

## Management of metal-on-metal hip implant patients: Who, when and how to revise?

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### Abstract

The debate on how best to manage patients with metal-

on-metal (MOM) hip implants continues. With over 1 million patients affected worldwide, the impact is far reaching. The majority of the aggressive failures of MOM hip implants have been dealt with by revision hip surgery, leaving patients with a much more indolent pattern of failure of devices that have been *in situ* for more than 10 years. The longer-term outcome for such patients remains unknown, and much debate exists on how best to manage these patients. Regulatory guidance is available but remains open to interpretation due to the lack of current evidence and long-term studies. Metal ion thresholds for concern have been suggested at 7 ppb for hip resurfacing arthroplasty and below this level for large diameter total hip arthroplasties. Soft tissue changes including pseudotumours and muscle atrophy have been shown to progress, but this is not consistent. New advanced imaging techniques are helping to diagnose complications with metal hips and the reasons for failure, however these are not widely available. This has led to some centres to tackle difficult cases through multidisciplinary collaboration, for both surgical management decisions and also follow-up decisions. We summarise current evidence and consider who is at risk, when revision should be undertaken and how patients should be managed.

**Key words:** Metal on metal hip; Management; Multi-disciplinary; Revision; Decision

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**Core tip:** Evidence supporting the management of metal on metal hips is lacking, and guidance is open to interpretation. Until supporting evidence is available, an evidence based multi-disciplinary approach on a case-by-case basis is considered a safe method to help surgeons make decisions and potentially improve patient outcomes.

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## INTRODUCTION

Considerable debate continues to surround the use and management of patients with failing metal-on-metal (MOM) hip implants. Over a million patients worldwide have been implanted with a MOM device<sup>[1]</sup>, and according to the United Kingdom National Joint Registry (NJR), their use peaked in 2006 [hip resurfacing arthroplasty (HRA)] and 2008 [large diameter total hip replacement (LDTHR)]<sup>[2]</sup>. However, due to several concerns of catastrophic soft tissue reactions leading to early failures and associated complications, medical device alerts were published<sup>[3]</sup>, and MOM hips were subsequently withdrawn from use by the British Hip Society in 2012.

It is clear that there are evolving and changing patterns of behaviour in the failure of MOM hips<sup>[4]</sup>. Many of the early, aggressive failures have been dealt with by revision hip surgery, and we now see a much more indolent pattern of failure in patients who have had devices *in situ* for more than 10 years.

This spectrum of patients from the well functioning, that require only monitoring, to the poorly functioning, which require revision continues to evoke debate among surgeons, especially since the bulk of patients fall between these two extremes Figures 1 and 2. Uncertainties surround thresholds for investigation, revision surgery and methods for surveillance<sup>[5]</sup>. Guidance from international regulatory agencies exists, but tend to reflect the needs of local health authorities, which accounts for some of the variation seen in the guidance<sup>[3,6,7]</sup>.

This review examines the literature on current clinical dilemmas facing surgeons and their patients with MOM hip replacements, and summarises current clinical guidance for how and when patients should be managed.

### MOM hip implants

MOM hip implants consist of two broad types, the HRA and the LDTHR. Since their inception in 1937<sup>[4]</sup>, they have gone through several key design changes and modifications, with the expected fluctuations in their use. Their use flourished in the 1990s with the introduction of the modern HRA and subsequently accounted for approximately a third of all hip replacements being implanted in the United States in 2008<sup>[1]</sup>.

The proposed benefits for using MOM bearings were to reduce the occurrence of polyethylene disease (aseptic loosening) and to allow the use of large diameter femoral head components to reduce the occurrence of hip dislocation<sup>[4]</sup>. However, the inception of highly cross-linked polyethylene and improved ceramic bearing

design, have diminished the perceived advantages of MOM over other bearing surfaces<sup>[8,9]</sup>.

Besides this, metal debris and corrosion products have led to inflammatory reactions within the soft tissues surrounding MOM hip implants and subsequently their early failure and need for revision<sup>[10-13]</sup>. This has led to the subsequent fall in use of MOM hips and intervention from regulators<sup>[3]</sup>.

