

Review

# Current Insights Regarding Metal-on-Metal Bearings for Hip Arthroplasty †

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† Metal-on-Metal bearings for hip arthroplasty: Cobalt-chromium-molybdenum alloy articulating against itself.

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**Abstract:** Modern small diameter metal-on-metal (MoM) bearings for total hip arthroplasty (THA) have been developed in the nineteen-eighties to address the problem of polyethylene wear related osteolysis. Subsequently large diameter MoM hip resurfacings (HRA) were designed for young and active patients to preserve bone and avoid dislocation. Large diameter MoM THA were originally meant as an easy femoral component-only revision solution for femoral neck fractures in HRA, but were then advocated for primary THA as well. In the last decade however, increasing numbers of revisions for adverse local tissues reactions (ALTR) to metal debris have been reported. These ALTR are due to excessive wear of the MoM bearings, usually related to malpositioning of the components leading to edge loading, or in rare cases to metal sensitivity. Besides the immunological reactions, metal particles and ions have a potential local and systemic toxicity. Wear and tribocorrosion at the taper-trunnion connections of MoM THA but also THA with polyethylene and ceramic bearings have also been recognized as a cause of ALTR with extensive tissue destruction. Despite the fact that the long-term survivorship and functional results of certain MoM HRA are excellent and better than THA in the young and active patients group, MoM bearings have become very unpopular and are likely to be replaced by bearing couples of other materials.

**Keywords:** metal-on-metal bearings; hip arthroplasty; hip resurfacing; wear particles; metal ions; edge loading; toxicity

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Metal-on-Metal (MoM) bearings for hip arthroplasty consisting of cobalt-chromium-molybdenum (CoCrMo) alloys were first introduced in the sixties by McKee and Farrar [1] and by Ring [2]. As early as 1968, Papps et al. published their findings on the toxicity of CoCrMo particles on tissue cultures [3], endorsed by the research of Trevor Rae, who, in 1979, concluded: ‘after the implantation of orthopaedic prostheses, metals can dissolve from the alloys used, some of the metals are toxic. [...] From the biological standpoint, in view of the very much higher levels of soluble metal produced, metal against metal bearings should be avoided.’ [4] By that time, however, MoM hip arthroplasties had been abandoned for the low friction metal-on-polyethylene (MoP) hip replacements developed by Sir John Charnley [5]. When an increasing number of these MoP total hip arthroplasties (THA) had to be revised because of progressive loosening and extensive osteolysis caused by a macrophage response to polyethylene (PE) wear particles [6] whilst hip simulator studies were demonstrating substantially less volumetric wear from MoM bearing surfaces [7,8], MoM hip articulations were reintroduced to solve the problem of polyethylene (PE) particle-induced osteolysis. The imperfections regarding geometry, tolerance and metallurgy (low-carbon content associated with higher wear) of the first generation MoM articulations were resolved in the second generation high carbon content Metasul® MoM bearings (Sulzer/Centerpulse, Winterthur, Switzerland, 1988), which exhibited very promising short- and medium term results [9]. Furthermore, in the nineties,

modern MoM hip resurfacing arthroplasty (HRA) (Figure 1) was proposed to address the inferior clinical results of THA in young and active patients, including the high dislocation rates of the 22 and 28 mm diameter femoral heads of the low friction MoP THA [10].



**Figure 1.** Radiograph of a Metal-on-Metal (MoM) Hip Resurfacing Arthroplasty (HRA).

Early HRA failure modes mainly consisted of femoral neck fractures [11] (Figure 2), treated by revising only the femoral component and preserving the acetabular component and the MoM bearing. Large diameter MoM femoral heads modularly fitting on a prosthetic femoral stem had been specifically designed for these femoral component-only revisions of HRA (Figure 3). Following the good initial results of the Metasul® MoM hips and the reduced risk of dislocation with large diameter femoral heads, these HRA revision big femoral head (BFH) components were also used for primary THA, despite the smaller coverage angle of the acetabular design, the introduction of an additional MoM articulation at the taper–trunnion head–neck junction and despite the fact that these components had not been thoroughly tested for this indication [12,13].



