 43.4) blood metal ions.

Implant no	Gender	Age (years)	Head size (mm)	Co (ppb)	Cr (ppb)	Time in situ (months)	Reason for revision	MRI result
1	Female	65	40	8.1	23.4	41	Aseptic loosening of cup	Fluid collection
2	Female	56	46	7.8	8.9	28	Aseptic loosening of cup	Fluid collection
3	Male	60	42	5.6	5.6	49	Unexplained pain	Fluid collection
4	Male	60	48	43.4	27.7	33	High metal ions	Soft tissue mass
5	Female	59	44	-	-	Unknown	Unexplained pain	Soft tissue mass
6	Female	67	40	14.0	9.0	67	Unexplained pain	-

Table 1: Implant and patient data of retrieved R3 acetabular systems

Visual analysis of each acetabular shell showed a circumferential band of debris on the inner surface, below the hard-bearing taper locking mechanism. The backside of the R3 metal liners illustrated evidence of surface damage and black debris in the corresponding area. The areas of corrosion were clearly demarcated into a ‘castle parapet’ shape (**Figure 1**). These areas of corrosion were found circumferentially at the equator of the metal liner. SEM micrographs of the backside of the liner illustrated evidence of pitting within the areas of corrosion and confirmed that the corrosive damage was clearly within the boundaries of the 'castle parapet' shape (**Figure 2**). EDX confirmed corrosive debris, rich in Ti (**Figure 3**).

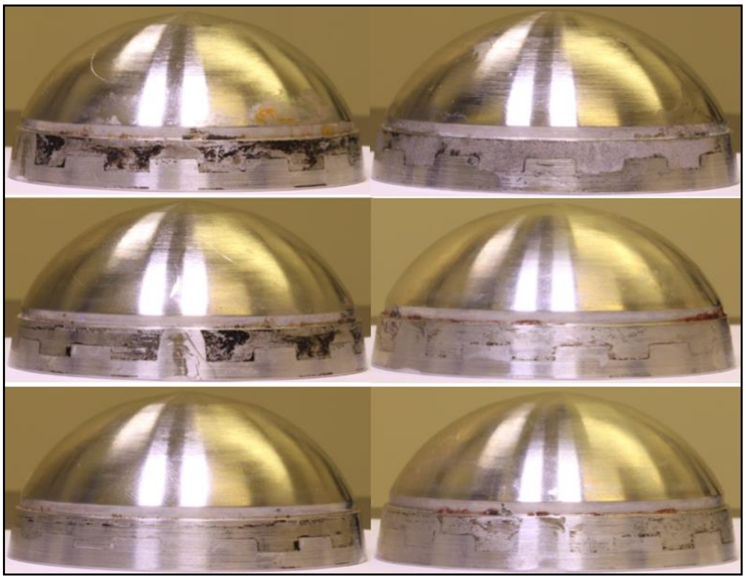

Figure 1: Photographs of 6 retrieved metal liners used in the R3 acetabular system illustrating a distinctive pattern of corrosion on the backside of the liners

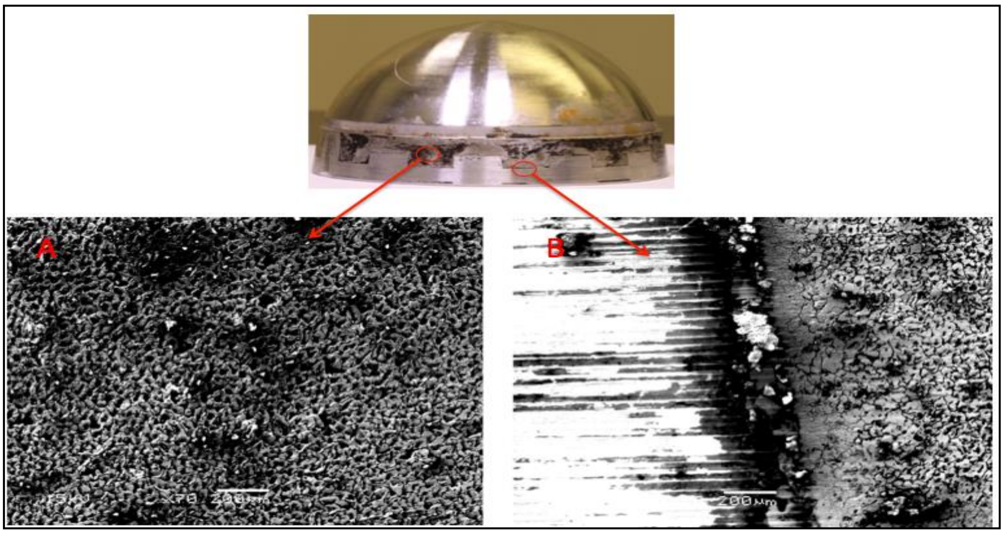

Figure 2: (A) Scanning electron microscopy image [x70] illustrating extensive pitting in areas of corrosion on the backside of the metal liner. (B) Scanning electron microscopy image [x70] illustrating a clear demarcation between the corroded [right of image] and non-corroded areas [left of image]

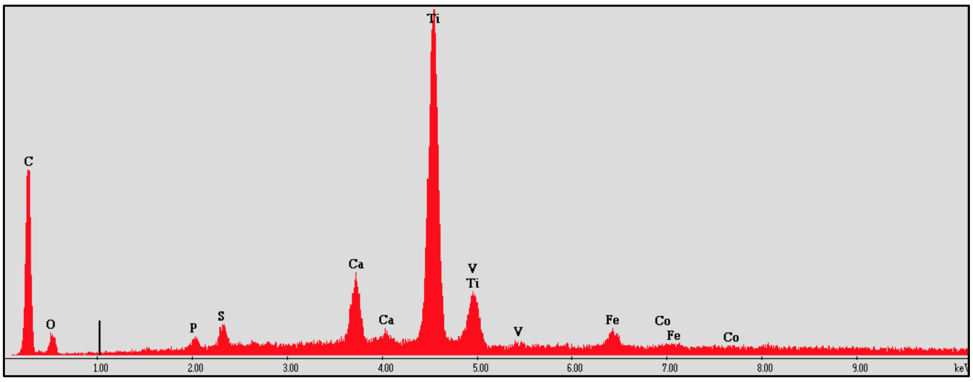

Figure 3: Energy dispersive X-ray spectroscopy of corrosive debris on the backside of the metal liner showing Ti rich deposits

Discussion

This study has shown a potential new mechanism of failure that affects the backside of the R3 acetabular system metal liners. Through detailed visual analysis, this study has identified the presence of corrosion on the backside of the metal liner, which appears to be clearly demarcated around the equator of the metal liner. Furthermore, the corrosion observed had a pattern correlating with the inner surface of the acetabular shell. The "castle parapet" outline of the areas of corrosion conforms with the grooved areas of the acetabular shell where the polyethylene liner antirotation tabs insert (Fig. 4). These results are important as they may help explain the high failure rates seen with the metal liner option of the R3 acetabular device and its subsequent recall. Recall of R3 metal liners was due to their association with a higher-than-normal failure rate. UK national joint registry data found a revision rate of 6.3% at 4 years, compared to 2.9% revision rate for all primary THA [194]. Similar results were found in the Australian joint registry, with 2.48 revisions per 100 observation years for the R3 metal liner, compared to 0.79 for all primary THAs [4]. Unpublished implant data from the national joint registries, which are available to manufactures, reported no dominant cause of failure according to Smith and Nephew, but there has been 1 study which has reported a failure rate of 24% due to adverse local tissue reactions [5]. However, the R3 acetabular cup used with polyethylene or ceramic liners ranks third most common acetabular component inserted in Australia [4], and Lee and Evans [6] found a cumulative revision rate of 0.15% for the R3 system when used with ceramic or highly cross-linked polyethylene in 646 patients from the Australian joint registry.

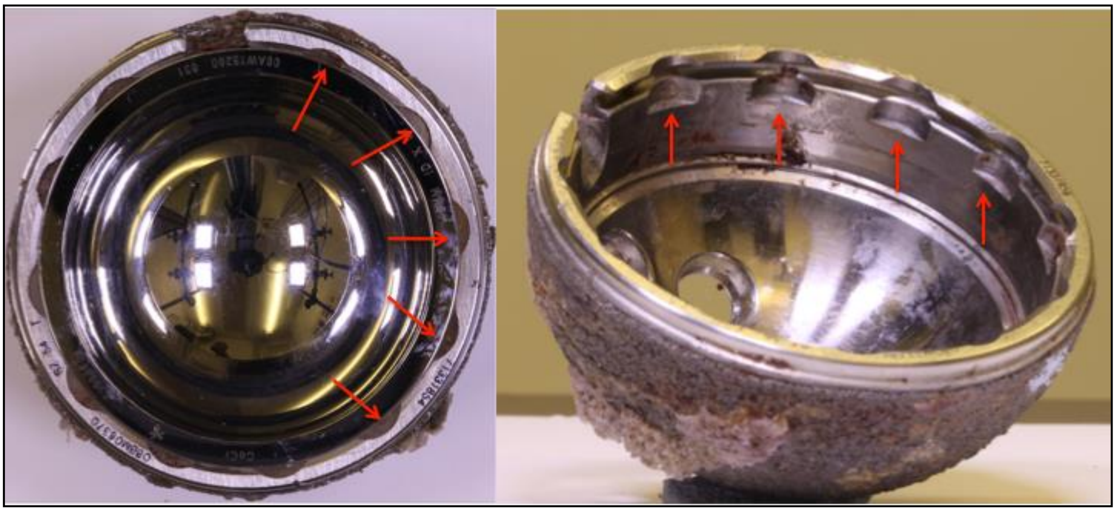

Figure 4: Photograph (100mm lens) of the R3 acetabular shell highlighting the insert for the polyethylene liner anti-rotation tabs (arrows)

There are a limited number of other studies that have investigated the R3 acetabular system. A radiostereometric analysis study by Grosser et al. of 14 patients who had undergone implantation of the R3 modular cup found proximal migration of 0.39 mm greater than the proposed safe level of 0.2 mm [7]. This result put the R3 system in the “at-risk range,” albeit at the lower end. Labek et al. [8] analysed datasets from 3 different countries regarding the outcome of the cementless tapered SL stem. This study showed that the combination with the R3 acetabular system showed a higher revision rate when compared with another more frequently used cup. However, there are no published studies investigating the cause of the increased failure rate of the R3 modular cup with a metal liner that led to its recall. In the study by Lee et al. which reported failures due to radiographic and histologic confirmation of adverse local tissue reactions, there was no analysis of retrieved components. All of the patients who underwent a pre-revision magnetic resonance imaging in this study showed evidence of adverse local tissue reactions; however, we cannot conclude that this was directly caused by corrosion at the backside of the metal liner, as metal debris can occur from the bearing and other modular surfaces. However, damage to the backside of a metal liner will increase the amount of metal debris, which previous studies report that corrosion at taper junctions of THA has resulted in extensive soft tissue damage [9-15].

The corrosion on the backside of the retrieved metal liners in this study appears to have a clear pattern. Micrographs highlighted that there was a clear border as to which areas were corroded. These areas are exactly matched to corresponding areas on the inner surface of the shell, illustrating that the geometry of the R3 acetabular shell does not fully conform to the metal liner. The R3 polyethylene liner is different to the ceramic and metal liners as it has antirotational tabs to prevent torque and allow a lock fit with the grooves on the acetabular shell. The insertions for the poly- ethylene tabs are visible on the inner surface of the R3 acetabular shell (Fig. 4). The metal liner does not have antirotation tabs, therefore having intermittent areas of contact between the shell and liner at its equator. Where there is close contact between 2 different metals, there is potential for corrosion. The acetabular shell is constructed from titanium, whereas the liner is constructed from a cobalt-chromium alloy. The mixing of different metals permits galvanic corrosion, and studies have shown that there is increased damage at taper junctions in mixed alloy implants [16-20]. When a metal liner is used in the R3 acetabular system, due to the antirotational tabs insertions on the equator of the shell it can permit joint fluid and debris to infiltrate the crevices between the liner and shell. This can cause an exacerbation of corrosion at this taper junction.