### Metal debris - A cause for concern?

Metal implants are considered biologically inert, however wear debris is not and is thought to evoke an immune response<sup>[14]</sup>. The release of material from metallic implants occurs by wear, corrosion and mechanical factors such as fretting and third body wear. Cobalt and chromium are the major constituents of alloy metal implants, and are the main cause for concern.

Metal particulate and ionic wear debris from the hip is released into the peri-prosthetic tissues and transported systemically throughout the body<sup>[15,16]</sup>. Studies have demonstrated a peak in blood cobalt levels at 6-mo post implantation and chromium levels at 9-mo, followed by a steady decline over time<sup>[17,18]</sup>. Following revision of a MOM implant to an alternative bearing, blood ion levels reduce but do not normalise in the post-operative period<sup>[19,20]</sup>.

Component design and positioning has been shown to be associated with increased wear and as a result raised metal ion levels<sup>[21-25]</sup>. Blood cobalt and chromium ion levels in patients with unexplained painful MOM hips are double those of well-functioning MOM hips<sup>[13]</sup>.

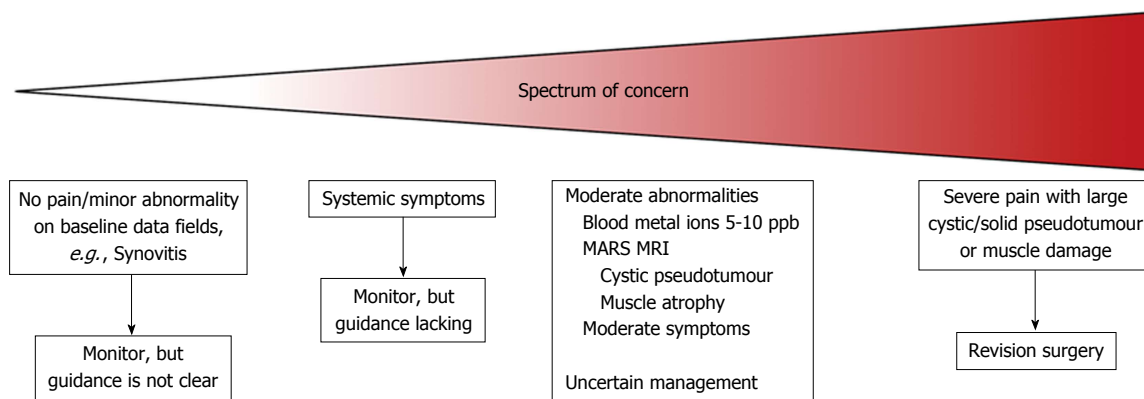
Wear debris can accumulate locally as seen by studies of joint fluid surrounding MOM hip implants<sup>[26-28]</sup>. The level of chromium is greater in joint fluid compared to cobalt, whereas the converse is true for blood analysis<sup>[28]</sup>. However it is believed that cobalt is the species with greatest reactivity causing local tissue inflammatory reactions due to its ready solubility<sup>[29-31]</sup>.