**Figure 2.** Early failure of an MoM HRA due to femoral neck fracture.

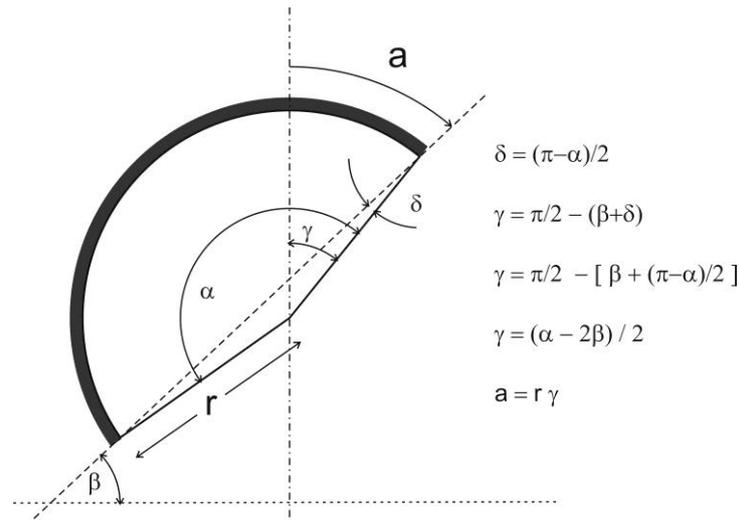


**Figure 3.** MoM total hip arthroplasty with large diameter femoral head.

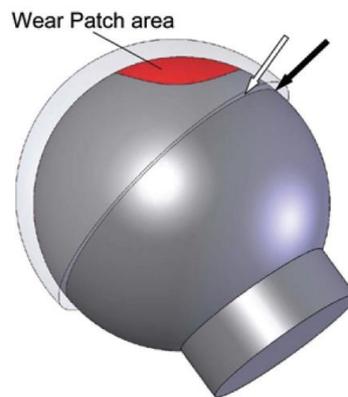
In the meantime, Trevor Rae's warnings remained buried under a load of papers on PE wear and PE particle disease, and were forgotten.

In 2005, Willert et al. published the first report on adverse tissue reactions to MoM hip arthroplasties, including 16 cases of 28 mm-diameter Metasul® bearings [14]. In 2008, the first paper on 'Pseudotumours associated with Metal-on-Metal Hip Resurfacing' from the Oxford group appeared [15] followed by many anecdotal reports on elevated metal ions, metallosis and soft tissue reactions from other centres [16]. In August 2010, the ASR (Articular Surface Replacement) MoM hip resurfacing and ASR-XL MoM THA (DePuy Orthopaedics, Warsaw, IN, USA) were recalled from the market for higher early revision rates due to adverse local tissue reactions (ALTR) to metal debris [17]. In the last decade, it has become apparent that design features including clearance and even more importantly the subtended articular arc (coverage angle) [18,19] (Figure 4) are crucial factors in the articular wear characteristics of MoM hip devices. In MoM hip arthroplasty, an important factor influencing the lubrication is the clearance, which is the difference in radius (radial clearance) or in diameter (diametrical clearance) between the acetabular and the femoral bearing surfaces [20]. (Figure 5). When the clearance is too large, the contact area between the femoral head and the acetabular cup during loading will be small (polar loading), which leads to high contact stresses and increased wear. When the clearance is too small, equatorial contact may occur during loading and both components will be jammed together, which also leads to increased wear (equatorial loading). In the ideal situation, a small wedge exists between the acetabular and femoral component via which a fluid film will be entrained during motion. Modern MoM hip arthroplasty designs and manufacturing have minimized the clearance problem by refining component geometry and reducing the tolerances, but with excessive wear e.g., at the edge, the altered clearance may become an additional factor accelerating implant failure [20]. The most important factor contributing to failure of modern MoM implants has been the coverage angle: a smaller subtended articular arc leads to a smaller contact patch to rim distance (CPR) (the distance between the point of intersection of the hip reaction force with the cup and the closest point on the inner side of the cup rim) [21]). A CPR < 10 mm leads to edge loading with higher wear [18,19,21] (Figure 6) and occurs more frequently with smaller femoral head sizes and when the acetabular component is placed at a higher inclination angle or at an inadequate anteversion angle [18]. This problem was most pronounced with the ASR designs exhibiting very low coverage angles but also with the smaller sizes of the BHR (Birmingham Hip Resurfacing, Smith&Nephew, London, UK) which had a smaller coverage angle and were more at risk for edge loading and increased wear, especially when not placed in the ideal position (Figure 7) [21,22]. Wear-related ALTR, as a result of innate macrophage-dominated immunological reactions to excessive wear debris (in casu metal particles) thus occurred more frequently with smaller sizes [23–25], in diagnoses associated with difficult surgical reconstruction because of anatomical anomalies such as developmental dysplasia of the hip (DDH) and post-traumatic osteoarthritis [23–25] and in