When a metal liner is used in the R3 acetabular system, there are areas between the grooves on the shell and the backside of the liner that are in close contact. This area of close contact between the dissimilar metals can create a crevice and a subsequent galvanic environment. SEM imaging showed evidence of pitting within areas of corrosion, which is suggestive of crevice corrosion. Differences in tolerances and also micromotion can exacerbate the potential for corrosion in this area. The presence of screw holes and decreased conformity between the liner and shell interface can permit fluid and debris into crevices. Previous studies have shown that fluid within a crevice can cause ion exchange and prevent a friction fit, increasing corrosion [21,22].

Due to the small number of retrievals in this study, we cannot conclude that backside corrosion occurs with all the metal liners of the R3 acetabular system. However, the clear corrosive patterning found during this retrieval study appears to be linked to the implant design and metallurgy. All R3 acetabular shells accommodate for the polyethylene inserts with the antirotational tabs. As all retrievals showed the same pattern of liner damage, this suggests that the metal liner may not be a suitable option for the R3 acetabular system. This problem ideally should have been discovered during in vitro testing. The results of this study suggest that through increasing implant adjustability, the R3 acetabular system long-term success could be compromised, as the shell may not be suited for its metal liner. Although larger studies are needed to confirm our results, we suggest that a testing standard for modular cups should be developed to reduce potential future issues like this occurring.

Backside corrosion can potentially arise with any acetabular system that contains a liner with metal on its backside. Therefore, acetabular systems with metal-backed ceramic liners and modular dual-mobility components may also be susceptible to this issue, in the long term. Further research is required to understand the significance of the backside liner corrosion. However, as an extra source of metal debris, close monitoring for evidence of metallosis and adverse tissue reactions is essential as advised by the medical and healthcare products regulatory agency for all metal-on-metal implants. Further information is required as to whether all acetabular systems with metal-backed liners, regardless of bearing surface, should be monitored.

Limitations

This study has analysed a small number of retrieved R3 com- ponents; therefore, the results may not be representative all R3

components with a metal liner. Also, we do not know whether the corrosion at the backside of the metal liner was a direct cause of failure; however, this is an undesirable outcome. Further analysis is required to investigate the significance of corrosion of the backside of the metal liner and whether any patients or surgical factors contributed to its failure.

Conclusion

This study has shown that the issue regarding the R3 acetabular system and its metal liner is due to the geometry of the inner surface of the shell. While allowing for antirotational tabs of the polyethylene liner, this appears to permit corrosion between the metal liner and shell, leading to corrosive damage of the backside of the liner. The modular design of the R3 acetabular system is not suited for the metal liner, and future designs of modular acetabular systems should take these findings into account.

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Appendix 3: Metal-On-Metal Total Hip Arthroplasty: Does Increasing Modularity Effect Clinical Outcome?

Ilo KC, Hothi HS, Skinner JA, Hart AJ. *Metal-on-metal total hip arthroplasty: does increasing modularity affect clinical outcome?* Hip Int. 2022 Sep;32(5):677-684. doi: 10.1177/1120700020979275. Epub 2020 Dec 16. PMID: 33322929.

Abstract

Background: Modularity of metal-on-metal (MoM) implants has come under scrutiny due to concerns regarding additional sources of metal debris. This study is a retrieval analysis of implants from the same manufacturer with the same MoM bearing surface. The difference between the implants was presence or absence of modular junctions.

Methods: This is a retrospective study of 31 retrieved implants from 31 patients who received a Conserve Wright Medical MoM hip prosthesis. The 31 implants consisted of 16 resurfacings and 15 implants with modular junctions; 4 conventional THAs and 11 modular-neck THAs.

Results: 43% of pre-revision MRI scans performed on resurfacing implants and 91% performed on the modular implants illustrated evidence of an adverse local tissue reaction. There was no difference in pre-revision blood metal ion levels or bearing surface wear between the resurfacings and modular implants. The neck-head tapers of the modular group showed low levels of material loss. However, the neck-stem tapers showed increased severity of corrosion and material loss

Conclusions: The modular implants had an increased incidence of adverse local tissue reaction. This could be related to the presence of modular junctions, particular the neck-stem junction which showed increased susceptibly to corrosion

Introduction

Modular implants were introduced to improve flexibility and restoration of individual biomechanics [1,2]. High failure rates have led to recalls of certain designs [3]. Dual-modular femoral stems such as the ABG2 and Rejuvenate (Stryker, Mahwah, NJ, USA) were recalled in July 2012 as a result of high revision rates. A PROFEMUR (Wright Medical Group Inc, Arlington, TN, USA) modular neck device; the PROFEMUR Neck Varus/Valgus cobalt chromium eight degree, was recalled in August 2015 due to unexpected rates of fracture. Although increasing modularity did initially appear attractive, higher than expected failure rates are alarming. In this study, we analysed failed implants from the same manufacturer with the same bearing surface. The only difference between them was the absence or presence of modular junctions. Our aim was to investigate whether implant function and survival was affected by the presence of modular junctions.

Methods

This is a retrospective study of 31 retrieved implants from 31 patients who had received a Conserve Wright Medical (Memphis, TN, USA) metal-on-metal (MoM) hip prosthesis. The bearing surface materials are the same for the different designs and are manufactured from high carbon cast cobalt chrome alloy. The Conserve Wright MoM hip designs are resurfacings, conventional THAs and modular-neck THAs (Figure 1). The THA designs have a range of different femoral stem choices.

Implants were collected at a national MoM implant retrieval centre (Table 1). The patient cohort included 13 men and 18 women with an average of 67 (range 35–79) years at the index procedure. The 31 implants consisted of 16 resurfacings and 15 implants with modular junctions; 4 conventional THAs and 11 modular-neck THAs. The modular neck components provided a combination of 4/8/15 degrees of anteversion or retroversion and 6/8/15 degrees of varus or valgus (neutral = 135°).

Figure 1. 3 different designs of the Conserve Wright MoM hip prosthesis.
(Left) Hip resurfacing, (middle) conventional THA, (right), modular neck THA

Design	No.	Bearing surface	Stem material (design)	Modular neck material	Neck angle	Neck length
Resurfacing	16	High carbon caste cobalt chrome alloy	-	-	-	-
THA Conventional	4	High carbon caste cobalt chrome alloy	Titanium (Profemur Gladiator)	-	135°	32.6mm
THA Modular neck	11	High carbon caste cobalt chrome alloy	Titanium (Profemur Gladiator) (4)	CoCr	Neutral long 8° varus short 4° retroverted/ 6° valgus long 8° valgus short	38.5mm 27mm 38.5mm 27mm
			Titanium (Profemur Z) (5)	CoCr	4° retroverted/ 6° valgus long [193] neutral short[193] 8° varus long	38.5mm 28mm 38mm
			Stem not explanted (30)	CoCr	8° varus short 8° varus short	27mm 27mm

Table 1. Characteristics of the retrieved implants (THA: total hip arthroplasty)

Demographic, imaging & blood metal ions data

Patient demographics were collected (Table 2). Pre-revision whole blood cobalt and chromium ion levels and imaging data were collected. All imaging (including magnetic resonance imaging [MRI]) were reported by an experienced musculoskeletal radiologist to evaluate any adverse local tissue reactions (ALTR).

Design	M:F	Age (years)		Time *in situ* (months)		Head size	
		Median	**Range**	**Median**	**Range**	**Median**	**Range**
Resurfacing (*n* = 16)	7:9	55	35–73	55	29–119	56	48–60
THA (*n* = 15)	6:9	59	51–71	60	18–85	48	44–58

Table 2. Demographic and prosthesis data (THA, total hip arthroplasty)

Measurement of material loss

Volumetric wear from the bearing surfaces and head taper junction was measured. Material loss from the bearing surfaces was measured using a Zeiss Prismo (Carl Zeiss, Ltd., Rugby, UK) coordinate measuring machine utilizing a previously described protocol [4]. Data was analysed using a previously described method, to determine volumetric wear from each bearing surface [5].

To assess the volume of material loss from the head-neck taper junction of the conventional and modular neck THAs, a Talyrond 365 (Taylor Hobson, Leicester, UK) out-of-roundness instrument was used to measure taper surfaces using a previously described protocol [5]. The female taper of the head-neck junction was measured as its material loss is a similar magnitude to the bearing surfaces, in contrast to the male taper.

Currently there is not reliable way of determining material loss from the neck-stem taper junction as the unworn shape of the taper surfaces cannot be accurately determined. To estimate the material loss of the neck-stem taper, we used the Talyrond 365 to take a series of 14 vertical straightness profiles along the axis of the neck-stem taper surfaces. These traces were used to estimate the maximum linear deviation (equal to the maximum depth of material loss) on each surface.

Visual analysis

All tapers of the THAs were assessed for corrosion. For the conventional proximal taper, each male and female taper surface was inspected macroscopically with a Leica M50 light microscope (Leica Microsystems, Germany) at up to x40 magnification. A well-published classification method was used to grade each surface with a score of 1 (no corrosion), 2 (mild corrosion), 3 (moderate corrosion) or 4 (severe corrosion). This method has been demonstrated as being repeatable and reproducible [6].

A visual analysis method, modified from Goldbergs' method [7], was performed for the distal neck-stem taper. Corrosion was scored using a scale of 1 (corrosion evident on <10% of surface) to 4 (corrosion evident on >50% of surface). Fretting was not quantified due to the difficulties in the identification and quantification of fretting from previous experience [6]. The explanted stems taper surfaces were also examined for evidence of surface damage. A scanning electron microscope (SEM, Joel JSM5500, Tokyo, Japan) was used to perform detailed microscopic analysis of areas of interest highlighted from the macroscopic inspection on the neck-stem male taper surface.

Sectioned stem

A modular stem was sectioned in order to facilitate visual analysis of its female taper. Energy-dispersive x-ray spectroscopy (EDX) was performed to analyse the chemical characterisation of corrosive debris within the modular junction.

Results

Indications for revision are illustrated in Table 3.

Reason for revision	Resurfacing	THA (conventional and modular neck)
Unexplained pain	4	7
Aseptic loosening	7	3
Adverse local tissue reaction	4	4
Infection	1	0
High metal Ions	0	1

Table 3. Reasons for revision of retrievals.

Blood metal ions

Whole blood cobalt and chromium levels are illustrated in Figure 2. In the resurfacings group the median cobalt and chromium levels were 8.3 ppb and 7.4 ppb respectively. In the modular group the median cobalt and chromium levels were and 8.4 ppb and 3.4 ppb respectively and there was no statistically significant difference in cobalt ($p = 0.683$) and chromium ($p = 0.440$) between the resurfacings and modular group. The mean ratio of Co/Cr was 1.08 in the resurfacing group and 1.45 in the modular group ($p = 0.358$).

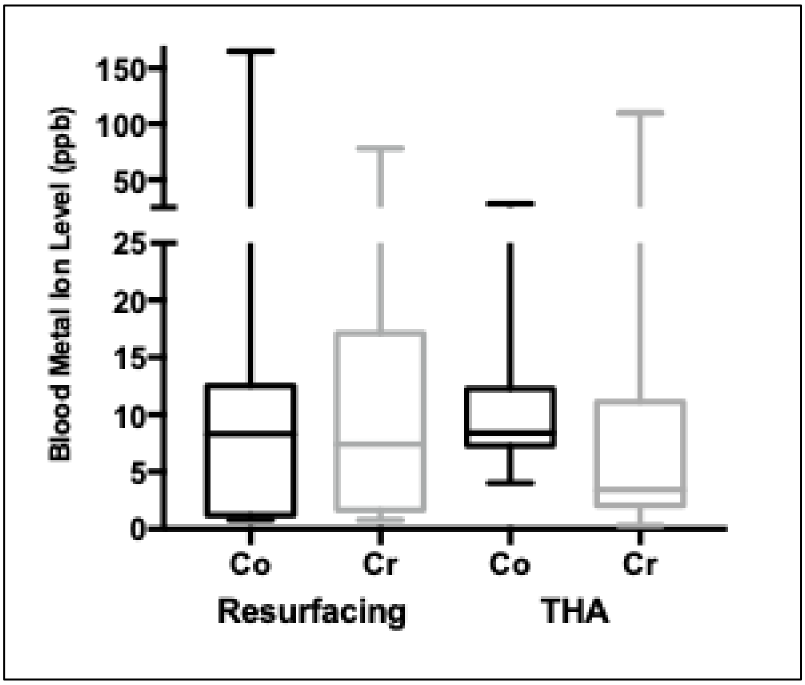

Figure 2. Blood metal ion levels of the resurfacing and modular group.