## WHO IS AT RISK?

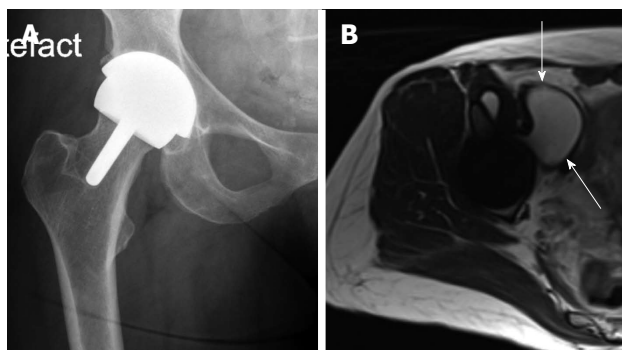
### Local soft tissue reactions

Pseudotumours are well described in patients with MOM hip implants, and can be either solid or cystic. Reported prevalence in both symptomatic and asymptomatic patients ranges from 0.1% to 69%<sup>[10,11,32-37]</sup>. The precise aetiology is not known, however the term aseptic lymphocytic vasculitis-associated lesion (ALVAL) is used to describe the histological features associated with metal hips<sup>[38]</sup>. It has been suggested that a delayed type IV hypersensitivity reaction to metal ions is the potential cause, however this has been challenged<sup>[12]</sup>. Pseudotumours were, however, shown to correlate with elevated blood and hip aspirate metal ion levels suggesting a relation to excessive implant wear<sup>[12,39]</sup>.

Recent evidence regarding the natural history of soft tissues abnormalities is conflicting. Studies report varying degrees of progression in size and grade of pseudotumours, however limitations in sample size,



**Figure 1** Diagram demonstrating the spectrum of concern for patients with metal-on-metal hip implants. The decision on how to manage patients at the extremes of the spectrum is relatively straightforward. However the majority of patients fall into to the middle category, where the management is uncertain or difficult. MRI: Magnetic resonance imaging; MARS: Metal artefact reduction sequence.



**Figure 2** Middle of the spectrum - A typical patient with moderate problems. This 58-year-old very active lady with a right hip resurfacing arthroplasty (A: X-ray AP hip) implanted 8 years ago. She has minimal symptoms and moderately raised blood metal ion levels (Cobalt 13 ppb, Chromium 7 ppb). A magnetic resonance imaging scan (B: Axial T2 weighted image) has revealed a 6 cm cystic pseudotumour anterior to the hip (arrows).

implant type and imaging modality do not readily allow the generalisability of the results<sup>[40-42]</sup>. It appears that when disease progression does occur, it is slow and therefore serial imaging annually is sufficient to identify change. The potential to cause local pressure effects causing necrosis and compression of nearby structures such as the iliac vessels, femoral vessels and the sciatic nerve is also a concern.

Muscle atrophy is now becoming an increasing concern, and is driving the debate regarding the timing of revision surgery in order to prevent irreversible damage. A recent publication demonstrated progressive muscle atrophy using serial magnetic resonance imaging (MRI) scanning in a mixed cohort of patients<sup>[43]</sup>.

**Systemic effects**

Several cases of systemic effects from metal hip implants have been reported, including cardiac, endocrine, neurological and dermatological complications, however this remains a relatively rare occurrence<sup>[44]</sup>. There is a mixture of cases reported in both fractured ceramic hips and in primary MOM hip patients<sup>[44]</sup>. Removal of the implant led to reduced metal ion levels and symptomatic

improvement in several of these cases. Additionally, chronic low dose exposure over several years revealed a negative effect on cardiac function and bone density<sup>[45]</sup>, however these were subtle and sub-clinical. Recent cases of cardiac toxicity have been further highlighted and novel diagnostic techniques are being explored<sup>[46,47]</sup>.

**MANAGEMENT - WHEN SHOULD PATIENTS BE REVISED?**

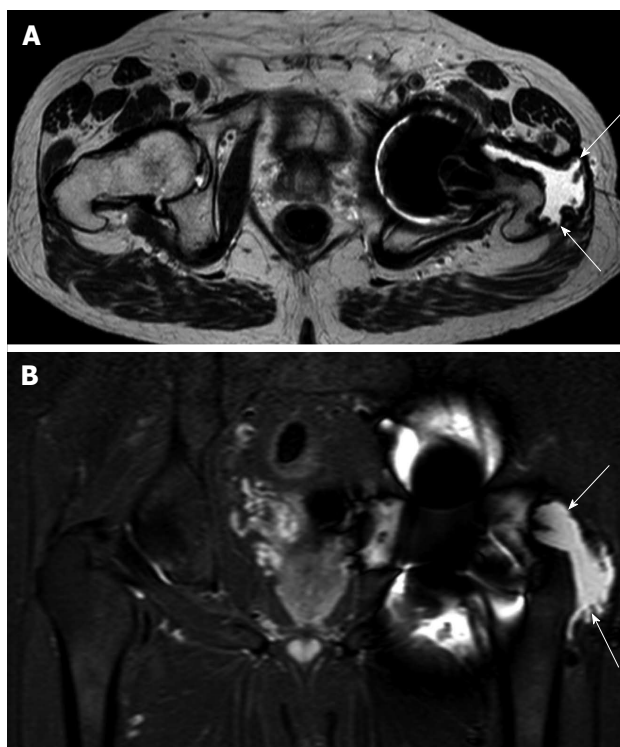
The local and systemic effects of metal particulate and ionic debris from MOM hips have led to increased rates of revision hip surgery. It has also led to significant levels of patient anxiety, not to mention the physical and financial burden of a failed metal implant on the patient and the health services.