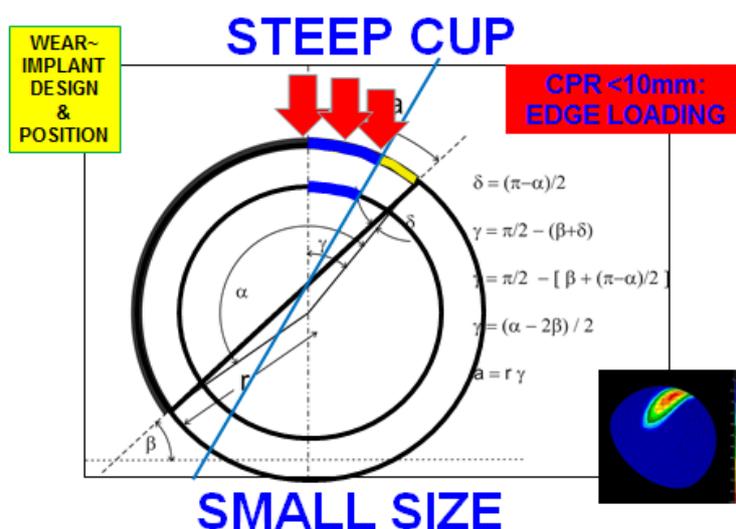
the hands of less experienced surgeons with a suboptimal surgical technique leading to inadequate component positioning [23,24,26,27]. Females are more at risk for ALTR because of all the aforementioned reasons including smaller size, more frequent diagnosis of DDH, and higher anatomical hip anteversion [20–22]. Additionally, women seem to be more prone to metal allergy; cases of ALTR not related to excessive wear but to adaptive immunological reactions to metal particles occurring more often in females [23,24,28]. It needs to be emphasized that the generation of metal particles is not an exclusive characteristic of MoM hip arthroplasty. In wear simulator studies with total knee arthroplasties (TKA), Kretzer et al. have demonstrated that 12% (in weight) of the wear products generated in these metal-on-polyethylene articulations were metallic purely related to wear and without measuring additional soluble metal ion generation by corrosion [29].



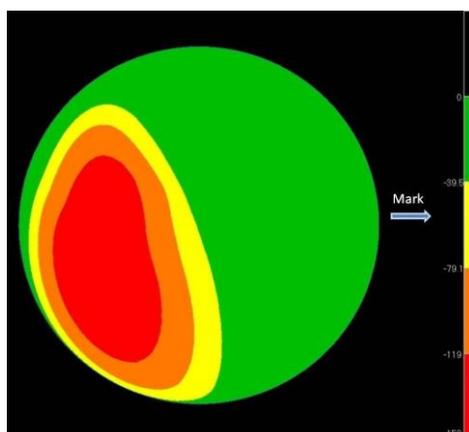
**Figure 4.** Subtended articular arc (a) (coverage angle) of a metal-on-metal articulation.