Bearing surface wear

There was no statistically significant difference between the wear rates of the cup ($p = 0.86$), head ($p = 0.103$) and combined ($p = 0.075$).

Taper junction wear

The taper of the THA acetabular heads was measured for material loss. The modular-neck implants (median 1.164 mm^3/year, range 0.16–3.94) did not have a statistically significant difference in the material loss at this taper junction when compared to conventional THA (median 1.93 mm^3/year, range 0.21–3.67).

Material loss at the neck-stem taper junction

Straightness traces of the 11 male, neck-stem taper demonstrated surface damage with areas of material deposition and material loss with a maximum depth of 58.17 microns (Figure 3).

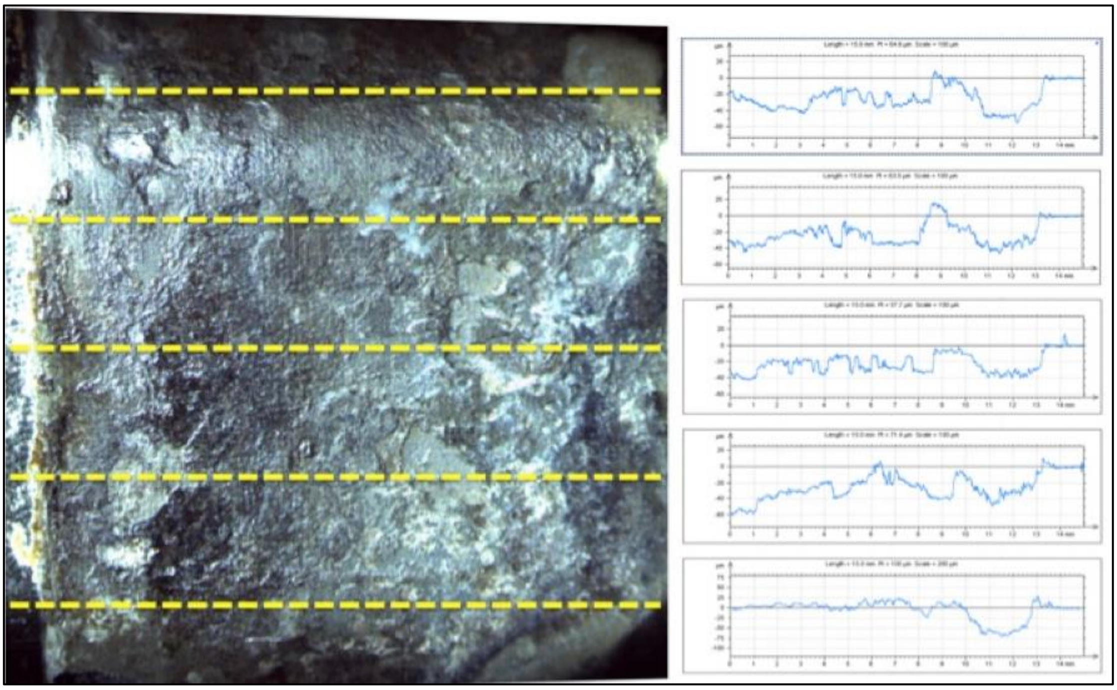

Figure 3. Optical microscopy image of a neck-stem taper of a modular neck component showing severe surface disruption with both areas of material deposition and material loss. Vertical straightness traces (right) confirmed these findings demonstrating areas of material loss with maximum depths of 58.17 microns. The traces were normalised using unworn areas measured below the contacting taper interface.

Visual analysis of taper junctions

All head-neck tapers of the modular group showed mild to moderate evidence of corrosion (mean 2, 95% confidence interval [CI], 1–2). However, the neck-stem taper showed mainly moderate to severe corrosion (mean 3, 95% CI, 2–3).

A modular neck stem was section to aid visual analysis. The trunnion showed evidence of corrosive debris present (Figure 4). Scanning electron microscope (SEM) images showed evidence of a corroded surface with corrosive debris and pitting (Figure 5).

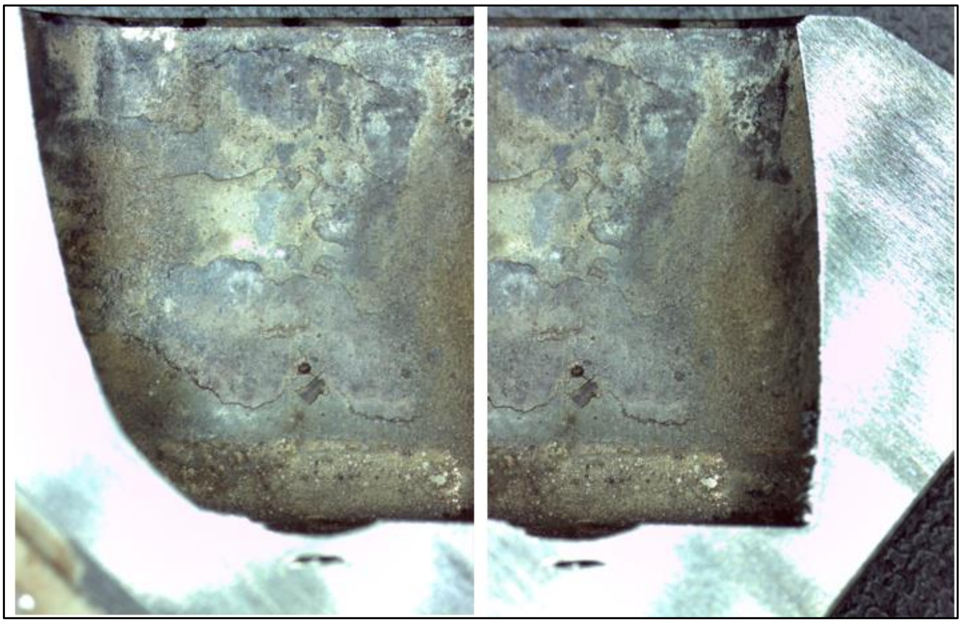

Figure 4. Optical microscopy image of sectioned modular neck stem illustrating a severely damaged trunnion surface.

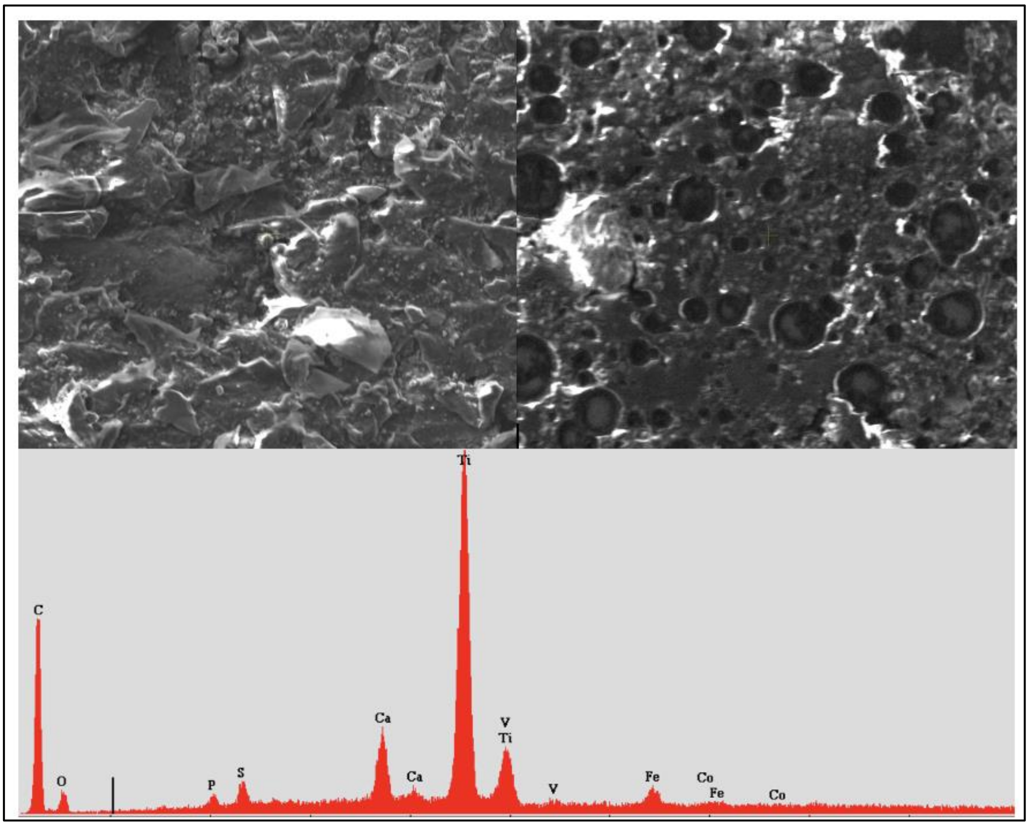

Figure 5. SEM and EDX analysis of sectioned stem illustrating evidence of black corrosive debris and pitting (200x and 400x).

Imaging

Pre-revision MRI scans were performed for all of the resurfacings group (n = 16) and 11 in the modular group (n = 15). 43% of pre-revision MRI scans performed on resurfacing implants and 91% performed on the modular implants illustrated evidence of ALTR. Radiographs were unremarkable apart from one modular neck implant showed extensive osteolysis of the greater trochanter.

Discussion

MoM bearing surface for THA improves wear properties in comparison to metal-on-polyethylene. Although this is desirable for hip prostheses, there are concerns regarding metal debris release [8,9]. Metal debris produced from bearing surfaces has a large surface area and is small in size, the small particle size leads to large number of particles for a given wear volume compared to metal-on-polyethylene bearings [10]. For resurfacings, metal debris release is from the bearing surface, whereas conventional and modular neck THA have taper junctions which are additional sources of metal ion release. Modular-neck THA permits optimisation of hip biomechanics but taper junction corrosion results in further biologically active metal debris [11]. This cohort showed no statistically significant difference in wear rates between resurfacings and modular implants. The majority of the retrievals had shown levels of wear within expected limits [12]. There were a small number of resurfacings which exhibited large amounts of volumetric wear from the head and the cup components. These implants illustrated a wear pattern equivalent to edge loading, which affects resurfacings more due to retention of the neck which can lead to impingement-type edge loading [13]. Edge-loading occurs in a mal-positioned prosthesis. It has been shown that other factors such as stem subsidence and tissue laxity could facilitate edge loading and lead to implant failure [13]. Nonetheless, there is significant importance in implant design and insertion in its optimum position [13].

Corrosion at taper junctions is reported to be a cause failure of hip implants [9,14]. Hip resurfacing implants are exempt as they do not contain a taper junction. In this study, the modular group consisted of conventional and modular-neck THAs. The head-neck male tapers were measured for material loss and this was relatively low, visual analysis of this junction also did not indicate severe corrosion. Measuring material loss from the neck-stem junction of dual-modular implants is challenging. Linear measurements of the male taper of the neck-stem junction illustrated that this surface can undergo severe damage and material loss. Mechanical *in vitro* studies of modular-neck implants show that at the neck-stem taper junction there is potential for micromotion resulting in fretting and corrosion [15]. We used visual corrosion scores to assess the changes at this taper junction. Matthies et al..[5] showed that scoring systems for corrosion and fretting are correlated with material loss, although this was for the neck-head taper. In this study, the stem-neck taper junctions exhibited a greater severity of corrosion than the head-neck taper junction. Nearly all stem-neck taper junctions of the modular-neck THA illustrated moderate to severe corrosion.