The British Hip Society was the first to publish their guidance through the Medicines and Healthcare Products Regulatory Agency (MHRA)<sup>[3]</sup>. The MOM task force (American Association of Hip and Knee Surgeons, the American Academy of Orthopaedic Surgeons, and The Hip Society) in the United States<sup>[48]</sup>, the European Hip Society (EHS) (2012)<sup>[6]</sup>, and most recently the European Commission’s Scientific Committee on Emerging and Newly Identified Health Risks, have also published guidance for surgeons<sup>[49]</sup>. However, uncertainties remain over decision making because of the difficulty - for any guideline - to define or quantify clinical symptoms, imaging findings and clinically important thresholds for blood metal ion results.

**Role of metal ions**

The MHRA currently recommends 7 ppb as the threshold for concern beyond which further investigations are recommended to diagnose complications associated with MOM hip implants. The Food and Drug Administration (FDA) does not currently set an action level, and SCENIHR acknowledge that the level for concern lies between 2-7 ppb based on questions raised regarding the current available evidence.

The population background level of cobalt in blood



**Figure 3** Axial (A) and coronal (B) magnetic resonance imaging. Example of abductor stripping secondary to a pseudotumour (marked by arrows). The pseudotumour can be seen traversing the posterior hip around the greater tuberosity onto its lateral aspect, which is now void of abductor tendon insertion.

has been shown to be 0.5 ppb. There is a correlation seen with wear rates, where 2 ppb can be expected with wear rates of 2 cubic mm per year<sup>[50,51]</sup>.

Since the 7 ppb level was derived from research based on hip resurfacings<sup>[51]</sup>, it has been postulated that this may not apply to stemmed implants. A study including a variety of implant types demonstrated improved sensitivity and specificity with a threshold cobalt level of 4.5 ppb<sup>[50]</sup>.

Various groups have argued for a blood metal ion threshold for revision. The prevalence of patients with blood metal ion levels over 25 ppb was 2.6% in HRA patients, and 3.1% in total Hip Replacement (THR) patients<sup>[52]</sup>. The sensitivity and specificity of the 7 ppb cut-off level have been reported to be 52% and 89%, respectively, indicating that the 7 ppb has relative poor ability to identify MOM failures. The lowering of the cut-off level to 5 ppb increases the sensitivity to 63% and lowers specificity to 86%<sup>[51]</sup>. The Finland group demonstrated that 25 ppb was 99% specific compared to 93% specificity at 7 ppb, however more notably revised patients with metal ions over 25 ppb had a significantly lower oxford hip score 12 mo after revision compared to those with ions less than 25 ppb. The re-revision rate was also higher in those patients with metal ions over 25 ppb<sup>[52]</sup>.

Based on current literature 7 ppb remains a safe level for concern in patients with a HRA implant, whereas the presence of a taper (LDTHR) would prompt a lower

threshold for concern.