Corrosion is an inevitable complication of implant design and metallurgy. Mixed alloy couples at modular junctions contribute to greater corrosion as the two alloys have different properties. The titanium alloy of the stem is softer and its oxide layer is more susceptible to fracture than the cobalt chromium alloy, therefore when coupled the corrosion and fretting resistance may be effected. However, conventional THA tapers and the modular neck-stem taper are both mixed alloy couples, yet the modular neck stem tapers exhibited greater corrosion. Mechanically-assisted crevice corrosion explains how mechanical loading can cause fretting, fracture of passive oxide films, repassivation and crevice corrosion [16]. The increased corrosion at the neck-stem junction is likely due to many factors. Greater micromotion at the neck-stem taper junction has been shown with modular-neck hip prosthesis, likely caused by a 20-fold larger lever arm between load application and taper engagement [17]. Also, tolerances of the neck-stem junction can lead to a gap between the taper surfaces [18]. This gap can facilitate micromotion and promote crevice corrosion. The mixing of metals at the neck-stem junction can hypothetically promote galvanic corrosion. This is concerning as metal debris from taper junctions may have a greater clinical impact than that from bearing surfaces [14]. In this study, one modular-neck stem component was sectioned to better visualise the stem trunnion. Severe damage secondary to corrosion was evident. A hypothetical benefit of modular implants is a well-fixed stem can potentially be left *in situ* during revision surgery. However, with dual modular prosthesis the question arises whether a well-fixed stem should still be explanted as the neck-stem taper is susceptible to damage secondary corrosion.

Chromium and cobalt alloys are popular for use in MoM prosthesis, excellent wear properties make it attractive for use in bearing surfaces. However, the clinical relevance of this debris is not fully understood. There are results showing that the elevated blood metal ion levels leads to a greater chance of an adverse outcome and that cobalt is the more clinically relevant metal responsible for adverse tissue reactions [19]. Also, exposure to high levels of these elements can lead to osteolysis, carcinogenic, teratogenic and allergenic responses [20,21]. Therefore, blood metal ion levels have been used to monitor MoM hip implants. In this cohort of retrievals, there was no statistically significant difference in blood metal ion levels between the resurfacing and modular groups, even though the modular groups had taper junctions which is additional source of metal ion release. There are reports that Co/Cr ratio might be a tool for detecting taper corrosion as it is speculated that there is a greater release of cobalt compared to chromium at taper junctions [22]. In a study by Laaksonen et al. [23], they found a Co/Cr ratio of 1.4 was highly sensitive to ALTR and independently predictive of ALTR presence. In this study, the mean Co/Cr ratio for the modular group was 1.45 (resurfacings=1.08). Pre-revision MRI scans showed that there was evidence of an ALTR in 43% of the resurfacing group and 91% of the modular group. Metal debris stimulates a host inflammatory response mainly due to macrophage activation [24]. A study by Xia et al.[25] showed that tissues from patients with dual modular implants have a higher amount of lymphocytes and tissue destruction when compared to conventional THA and resurfacings. The amplified inflammatory response to taper debris may explain the increased presence of ALTR within the modular group of retrievals.

In this study, there was one modular-neck implant which radiographs illustrated worsening osteolysis of the greater trochanter that occurred over a period of time. The retrieved implant showed wear of the bearing surface wear and the neck-head taper within expected limits, however visually the stem-neck taper had moderate corrosive damage. There are reports of ALTR reactions caused solely by metal debris from taper junctions, in the presence of a non-metal articulating surface [26]. For MoM implants, it is difficult to ascertain whether such reactions can be attributed to metal debris solely from taper junctions, bearing surfaces or from all sources. ALTR are not always associated with high wear volumes [27]. Both cobalt and chromium are known to be cytotoxic and can initiate an immune response [28]. This can result in periprosthetic osteolysis but some studies have shown cobalt and chromium to be mutagenic and genotoxic [29]. It is beneficial to minimise the volume of wear debris, but patient-related factors need to be further understood. The combination of macrophage-induced necrosis and T-lymphocyte mediated hypersensitivity reactions may explain differences in thresholds of toxicity, sensitivity and response to metal debris amongst individuals [29]. This may explain why there are many well-functioning hip implants with MoM bearing surfaces and modular junctions [30]. Further research is required to understand the clinical significance of modular junctions and patient related factors which may increase susceptibility to metal debris.

Limitations

This study discussed findings from a small cohort of retrieved Conserve hip implants and, therefore, does not represent all of those implanted. We are not able to comment on the failure rate of the Conserve hip compared to other manufacturers and designs. Also, the number of retrievals is not enough to draw significant conclusions regarding the performance of this implant.

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Appendix 4: Does Modularity Of MOM Implants Increase Blood Cobalt:Chromium Ratio?

Ilo KC, Aboelmagd K, Hothi HS, Asaad A, Skinner JA, Hart AJ. *Does modularity of metal-on-metal hip implants increase cobalt: chromium ratio?* Hip Int. 2021 Jan;31(1):109-114. doi: 10.1177/1120700019873637. Epub 2019 Sep 8. PMID: 31496282.

Abstract

Background: Blood metal ion levels are used in the surveillance of metal-on-metal (MoM) hip implants. Modular implants contain an extra source of metal debris that may affect the ratio of metal ions in the blood.
Methods: This was a retrospective study of 503 patients with hip replacements made by a single manufacturer (Smith & Nephew, Warwick, UK) with the same bearing surface. There were 54 total hip arthroplasties, 35 Birmingham Mid- Head Resections and 414 hip resurfacings. Whole blood metal ion levels and their ratios were analysed to investigate the effect of a modular junction.
Results: The cobalt:chromium ratios were greater in the total hip arthroplasty group (mean 2.3:1) when compared to the resurfacings group (mean 1.3:1, p=<0.05) and Birmingham Mid-Head Resection group (mean 1.1:1, p=0.11)
Conclusions: This study demonstrated a trend for a higher cobalt:chromium ratio in patients with MoM total hip replacement that may be due to metal debris from the modular stem-head junction. Further work is required to correlate clinical data with retrieval analysis to confirm the effect of taper material loss on the cobalt:chromium ratio.

Introduction

Due to its success, the use of total hip arthroplasty (THA) has been extended into younger age groups. In these patients, bone-conserving implants are attractive. Hip resurfacing and mid-head resection arthroplasty are good examples. Unfortunately, these require metal-on-metal (MOM) bearings to provide the wear resistance needed. With resurfacings, metal ions are only released from wear at the bearing surface. However, with MOM THA and mid-head resection arthroplasty there is potential metal ion release from wear of the bearing surfaces[1], and wear and corrosion at the head-neck taper[2]. The widespread use of MOM bearings, led to the identification of complications that have resulted in a reduction in the use of MOM implants.

Blood metal ion levels are utilized in the surveillance of patients with MOM implants[3]. The main source of metal debris is as a result of wear from the articulating bearing surface. Mechanical and corrosive damage at modular junctions have also been shown to be a cause of metal debris formation[2, 4]. Blood metal ion levels may provide useful information regarding the production of metal debris in-situ. Blood metal ion levels can be affected by various implant and patient factors[3, 5]. It has been previously reported that the addition of modular junctions increases blood metal ion levels[6]. Conversely, current interpretation of blood metal ion levels are unable to provide information regarding the integrity of the modular junction. Any information we can gather regarding the in vivo performance of the implant would be beneficial. The aim of this study was to investigate whether modularity leads to a difference in blood metal ion levels and their ratios.

Method

This was a retrospective, non-randomized study performed at a tertiary referral centre for MOM implants. In order to compare the effect of modularity on blood metal ion levels, we identified implants from a single manufacturer with the same bearing surface design and metallurgy with and without a modular junction. Smith and Nephew's (Warwick, United Kingdom) MOM Birmingham Hip system consists of high carbon content cobalt chrome molybdenum (CoCrMo) alloy bearing surfaces that is utilized as different types of arthroplasty (Figure 1).

The Birmingham Hip resurfacing is a joint resurfacing implant which contains no modular junction. Conversely, the Birmingham Hip Total Hip Arthroplasty[7] has a modular taper junction within the femoral head component which can be used with a variety of femoral stem implants. One of these options uses an alternatively designed femoral component which is positioned within the femoral neck and not the shaft. This bone-conserving arthroplasty is the Birmingham Mid-Head Resection arthroplasty (BMHR).

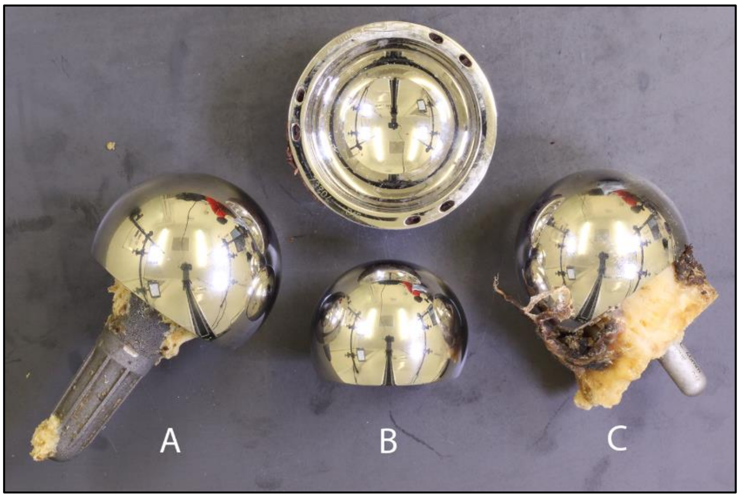

Figure 1: Photograph image (100mm lens) of MMT/Smith and Nephew metal-on-metal bearing surface utilized as different implants; (A) Birmingham Mid-Head Resection, (B) total hip arthroplasty, (C) resurfacing

A total of 503 patients were identified that had undergone a unilateral hip replacement with a MOM Birmingham Hip bearing system. Patient demographic data and the blood metal ion levels were collected for all implants. Data was collected in the period from July 2009 to May 2013. Of the 503 patients identified with a MOM Birmingham Hip bearing system, there was a total of 414 hip resurfacings, 54 THAs and 35 BMHRs.

Statistics

All statistics were performed using the statistical software package SPSS 22 (Spss Inc., Chicago, Ill). The Mann-Whitney U test was utilized to determine a significant difference between the different implant groups. A significance level of $p < 0.05$ was utilized.

Results

Amongst the 414 patients with hip resurfacings; 308 had subsequently been revised, whilst 106 had well-functioning implants. The 54 patients with THAs had all been revised, whilst all 35 patients with a BMHR were all well-functioning. A well-functioning implant was defined clinically as an asymptomatic implant which had no indication for revision (unexplained pain, pseudotumour, loosening etc) and was purely under surveillance in accordance with Medicine and Healthcare Regulatory Authority (MHRA) guidelines. Patient demographic data is illustrated in Table 1. Reasons for revision are illustrated in Table 2. Whole blood cobalt (Co) and chromium (Cr) levels were collected for all patients. For revised implants the pre-revision blood metal ion results were used and for the well-functioning patients; the most recent result.

Implant	**M:F**	**Age (years) Median**	**Range**	**Head size (mm) Median**	**Range**	**Time in situ (months) Median**	**Range**
THA (n = 54)	25:29	69	39-84	46	38-58	53	11-128
BMHR (n = 35)	20:15	56	30-71	48	44-56	73	37-92
Resurfacing (n = 414)	219:95	68	26-84	48	38-54	140	5-158

Table 1: Patient demographic data for implant groups

Revised Implant	**Unexplained pain**	**Aseptic loosening**	**infection**	**Psuedotumour**	**instability**	**High metal ions**	**Fracture**	**Impingement**
THA (n = 54)	25	5	4	19	1	0	0	0
Resurfacing (n = 308)	142	34	10	49	7	41	14	11

Table 2: Reasons for implant revision

Blood metal ions levels and ratios of different implant types

Blood metal on levels are illustrated for the different implant types in Table 3, Figures 2 and 3.

Implant Type	**Cobalt (ppb)**			**Chromium (ppb)**			**Ratio**		
	Min	**Mean**	**Max**	**Min**	**Mean**	**Max**	**Min**	**Mean**	**Max**
THA	0.83	15	119	0.7	7.8	43	0.62	2.3	10
BMHR	0.18	2.8	10	0.36	3	12	0.38	1.1	4.4
Resurfacings	0	19	250	0.3	16	343	0	1.3	60

Table 3: Blood metal ion levels and ratios of different implant types

The only statistically significant difference in cobalt levels was between the resurfacings group and the BMHR group (p=0.0115). The only statistically significant difference in chromium levels was between the resurfacings group and the BMHR group (p=0.0222). The only statistically significant difference in Co:Cr ratio was between the THA group and the resurfacings group (p=0.0426).

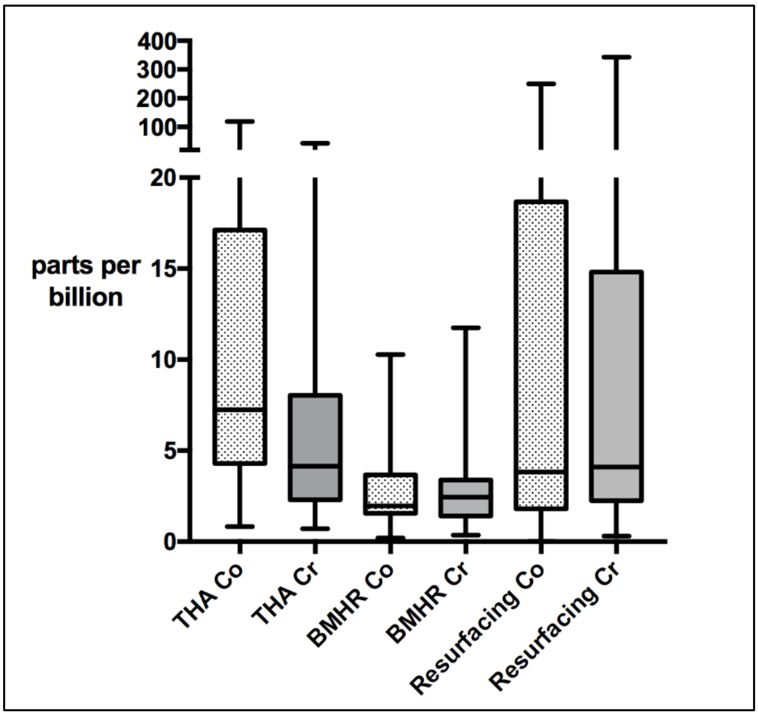

Figure 2: Graph illustrating blood metal ion levels of different implant types

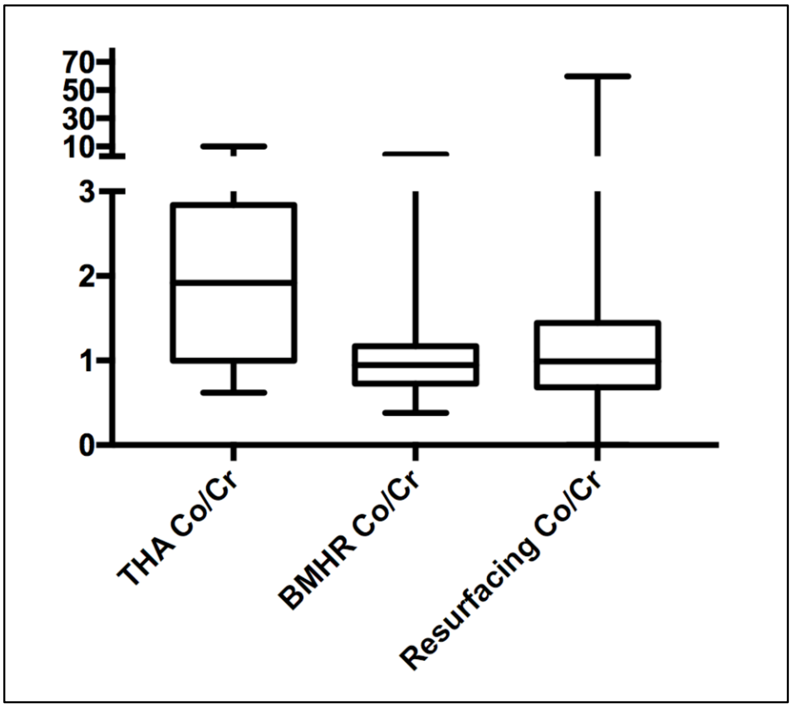

Figure 3: Graph illustrating Co:Cr ratio of different implant types

Blood metal ions levels and ratios of revised and well-functioning implants

There was no statistically significant difference between cobalt levels and Co:Cr ratios of the THA group (all revised) and the revised Resurfacings group. Although there was a trend for a higher Co:Cr ratio in the THA group (mean 2.3, range 0.62-10) in comparison to the revised Resurfacing group (mean 1.5, range 0-60). The Chromium levels were statistically different ($p=0.0079$).

There was no statistically significant difference between chromium, cobalt and Co:Cr ratio of the BHMR group (all well-functioning) and the functioning Resurfacings group. Comparing all functioning implants with revised implants. Revised implants showed statistically significant higher cobalt ($p<0.001$), chromium ($p<0.001$) and Co:Cr ratios ($p=0.0204$).

Correlation of time with blood metal ion levels

Time in situ was positively correlated with Cr and Co levels but not Co:Cr ratios. None of the correlations were significant.

Discussion

Modularity of implants permit the use of different components that allow better replication of individual hip biomechanics. However, failure of the modular taper junction has become a cause of concern regarding metal ion release with THAs [8-13]. Metal ions are not inert and can cause an inflammatory reaction which can be localized and systemic. There are reports of localized lesions which can be destructive and high incidences of unexplained pain. Nonetheless, there have been vast numbers of MOM hip replacements implanted and are under surveillance as advised by the MHRA. The utilization of blood metal ions provides a marker of the in-vivo performance of MOM bearings but the effect of modularity is unknown. This study aims to further understand blood metal ion levels and their ratios.

Three different implants that have the same bearing surface, with and without a modular junction were included in this study. Two of these implants had a modular junction (THA, BMHR) whilst the other did not have a modular junction (resurfacings). Analysis of blood metal ions between the implants showed that the resurfacings group had higher individual cobalt and chromium levels, than the other implants. However, the resurfacings blood metal ion levels were only significantly higher than the BMHR group. the ratio of cobalt to chromium was highest in the THA group and this was significantly greater than the resurfacings group.

As this was a retrospective study including all implants with the same bearing surface, the different implant groups were not matched demographically or functionally. Some of the implants had subsequently been revised. The THA group had all been revised and therefore their blood metal ion levels were further compared to revised resurfacings. The failed resurfacings had a higher Co and Cr level but the THA group had a higher Co:Cr ratio. This was not statistically significant, however there was one anomalous result in the failed resurfacing group, which was a Co:Cr ratio of 60. Removing this result from the analysis did result in a significantly greater Co:Cr ratio in the THA group when compared to failed resurfacings ($p<0.0001$). The BMHR group were all well-functioning and therefore their blood metal ion levels were compared to well-functioning resurfacings. There was no difference in Co, Cr and Co:Cr ratios between the two groups of well-functioning implants. We also compared the functioning implants to the revised implants. This did show significantly greater Co, Cr and Co:Cr ratio.

There are reports which have not shown Co:Cr to be useful, especially for diagnosing ALTR[14, 15]. This has been attributed to variabilities in alloy composition, solubility of metal ions and excretion. In this study, we have shown that well-functioning implants have lower blood metal ion levels than failed implants with the same bearing surface. However more importantly there was an increase in Co: Cr ratio with modularity. There are other studies that have shown elevated Co levels compared to Cr levels in modular implants [14,16–18]. In a prospective randomized clinical trial, Garbuz et al. [18] compared clinical outcomes of resurfacings to large diameter head THAs. At one year the THA group showed a marked elevation of Co in relation to Cr when compared to the resurfacing group. The elevation in the Co:Cr ratio may be due to the production of a Cr oxide passivation layer that develops at the head-neck junction. The consumption of Cr ions to form the passivation layer could potentially decrease the amount of Cr ions reaching systemic circulation. Hypothetically, this will increase the Co:Cr ratio.

Metal ion debris is produced from several sources, subsequently their levels are affected by material loss from the bearing surface, taper junction and component impingement. The influence of the taper junction will prove difficult to isolate. In this study, we have investigated implants with the same manufactured bearing surface with and without a modular junction. This study found an increase in Co:Cr ratio in the THA group when compared to resurfacings and the BMHR. We may have expected that because the BMHR also has a modular junction the Co:Cr ratio should be increased. However, the tapers of the BMHR and the THA are different. The BMHR has a collar just below the taper for the head to sit on, which the THA doesn't. This could protect this taper from fluid and debris that can exacerbate corrosive material loss at this junction. Also, due to the geometry of the BMHR implant the forces that act through this are similar to a resurfacing and the implant is well supported by the native femoral neck. In contrast the THA undergoes forces, which are transferred through the implant and the unsupported taper junction allowing the potential for micro-movement that exacerbates corrosion at the taper junction[19].

Moharrami et al. [20] showed that the oxide layer produced by the titanium alloy (commonly used in femoral stems) was both harder and thicker than the oxide layer produced from the CoCr alloy. This difference in hardness causes abrasive wear of the female CoCr taper resulting in wear debris and ion release. As the Cr ions are utilized in the formation of the passivation layer this would lead to an increase in Co with a lesser increase in Cr. In this study, all groups utilized the same bearing surface design and metallurgy, therefore the increase in Co ions greater than Cr ions in the THA group is possibly due to release from the taper head-neck junction. Clinically there has been a significant difference regarding the performance of the Birmingham Hip Resurfacing and the Birmingham THA. In this study there was a higher incidence of ALTR in the failed THA group when compared to the failed resurfacings. Data from the national joint registries of Australia and England and Wales have shown that revision rates are higher for the Birmingham THA when compared to other conventional hip replacements[21]. However, the Birmingham resurfacing has a much lower revision rate and performs well when compared to other resurfacings. As both implants utilize the same bearing surface, the issue may result from the taper junction. There are a range of conventional stems that can be and are used with the Birmingham Hip modular head. This mixing and matching of components could be the underlying issue. Unfortunately, in this study information regarding the different stems used was not available.

Addition of another metal-metal interface leads to corrosion related complications, especially when differing metals are combined[17,18]. Collier et al.[22] looked at the taper interface between 139 modular femoral components. In 91 femoral head and stem couples the same alloy was used and none of the implants examined in this group showed evidence of corrosion. Of the 48 implants that utilized a titanium stem with a CoCr head, 25 showed evidence of corrosion[22]. The mixing of metals in THA is one of the factors that contribute to corrosion at the taper junction as this can permit galvanic corrosion. Although the material loss at the junction is relatively small as shown in a study by Matthies et al.[2], the relative greater increase in Co rather than Cr may give an insight into the integrity of the taper junction. Cooper et al. reported on 10 patients with metal-on-polyethylene bearings that underwent revision for symptoms including pain, instability and swelling. Co levels were found to be higher than Cr levels and it was concluded that corrosion at the head neck taper can cause adverse local tissue reactions[23]. This suggests that Co:Cr ratio could potentially aid in discovering whether the culprit of problematic metal debris is from the bearing surface or the modular junctions. However cobalt is more soluble than chromium, therefore cobalt is more readily dissolved into the blood and this may affect the Co:Cr ratio. If this proves to be the case then it questions whether a well-fixed stem should be revised if the Co:Cr ratio suggests that the modular junction is a cause for concern.

Blood metal ion levels play an important role in the surveillance of MOM implants. The MHRA have suggested a threshold of 7ppb, above which suggests possible further investigations for the symptomatic patients[24]. However, blood metal ions below this threshold does not fully equate to a well-functioning implant. In this study, we have shown that in failed retrievals there are a large number below this level. The increase of Co and Cr, especially in implants with a modular junction does not appear to be equal. In modular implants, it appears that the Co increases more than Cr and this may be due to the taper junction. The Co:Cr ratio could possibly be used to risk stratify implants that undergo taper failure. Therefore, a possible alteration to the reporting of clinical reference levels used to monitor patients with implants that contain Co and Cr levels, could possibly include a Co:Cr ratio. The threshold of 7ppb for Co and Cr levels set by the MHRA may need to be augmented for modular implants to acknowledge the influence of the taper junctions.