### **Role of diagnostic imaging**

The MHRA advise metal artefact reduction sequence MRI (MARS MRI) or ultrasound scan as part of the investigation algorithm<sup>[3]</sup>. MARS MRI appears more appropriate, due to excellent sensitivity and specificity for detection of both superficial and deep lesions<sup>[53-55]</sup>, and also muscle atrophy. Ultrasound is a satisfactory modality for identifying tendon abnormalities<sup>[54]</sup>. Current MARS MRI techniques do suffer from metal artefact that limits the diagnosis of osteolysis, however, improved techniques are being developed<sup>[56]</sup>. Currently computed tomography (CT) scanning is ideal for visualising osteolysis if it is suspected on plain radiographs<sup>[57]</sup>.

In patients where the cause of pain is unexplained, single-photon emission CT (SPECT-CT) has been recommended<sup>[58]</sup>. SPECT-CT was shown to be clinically valuable in diagnosing the cause of pain and influenced management decisions in over half of patients with unexplained pain following a MOM hip arthroplasty despite inconclusive conventional investigations.

### **Pseudotumours**

There is a lack of evidence surrounding the need for revision secondary to pseudotumours, particularly regarding the outcome following revision surgery and the long-term natural history of pseudotumours. This is reflected in the current guidance by the limited detail in how to interpret MRI findings.

It has been shown that revision for pseudotumour is associated with significant post-operative complications<sup>[59]</sup>. In addition, recurrence after revision with excision is possible and may be as high as 30%. If pseudotumours, cystic or solid, are large enough to cause pressure necrosis or stretch of soft tissues, then this is usually an indication for revision surgery (Figure 3).

Large pseudotumours with intra-pelvic extensions along the psoas sheath or arising wholly within the pelvis are of particular concern. These have the potential for compression of neurovascular structures including the iliac vessels. In addition, surgical excision becomes more difficult and often a multi-disciplinary surgical approach with vascular surgeons is required (Figure 4).

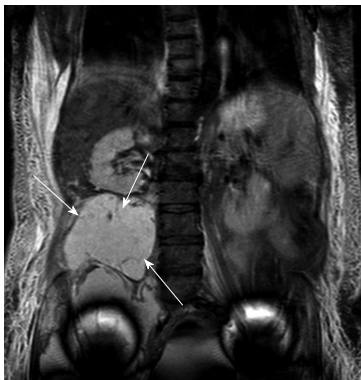
### **Osteolysis**

Osteolysis surrounding MOM hip implants is a further concern that needs to be addressed<sup>[60]</sup>, and one should be vigilant in the presence of very high metal ions. Progressive osteolysis may be an indication for early intervention if the potential for peri-prosthetic fracture is apparent.

### **Muscle atrophy**

There is growing evidence supporting early revision to a non-MOM hip implant to prevent irreversible damage<sup>[38,61]</sup>. Campbell *et al*<sup>[62]</sup> observed that patients can expect a good outcome if their soft tissues remain





**Figure 4** A 58-year-old patient with bilateral large diameter total hip replacement metal-on-metal implanted 9-years ago, moderate hip symptoms and raised metal ion levels (Cobalt 17 ppb, Chromium 13 ppb). She presented to the general surgeons with abdominal pain and distension. Coronal magnetic resonance imaging scan (above) demonstrated a large cystic pseudotumour extending into the pelvis up to the level of the L2 vertebra and abutting the right kidney in the retroperitoneal space (arrows). The cystic pseudotumour was drained prior to surgical excision with both orthopaedic and vascular surgeons present.

intact. A recent study demonstrated progressive muscle atrophy over a period of 12 mo using serial MRI, and noted an association with high metal ion levels<sup>[43]</sup>. Liddle *et al*<sup>[63]</sup> highlight the degree of misdiagnosis possible when planning for revision of MOM hip implants. They describe that pre-operative imaging can underestimate the degree of soft tissue abnormalities seen at revision surgery including a high rate of severe abductor muscle atrophy and stripping of the tendinous attachment<sup>[63]</sup>. If progressive and destructive soft tissue change is possible, predicting those patients that are likely to fail is paramount so that revision can be undertaken early to ensure a better outcome (Figure 3).

Broadly however, a decision to revise should not be based on a single investigation, instead the decision should take into account patient symptoms, activity level, implant type, metal ion levels and imaging findings.