Limitations

We acknowledge that there are several limitations to this study. This study has investigated different groups of patients that have not been demographically matched which can introduce confounding factors to our results. Patient factors such as kidney function, occupational exposure and dietary supplementation were not identified. In this study, there were no well-functioning THAs and failed BMHR to compare results to. The cause of failure was not determined for every implant and possibly could affect the blood metal ion levels, such as component impingement. The analysis of blood metal ion levels were performed at different laboratories that can introduce measurement differences. In our group of failed THAs there was a number of various stems used which will affect the geometry and characteristics of the modular taper junction. Unfortunately, not all stems could be identified as some stems were well fixed and left in situ, therefore not revised.

Conclusion

The full significance of blood metal ion levels and their correlation with the in-vivo performance of MOM bearings are not fully known. There are a large number of MOM bearings, which have failed with blood metal ion levels less than 7ppb. However, till more is known about the significance of blood metal ion levels we cannot advise on how this value should be altered. This study which focused on implants with the same metallurgy showed a trend of higher Co:Cr ratio in patients with a MOM THA that may be attributed to metal debris from the modular stem-head junction. Further work is required to correlate retrieval analysis with blood metal ions to investigate the effect of material loss from modular junctions on blood metal ions and ratios.

Acknowledgements

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Appendix 6: Custom Femoral Stems: A Needed Solution To Modularity

Ilo K, Hallikeri P, Naathan H, Van Duren B, Higgins M, McNamara I, Smith T. ***Outcomes of primary total hip arthroplasty using custom femoral stems in patients with a secondary hip osteoarthritis: a systematic review.*** **Arthroplasty Today 2024 DOI: 10.1016/j.artd.2024.101504**

Abstract

Aims: This systematic review aims to evaluate the effectiveness and safety of custom femoral stems in primary total hip arthroplasty (THA) for patients with secondary osteoarthritis with abnormal hip anatomy.

Methods: Following PRISMA guidelines, databases were systematically searched for studies published on primary THA utilizing custom femoral stems. Inclusion criteria were studies on patients with secondary osteoarthritis receiving custom stems, with outcomes including implant survival, revision rates, and functional scores. Data were extracted from eligible studies, with a focus on overall and cause-specific revision rates.

Results: 689 studies were screened, 13 met the inclusion criteria, encompassing 806 patients and 951 custom THA procedures. The collective follow-up period averaged 11.6 years, with a mean age of 44.6 years. The mean reoperation and revision rates were 6.9% (95% CI: 3.24 – 10.13) and 8.25% (95% CI: 4.02 – 12.47) respectively. The mean intraoperative fracture rate was 3.23% (95% CI: 1.35 – 5.11) and the mean postoperative leg length discrepancy was 4.25mm (95% CI: 1.57-6.93). Mean improvement of postoperative Harris Hip Score as 40.32 (range 30-56).

Conclusions: Custom femoral stems in primary THA demonstrate promising results in terms of implant survival and functional outcomes for patients with complex hip anatomy due to secondary osteoarthritis. These findings support the consideration of custom implants as a viable option for this patient demographic, though further research is warranted for long-term outcomes and direct comparisons with standard prostheses.

Introduction

Total hip arthroplasty (THA) is increasingly being utilised to treat younger, more active patients who have developed secondary hip osteoarthritis due to congenital or acquired conditions[1, 2]. This poses new challenges in surgical practice and implant design, especially when addressing patients with complex hip anatomy[3]. Cemented femoral stems have been the preferred solution for addressing femoral abnormalities due to their versatility and flexibility during surgery to recreate a patient's normal hip biomechanics[4, 5]. However, there are concerns regarding the durability of cemented fixation in younger and more active patients[6, 7]. Furthermore, recent studies have highlighted an increased risk of periprosthetic fractures with certain designs of cemented femoral stems[8-10]. As a result, cementless and biological fixation is desirable[11]. Custom cementless femoral stems have the potential to address such issues, especially for patients with femoral deformities. Achieving primary stability is crucial for THA success, but it can be challenging with standard cementless femoral stems, especially in the presence of anatomical irregularities as the proximal femur has a wide range of anatomical variations[12]. These variations make it difficult to achieve an optimal fit-and-fill of the metaphysis with commercially available prostheses, despite the availability of various anatomical designs and sizes[13].

Custom femoral stems, designed and tailored through advanced preoperative three-dimensional (3-D) imaging techniques, are a promising solution (Figure 1). They have shown considerable utility in treating a range of conditions, including primary osteoarthritis, osteoarthritis secondary to abnormal anatomy, and revision surgery [14-17]. By tailoring the design to the individual's specific anatomy, custom stems ensure a more precise fit, recreating normal hip mechanics and stability, in theory improving their overall outcome[18-21]. For patients with femoral deformity and a long-life expectancy, custom cementless femoral stems represent an encouraging alternative to standard femoral stems. This approach addresses the unique challenges posed by the patient's anatomy and age, offering a solution that aligns more closely with their physiological requirements.

Despite the potential of custom femoral stems, there is a lack of comprehensive clinical outcomes data for custom femoral stems in primary THA, especially in patients with abnormal hip anatomy. This review aims to address this need by examining the clinical outcomes associated with the use of custom femoral stems in secondary hip osteoarthritis, focusing on patients with abnormal hip anatomy and deformity and exploring their benefits and challenges in modern orthopaedic practice.

Figure 1: Design of a custom femoral stem utilising computer tomography imaging]for abnormal proximal femur anatomy

Methods

This systematic review adheres to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[22]) and has been registered with PROSPERO (Registration: CRD42023488321).

Search Strategy

The search strategy involved an electronic literature search conducted on November 1, 2023, encompassing Medline, Embase, Cochrane, and CINAHL databases. The search terms, including variations of "custom," "stem," and "total hip arthroplasty" were crafted to identify relevant studies (full search strategy in supplementary material). In addition to database searches, reference lists of selected articles, and trial registries were scrutinised to identify further relevant studies.

Eligibility Criteria

Inclusion criteria comprised of studies reporting clinical outcomes of custom femoral stems designed from preoperative 3-D imaging in secondary hip osteoarthritis. Studies where the population group majority (>50%) was primary osteoarthritis were excluded. The exclusion criteria also encompassed non-English studies, those published before 2000, revision THA studies, custom femoral stems not made with 3-D imaging, cemented stems, narrative reviews, expert opinions and case reports.

The titles and abstracts of all references from the search results were screened for inclusion by two independent reviewers (KI, PH). These authors then reviewed the full-text of the studies, and disagreements between the two reviewers were resolved through review and consensus with a third reviewer (HN).

Data Extraction

Three reviewers (KI, PH, HN) independently reviewed each study and extracted relevant review data. This included: year of publication, population characteristics, indication for surgery, type of stem, surgical approach, follow-up duration, type of acetabulum component and patient demographics. Outcomes including revision rates, reoperation rates, post-operative leg length discrepancies, survival rates of the femoral stem and both components, and pre- and post-operative patient-reported outcomes were also collected.

Outcomes

The primary outcome was reoperation events. Secondary outcomes included revision and survival, intraoperative complications, post-operative complications, leg length discrepancy, patient-reported outcome measures and health resource use/cost-effectiveness analysis data.

Critical Appraisal

The quality of each study was evaluated using the Joanna Briggs Institute Checklist, an appraisal tool for case series which is an approved method to assess the methodological quality of these studies [23]. This checklist consists of 10 questions and a point was scored for each, giving a maximum of 10 points. Assessments were performed by one reviewer (KI) and independently verified by two other reviewers (HN & PH).

Data Synthesis

Outcomes from the studies were recorded. Arithmetic and weighted means were calculated. Data extraction tables were reviewed for study heterogeneity. Where there was substantial heterogeneity in study design, population characteristics and surgical procedure, a narrative analysis were performed. Continuous data were assessed using a mean difference and presented with 95% confidence intervals. Dichotomous data were assessed with relative risk and presented with 95% CI. All data were analysed using Prism 10 (Prism 10, GraphPad Software, San Diego, USA).

Results

Search results

A total of 689 studies were identified, of these 202 were duplicates (Figure 2). A further 41 studies were removed as they were prior to the year 2000 and not in English. The remaining, 438 studies were screened using title and abstract. This resulted in the inclusion of 51 studies for full-text screening. Out of these, 13 studies met the criteria for inclusion in the systematic review. All 13 studies reported on the clinical outcomes of primary THA using custom stems designed from 3-D imaging in patients with secondary hip osteoarthritis. One study (Jacquet et al.), reported on two series of patients[24]. All included studies were case series[17, 24-35].

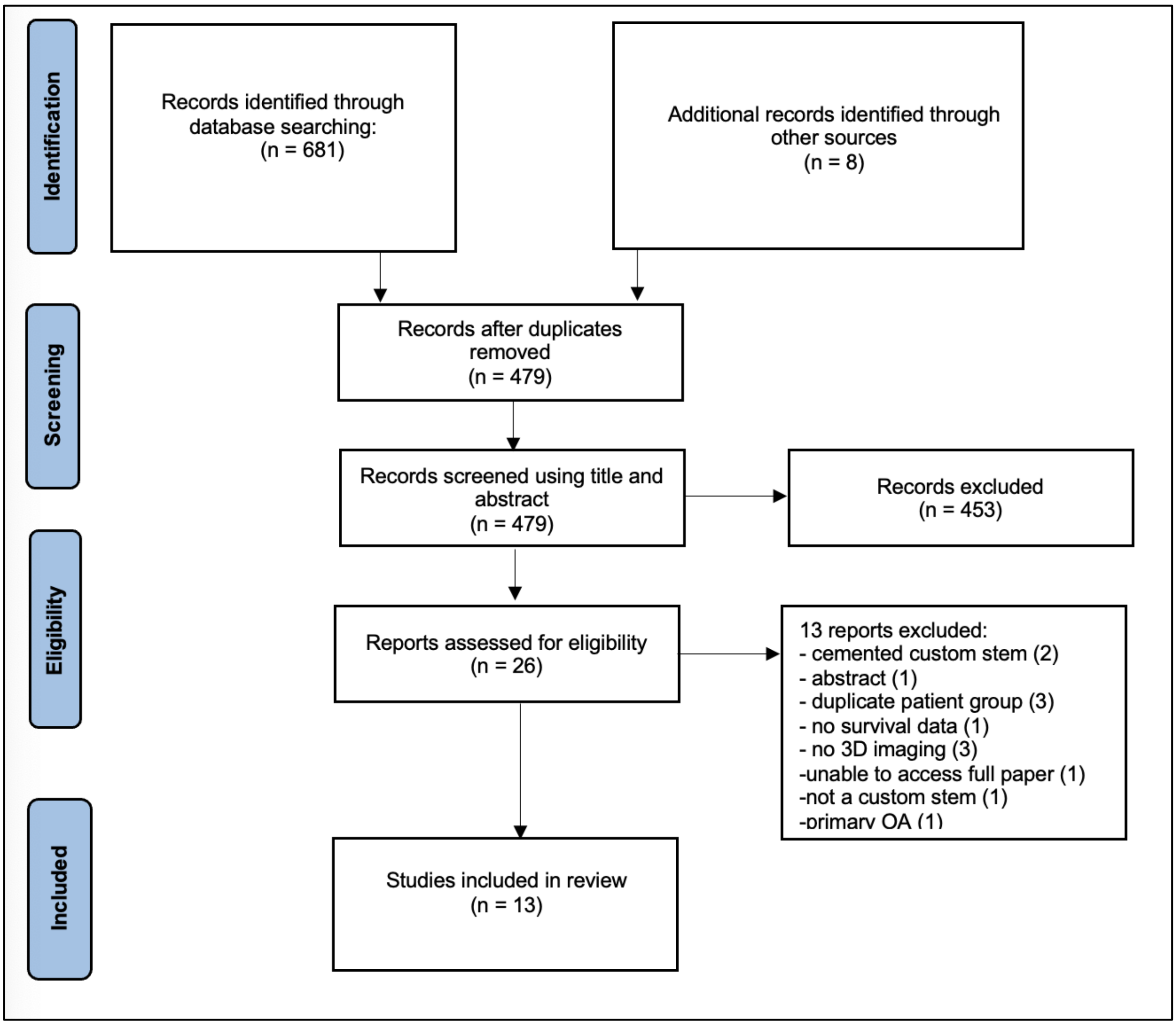

Figure 2: PRISMA flow diagram

Study Characteristics

The included studies exhibited a mean follow-up duration of 11.6 years (95% confidence interval (CI), 9.48-13.74). The collective patient pool across the studies comprised 806 individuals and 951 custom femoral THAs (Table 1). The mean number of custom femoral stems included in each study was 67.9 (95% CI 36.1-99.8). The mean age of patients who received a custom femoral stem was 44.6 years (95% CI 38.4-50.9) with a mean BMI (four studies included the mean BMI) of 25.4kg/m² (95% CI 23.7-27.0). The indications for THA in each study are summarised in Table 1. There were no studies that compared patients with secondary hip osteoarthritis to patients with primary hip osteoarthritis. There were also no studies that compared custom femoral stems to off-the-shelf stems.

Study	No. patients	No. hips	Indication	Approach	Mean age (range)	Male No. (%)	Mean BMI (range)
Jacquet et al. 2020	212	233	Primary OA 17.6%, Secondary OA 49.4% AVN 33% DDH 37.8%, Post traumatic 11.6%	Anterolateral	39.6 (20-50)	106 (50%)	25 (16-48)
	21	26	DDH (Crowe 3 and 4)	Anterolateral	45 (17-73)	13 (61.9%)	27.2 (16-52)
Flecher et al. 2018	23	23	Hip fusion	Watson Jones	49 (28-69)	13 (56.6%)	25 (19-33)
Pakos et al. 2015l	67	86	DDH	Posterolateral	Median 48	7 (10.50%)	Median 26.81
Akbar et al. 2009	61	72	Dysplasia 34.7% Hip dislocation 11.1% AVN 11.1% OA 2.8% Post-traumatic 16.7% Perthes 11.1% RA 9.7% SUFE 2.8%	Anterolateral	35 (22-40)	33 (54%)	26 (18-41)
Flecher et al. 2007	79	97	Congenital hip dislocation Crowe 1 =38.1% Crowe 2= 28.9% Crowe 3= 13.4% Crowe 4= 19.6%	Watson Jones	48 (17-72)	5 (6.3%)	Not stated
Al-Khateeb et al. 2014	14	15	Perthes	Anterolateral or Posterior	32.8 (23-55)	6 (42.9%)	Not stated
Koulouvaris et al. 2008	38	48	Congenital dislocation of hip	Posterolateral	47 (22-69)	Not stated	Not stated
Benum et al. 2010	83	83	Primary OA 19% Dysplasia 57% Perthes 12% RA 6) Post-traumatic 1% AVN 2% Other 2%	Direct lateral	46 (20-60)	36 (43.4%)	Not stated
Sakai et al. 2006	77	99	Congenital hip dysplasia Crowe 1= 47.5% Crowe 2 = 41.4% Crowe 3 = 11.1&	Posterolateral	54 (40-73)	7 (9.1%)	23.6 (17.3-30.6)
Sewell et al. 2011	25	40	Skeletal dysplasia	Anterolateral or Posterior,	37.5 (18-61)	15 (60%)	Not stated
McCullough et al. 2006	25	42	Inflammatory Polyarthropathy	Not stated	21(11-35)	7 (28%)	Not stated
Kawate et al 2009	53	55	Dysplastic hips	Posterolateral	60(40-73)	5 (9.4%)	Not stated

Masuda et al. 2016	28	32	Dysplastic hips with previous osteotomy	Posterolateral	62(29-77)	2 (7.1%)	Not stated

Table 1: Characteristics of included studies (AVN = avascular necrosis; DDH = developmental dysplasia of hip; No. = Number; OA = osteoarthritis; RA = rheumatoid arthritis; SUFE = Slipped Upper Femoral Epiphysis)

Design of Custom Stems

Of the 13 included studies of custom femoral stems, there were six different manufacturers, and in one study, the manufacturer was not stated (Supplementary File 2). All custom stems were designed from computer tomography (CT) imaging. They were all uncemented, and 11 studies specified a coating with hydroxyapatite, however not always stating whether fully or partially. Additionally, 10 studies mentioned the material of the femoral stem (titanium alloy), while others did not provide specific material details. The lengths of the custom femoral stems were stated in four studies.

Survival Rates, Revisions, and Reoperations

Eleven studies (N=780) presented reoperation rates (Table 2). At a mean follow up of 11.6 years, the overall mean reoperation rate was 6.9% (95% CI: 3.24 – 10.13). The range of reoperation rates in the studies was 0%-16%. The overall weighted mean reoperation rate was 5.6%.

Eleven studies (N=780) presented their revision rates (Table 2). At a mean follow-up of 11.5 years, the overall mean revision rate for custom femoral THA prostheses was 8.25% (95% CI: 4.02 – 12.47). The range of revision rates in the studies was 0% to 23.10%. The overall weighted mean revision rate was 7.0%.

Kaplan Meier survival was reported in 11 studies (Table 3). Stem survival with aseptic loosening as an endpoint was reported in 11 studies (N=869). Eight studies (N=488)[26-29, 32-35] reported this as 100% with a follow-up ranging from 6 to 14 years. Three studies (n=381)[17, 24, 25] reported survival of 87.5%-99% with a follow up ranging from 9.3 to 20 years.

Study	Follow-up period in years (range)	Revisions (%)	Reason for Revision	Reoperations (%)	Reason for Reoperation
Jacquet et al. 2020	20 (14-27)	23 (9.9%)	Cup -7 for AL - 6 for PE wear Both implants -3 for AL -7 for infection	12 (5.2%)	4 infections 3 symptomatic HO 1 PP femur fracture 1 liner dislocation 1 painful trochanteric wire 1 GT fracture non-union 1 dislocation
	16 (10-22)	6 (23.1%)	Cup -2 for dislocation -1 for AL Stem -for PP fracture -2 for AL	1 (3.8%)	1 PP femur fracture
Flecher et al. 2018	15 (9-22)	1 (4.35%)	Stem -1 for AL	2 (8.7%)	1 infection 1 head fracture
Pakos et al. 2015	10.6	8 (9.30%)	Cup -3 for AL -1 for PE liner wear Stem -2 for AL Both implants -2 for infection	3 (3.5%)	2 dislocations 1 HO
Akbar et al. 2009	14 (10-16)	3 (4.17%)	Cup -3 for AL	-Not stated	-Not stated
Flecher et al. 2007	10.25 (83-182)	6 (6.2%)	Cup -2 for AL -2 for dislocation Stem -1 for stem fracture Both implants -1 for infection	1 (1.0%)	1 dislocation
Al-Khateeb et al. 2014	10.1 (5-15)	3 (21%)	Cup -3 for AL	2 (13.3%)	1 symptomatic HO 1 infection
Koulouvaris et al. 2008	6 (4-8)	3 (6.25)	Cup -1 for mechanical failure Both implants -2 for infection	2 (4.2%)	1 dislocation 1 symptomatic HO
Benum et al. 2010	10	2 (2.41%)	Stem -2 for PP fracture	7 (8.4%)	1 PP femur fracture 4 PE wear 2 pain
Sakai et al. 2006	9.25	1 (1.01%)	Stem - 1 for AL	-Not stated	-Not stated
Sewell et al. 2011	10.1 (4.3-18.2)	4 (10%)	Cup -2 for AL Stem - 1 for infection Both implants -1 for AL	4 (16%)	1 dislocation 2 intraoperative fracture 1 infection
McCullough et al. 2006	11.2 (8-13)	4 (9.5%)	Cup -2 for AL Stem -2 for AL	6 (14.3%)	1 stem subsidence 4 exchange PE line 1 PP fracture
Kawate et al. 2009	7 (5-11)	0	0	1 (1.8%)	1 dislocation
Masuda et al. 2016	13 (10-19)	-	-	3 (9.38%)	3 dislocation

Table 2: Rates and reasons for revision and reoperations in included studies (AL = aseptic loosening, PE= polyethylene, HO = heterotopic ossification, GT = greater trochanter, PP = periprosthetic)

Study	Stem revision for aseptic loosening		Revision of any component for any reason	
	Follow up years	KM survival (95% CI)	Follow up years	KM survival (95% CI)
Jacquet et al. 2020	20	96.8% (95.1-98.5)	20	77.7% (72.4-84)
	15	87.5% (76.5-99.1)	15	72.60%
Flecher et al. 2018	15	95.6% (92.4-98.8)	Not stated	Not stated
Pakos et al. 2015	10	100%	10	95.4%%
Akbar et al. 2009	14	100%	14	86% (64-95)
Flecher et al. 2007	13	100%	13	89.5% (89.2-89.8)
Al-Khateeb et al. 2014	10.1	100%	10.1	79%
Koulouvaris et al. 2008	6	100%	Not stated	Not stated
Benum et al. 2010	10	100%	Not stated	Not stated
Sakai et al. 2006	9.3	99% (0.97-1)	9.3	99% (0.97-1)
Sewell et al. 2011	Not stated	Not stated	Not stated	Not stated
McCullough et al. 2006	Not stated	Not stated	12	71.4%
Kawate et al. 2009	7	100%	Not stated	Not stated
Masuda et al. 2016	13	100%	Not stated	Not stated

Table 3: Kaplan Meir survival data for included studies (CI = confidence interval; KM = Kaplan Meir).

Intraoperative Fractures and Leg Length Discrepancy

Intraoperative fracture rates were reported in 11 studies (N=595) with a mean rate of 3.23% (95% CI: 1.35 – 5.11). The overall weighted mean was 3.19%. All cases of intraoperative fractures were treated with cabling, except one which required no intervention. Leg length discrepancies postoperatively were reported in five studies with a mean discrepancy of 4.25mm (95% CI: 1.57-6.93). The overall weighted mean was 3.08mm.

Postoperative Patient-Reported Outcomes (PROM)

All studies included reported patient outcomes. Ten studies reported their outcomes using Harris Hip Score(HHS; Figure 2)[36], four studies presented Merle D'Aubigne scores[37] and one study presented Hospital for Special Surgery system scores[38]. There was insufficient data to permit meta-analysis with studies not reporting inter-quartile range or standard deviation values for specific timepoints. The mean preoperative HHS was 47.26 (range 41-59), and post-operative HHS was 87.58 (range 80-98). The mean improvement in HHS was 40.32 (30-56). The mean preoperative Merle D'Aubigne score was nine (range 7.6-10) and postoperatively the mean score was 16.63 (range 15.9-17). The one study presenting the hospital for special surgery system score showed an improvement from a median 14 preoperatively to a median 30 postoperatively.

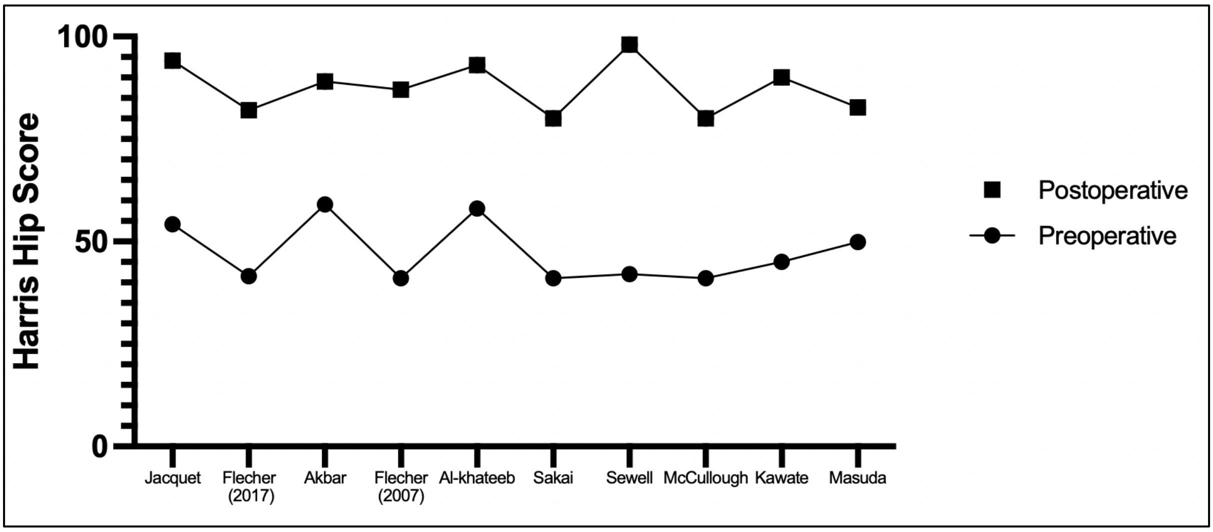

Figure 2: Graph illustrating mean preoperative and postoperative Harris Hip Scores