## WHEN SHOULD PATIENTS BE FOLLOWED UP?

Current guidance stratifies patients by risk depending on the type of implant they have *in situ*. Small diameter THR and hip resurfacing arthroplasty is considered low risk, whereas the large diameter THR and the DePuy ASR implants are considered high risk<sup>[3]</sup>. A recent publication went one step further and stratified all current generation MOM hip implants into low, medium and high risk categories<sup>[5]</sup>, based on registry and regulatory advice. More recently however the Regulators state that low risk implants that are functioning well should be monitored according to local hospital protocols, whereas high-risk implants require follow-up for the life of the implant. The Birmingham Hip Resurfacing (Smith and Nephew, London, United Kingdom) has been the best performing hip resurfacing, however concerns have always existed regarding their

use in female patients, and patients with small diameter femoral heads (< 48 mm). As a result of these concerns the MHRA have released further guidance advising against their use in this population and additional advice on the management of patients with these implants *in situ*<sup>[64]</sup>.

However the majority of guidelines do not offer detail on what constitutes follow up, and more importantly which patients require more frequent monitoring. A pragmatic approach would be to take this on a case-by-case basis where the frequency of follow up needs to be tailored to the individual based on the implant risk stratification and the patients clinical status.

Based on the literature, with particular reference to the natural history of soft tissue changes, annual follow up would suffice for those with a medium to high risk implant. Follow up should consist of a history, clinical examination, functional scoring, blood metal ions measurement and X-ray. If clinical concern exists then cross sectional imaging with MARS MRI would be indicated. For low risk implants in individuals with a low risk profile, then less intensive follow-up would be indicated, such as annual questionnaires and 5-yearly clinical review.

One must be mindful of applying a simplistic approach based on implant risk stratification alone, since certain aspects of the patients clinical and surgical history would suggest a heightened risk even in the best performing hip implants. Low risk implants in patients with hip symptoms, evidence of soft tissue abnormality or high metal ions would require closer monitoring. In addition, excessive acetabular cup inclination can lead to edge loading and early failure<sup>[65,66]</sup>, and also female patients with small femoral head size hip resurfacing arthroplasties and females with primary hip dysplasia have worse long term outcomes<sup>[48]</sup>.

## HOW - MULTI-DISCIPLINARY TEAM APPROACH

Some clinical cases are straightforward and decision-making is relatively easy. However, in many instances surgeons experience considerable uncertainty in decision-making because of the lack of guidelines or the difficulty in applying guidelines in complex cases. This gap has led to the use of a multidisciplinary teams (MDT) approach to help interpret the guidance published by the regulatory agencies, with the aim of using surgical experience, tacit knowledge, and evidence-based current best practice to reduce the uncertainty surrounding the management of patients with MOM hip implants<sup>[5]</sup>.

This highlights the need for a more collaborative approach between surgeons, regulators and industry representatives to improve the available evidence and the guidance offered to aid the management of patients with MOM hip implants.

### Role of retrievals

In a recent commentary by Jacobs *et al*<sup>[67]</sup>, the im-

portance of implant retrieval analysis by centres with access to large retrieval cohorts was emphasized as significant in understanding mechanisms of failure and also for developing future preclinical testing models. This reflects the number of developments established through retrieval analysis and includes the relationship with cup position and edge loading<sup>[68]</sup>, the correlation of wear rates with blood metal ion levels<sup>[66]</sup> and the role of frictional torque and fretting currents in LDTHR<sup>[69]</sup>.

## CONCLUSION

The management of patients with MOM hip implants continues to cause concern and difficulties for patients and surgeons alike. The evidence is lacking in certain scenarios, and regulatory guidance can be interpreted differently. When considering which patient requires revision, no single investigation or aspect of the history should be taken in isolation. Decisions should be taken on a case-by-case basis, with consideration given to all aspects of the patient's clinical history and investigation results. A multi-disciplinary approach with shared decision-making, tacit knowledge and surgical experience appears to be a safe and practical approach to improving patient's outcomes.

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