Quality of Evidence

The Joanna Briggs Institute score, reflecting the quality of evidence, indicated a mean score of 6.08 points out of a maximum of 10, with a range of 3 to 9 points (Table 4). Consistently reported strengths in the literature included clearly reported follow-up results of cases (N=12; 92.3% studies), clear criteria for inclusion in the case series (N=11; 84.6% studies) and clear reporting of the demographics of the participants of the study (N=12; 92.3% studies). Repeated limitations in the evidence included insufficient methods used for identification of the condition for all participants included (N=11; 84.6% studies) and the condition was not measured in a standard, reliable way for all participants included (N=9; 69.2% studies)

Study	JBI Checklist Score
Jacquet et al. 2020	6 (non-comparative, retrospective)
Flecher et al. 2018	4 (non-comparative, retrospective)
Flecher et al. 2018	7 (non-comparative, retrospective)
Pakos et al. 2015	8 (non-comparative, prospective)
Akbar et al. 2009	8 (non-comparative)
Flecher et al.	7 (non-comparative, retrospective)

2007	
Al-Khateeb et al. 2014	9 (non-comparative, prospective)
Koulouvaris et al. 2008	0 (non-comparative, prospective)
Benum et al. 2010	8 (non-comparative, prospective)
Sakai et al. 2006	7 (non-comparative, retrospective)
Sewell et al. 2011	5 (non-comparative)
McCullough et al. 2006	7 (non-comparative)
Kawate et al. 2009	3 (non-comparative, retrospective)

Table 4: Illustrating Joanna Briggs Institute (JBI) Checklist Score and study type

Discussion

Custom femoral stems offer tailored solutions for deformed proximal femurs, optimizing fixation for unique anatomical challenges. However, their use has limitations, requiring a balanced consideration of benefits against potential challenges in clinical practice. The findings of this systematic review indicate the impressive performance of custom femoral stems in complex patient groups, where achieving durable fixation in abnormal proximal femoral bone is a concern[39, 40]. These custom stems demonstrate excellent survival rates against aseptic loosening, with figures ranging from 87.5% to 100% over follow-up periods of 6-20 years. Multiple studies have emphasised that custom femoral stems excel in achieving enhanced metaphyseal fit and fill, a critical factor in boosting both rotational and axial stability[18, 41]. The integration of computer-aided design and manufacturing (CAD-CAM) technologies in crafting these stems has been instrumental in achieving this[42, 43]. This approach not only preserves bone mass but also optimizes load distribution across the hip joint, characteristics vital for femoral stems, particularly in complex clinical scenarios[42, 44]. While the overall survival rate for all components (considering any cause) is somewhat lower, it remains promising in a challenging patient demographic. Notably, most revisions were related to acetabular issues such as loosening and wear, underscoring known challenges with acetabular fixation and durability in these patients[45, 46]. The relatively fewer revisions pertaining solely to the femoral component are reassuring.

Custom femoral stems are designed to achieve optimal fit and fill in the metaphyseal region. This is particularly significant in patients with atypical proximal femoral anatomy, who may also present with abnormal bone quality. Such scenarios inherently raise the possibility of intraoperative challenges, including the risk of fractures and potential discrepancies in limb length, should the custom femoral stem not fit as intended[25, 47]. Encouragingly, the incidence of intraoperative fractures with custom stems has been reported to be low, even falling below the reported rate of up to 5% for cementless stems in primary THA[48-50]. This is a noteworthy achievement, considering the complexity of cases involving custom stems. Furthermore, the rates of postoperative leg length discrepancy with custom stems have also been low. When contrasted with the average discrepancies reported in the literature, which range from 3 to 17mm, the precision achieved with custom stems is commendable[51]. This suggests that with meticulous surgical planning and technique, the risks typically associated with custom stem implantation, such as intraoperative fractures and leg length discrepancies, can be effectively mitigated whilst adequately replicating centre of rotation of the femoral head. Therefore, avoiding impingement and reproducing the original foot progression angle[52, 53]. These findings underscore the importance of careful preoperative assessment and planning in ensuring successful outcomes with custom femoral stems in THA.

Custom femoral stem manufacturing has evolved over the past three decades, shifting from intraoperative silicone mould crafting to preoperative design using radiographs and 3-D imaging. Manufacturers differ in their approach; some modify off-the-shelf models, while others use detailed imaging for a precise anatomical fit. These stems vary in dimensions, shapes, and materials, reflecting diverse manufacturing practices and necessitating treating each stem as a unique, patient-specific implant. This variability challenges standard classification and comparison, as noted in a previous systematic review[54]. Custom stems, designed based on individual patient anatomy and surgeon preferences, offer unique surgical solutions but face challenges like higher costs and extensive preoperative planning[55, 56]. Advancements in technologies such as CAD-CAM and 3-D printing are revolutionizing the manufacturing of custom stems, by making the process more efficient and cost-effective. Although the initial cost of these advanced manufacturing techniques might be higher, this could be offset by reduced risk of revision. These techniques offer enhanced precision and customization, which enable surgeons to provide more tailored and patient-specific solutions, particularly in complex cases where standard implants may not be adequate. As we continue to embrace these innovations, the future of hip replacement surgery looks to offer more personalized treatment options in order to significantly improve patient outcomes and satisfaction.

This review highlights that existing research lacks direct comparative studies between custom and standard femoral stems in secondary hip osteoarthritis, limiting understanding of custom designs' benefits in complex scenarios. The decision to utilise a custom femoral stem, requires deep knowledge of patient anatomy, standard implant limitations, and custom design benefits and challenges. Expertise in preoperative planning and intraoperative techniques is crucial to reduce complications. Current comparative studies show no significant differences, indicating a need for more robust comparative research involving larger cohorts[18, 20, 21, 57-59]. Future studies should include long-term follow-ups to assess custom stems' performance, durability, and effectiveness in mimicking natural biomechanics.

Limitations

Our review is not without limitations. The potential for publication bias, the heterogeneity of the included studies, and the variability in methodologies, follow-up periods, and patient demographics across studies may affect the generalisability of our conclusions. Furthermore, there is variability in the design and manufacturing of custom femoral stems that cannot be controlled and may result in a difference of outcomes. Data for each included study was not available so a meta-analysis of the PROMs could not be performed.

Conclusion

In conclusion, custom femoral stems in primary THA for secondary hip osteoarthritis offer a potentially accurate and reliable solution that can significantly improve patient outcomes. However, their use requires careful consideration of the individual patient’s anatomy, surgical expertise, and the challenges associated with custom implant design and manufacturing. Future research should aim to directly compare results and cost effectiveness of custom and standard femoral stems and provide more robust evidence to guide clinical practice. As orthopaedic surgery continues to evolve, the quest for optimal solutions in complex primary THA will undoubtedly fuel ongoing research and innovation.

<u>Supplementary Material</u>

Supplementary File 1: *Electronic database search strategy*

(custom OR custom* OR “patient specific”) AND (stem OR stems) AND (“total hip arthroplasty” OR “total hip replacement” OR “total hip implants” OR THA OR THR)

Supplementary File 2: *Details of custom femoral stems included in studies (Ti = titanium, HA = hydroxyapatite, 3-D = three dimensional, CT = computer tomography)*

Study	Stem manufacturer	Description
Jacquet et al. 2020	Symbios Ti-Alloy, HA coated	No further details
Flecher et al. 2017	Symbios Ti-Alloy, HA coated	Fitting intramedullary proximal femoral anatomy and accommodating neck offset to the new centre of the joint for patient according to the 3-D CT-based preoperative planning
Flecher et al. 2018	Symbios Ti-Alloy, HA coated	Thick layer coating of porous hydroxyapatite at the proximal part. The HA layer was air plasma sprayed and had a thickness of 75 ± 25 µm. All femoral stems were designed to restore the prosthetic neck anteversion to a normal of 15°. The median femoral neck angle was 130° (IQR 126°–133°) and the median neck length was 48mm (IQR 41.75 mm–56.00 mm). The offset of the prosthesis was calculated according to the opposite hip. If abnormal opposite hip, a 4cm offset for small patients with narrow pelvis and a 4.5cm offset for heavy, obese patients.
Pakos et al. 2015	OS orthopaedic services, GmbH, CT3D-A femoral stem, Ti-alloy, proximal HA-coated	Filling and fitting in the proximal metaphysis. Distal diaphyseal fixation was avoided by reducing the diameter of the stem. The length of the stem ranged from 140 to 160 mm. The macro-structure with a medial bridge and arched structure effectively strengthens both the axial and the rotational stability. A coating layer of hydroxyapatite (HA) (thickness, 80–150µm) was applied to the proximal two-thirds of the implant.
Akbar et al. 2009	- Titanium, HA coated	fitting the intramedullary proximal femoral anatomy and accommodating the offset of the femoral neck to obtain the correct hip centre was then inserted the femoral component was designed to produce proximal loading on the femur and was tapered distally. The mean prosthetic neck-shaft angle was 131.8° (102°-143°)
Flecher et al. 2007	Centre for Biomechanical Engineering, UCL Ti-alloy, HA coated	It had a collar proximally and a lateral flare. The intertrochanteric portion had numerous macro-grooves measuring 1.5mm in depth and 3 mm in width to increase the surface area for osseointegration. The distal end had longitudinal cutting flutes with a polished finish at the tip to optimize insertion. The implant surface was plasma-sprayed and coated with highly crystallinized HA.
Al-Khateeb et al. 2014	-	The custom prosthesis has a custom grit-blasted broach, which is undersized by 2 mm and is used for impaction of the cancellous bone of the femoral canal.
Koulouvaris et al. 2008	Unique; Scandinavia customized prosthesis, Trondheim, Norway) Proximal HA coated	Designed with a neck that gives a femoral neck anteversion of 10° after insertion unless surgeon decides otherwise. Stems were grit-blasted, and the proximal part of the stem was covered with HA only (CAM Implants, Leiden, the Netherlands) and sterilized by gamma technique (Gamma-Master BV, the Netherlands)
Benum et al. 2010	Cremascoli, Milano, Italy TI-Alloy, sandblasted	maximum proximal canal filling. The mean stem length was 121mm (range, 103–135mm). Curved anatomic shape with semicylinder-shaped surface grooves with a radius of 0.5mm were added to the implant in a 5mm grid to enhance mechanical locking onto the bone, femoral components were sandblasted with mesh sand (Al_2O_3, 106–250 um) under 4 bar pressure for a few minutes at room temperature to provide a 4.95 ± 1µm surface finish.
Sakai et al. 2006	Centre for Biomechanical Engineering, UCL (assoc. Stanmore implants) Ti-Alloy and proximally HA coated	Collared, lateral flare, intertrochanteric portion had numerous macrogrooves measuring 1.5mm in depth and 3mm in width to increase the surface area for osseointegration. The distal end had longitudinal cutting flutes with a polished finish at the tip to optimize insertion. The implant surface was plasma-sprayed and coated with highly crystallinized hydroxyapatite.
Sewell et al. 2011	Centre for Biomedical Engineering, UCL proximally HA coated	All had HA proximal third, high-crystallisation HA was used with a thickness of 75 µm to 100 µm. in the first 14 hips, straight-stem femoral components were used, while the subsequent 28 implants had the addition of a proximal lateral flare.
McCullough et al. 2006	Expert stem version 1 Japan Medical Material, Ti-Alloy and proximally HA coated	To obtain the proximal fixation, the distal part was gradually tapered. The stems did not have collars and the proximal one third was coated using 400µm thick porous coating covered with 20µm HA coating. The average stem length was 10cm (range, 8.7-11.4cm) and average diameter was 8.8 mm (range 6.9-11.8mm)
Kawate et al. 2009	Expert stem version 1 Japan Medical Material, Ti-Alloy and proximally HA coated	collarless and the proximal third was coated with a 400µm thick porous coating covered with 20µm HA coating. The centre third was coated using sand blasted coating. Average stem length 10.5cm (range 8.9 – 18.8)

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