**Figure 5.** The clearance is difference in radius (radial clearance) or in diameter (diametrical clearance) between the acetabular (white arrow) and the femoral (black arrow) bearing surfaces. Lubrication of the articulation is achieved by fluid being entrapped in that inter-bearing space.



**Figure 6.** Edge loading associated with small coverage angle, steep cup position and/or small size.



**Figure 7.** Retrieval of high wear Birmingham Hip Resurfacing (BHR) HRA, head size 52 mm, implanted in a 59-year-old male with primary osteoarthritis. This was revised after 58 months for cup malpositioning (EBRA measurement inclination 57°; anteversion 51°) associated with very high metal ions (Cr: 25.1 µg/L; Co 72.4 µg/L) and a soft tissue mass. This coordinate measuring machine derived wear depth map shows high wear due to edge loading, (maximum 158 microns).

Besides the generation of metal particles, metal ions are released by corrosion of the metal implant surfaces and also the metal wear particles. The most studied ions in relation to MoM hips are chromium (Cr) and cobalt (Co). Cr ions from MoM hip surfaces usually consist of trivalent Cr<sup>3+</sup> ions that rapidly bind with hydroxides and anions to form Cr hydroxides, oxides and salts used for the regeneration of the passive film on the metal surfaces [30]. These ions are thus less available for bonds with biomolecules (proteins, RNA, DNA) intra- and extracellularly and potentially less toxic. Co ions, on the other hand, remain in a soluble state for a longer time and may bind to intra- and extracellular biomolecules with a potential systemic toxic effect [31].

Elevated systemic (whole blood, serum or urine) levels of Co and Cr are indicative of higher wear or failure of an MoM hip articulation, after exclusion of other sources of metal ions such as occupational exposure, other metal implants or medicinal intake [17,29]. Safe upper levels have been established in unilateral (Cr < 4.6 µg/L; Co < 4.0 µg/L) and bilateral HRA (Cr < 7.4 µg/L; Co < 5 µg/L) [19,32]. These safe levels are confirmed in other studies [33]. Additionally, well performing MoM hips have been associated with decreasing ion levels [33]. Analysis of consecutive ion levels in HRA demonstrated a statistically significant overall decrease of Cr and Co levels with time [34]. In 25% of

patients, ion levels were undetectable at  $\geq 10$  years postoperatively. Increasing metal ion levels correlated with greater cup inclination angles and levels  $>10 \mu\text{g/L}$  were associated with poorly functioning or malpositioned MoM HRA leading to metal particulate debris [34]. The in vivo decrease of metal ion levels with time is in accordance with tribocorrosion studies indicating a lower-wear bedding-in phase after the initial running-in phase of higher wear [35]. These studies also describe the formation of a passive protective film on the articulating metal surfaces after the initial wear-in, preventing further corrosion [35,36]. Ions are then mainly formed by corrosion of the metal particles provided there is no additional surface wear.

The upper acceptable levels outlined above refer to ion measurements of patients with MoM HRA and do not include MoM THA with a large diameter femoral head. Several authors have demonstrated higher levels of Co and Cr ions with MoM large diameter head THA compared to MoM HRA [37,38]. The extra burden of metal particles and ions is probably related to wear due to high tolerances leading to toggling, to the introduction of ridged surfaces on tapers/trunnions to accommodate ceramic heads as well and/or to inadequate load distributions [39–41]. However, crevice corrosion at the taper–trunnion connection between the modular head and the prosthetic femoral neck is probably the most important factor leading to ALTR [42]. The trunnion refers to the proximal conal extremity of the femoral stem or the ‘male’ component of the modular junction. The taper refers to the ‘female’ component of the modular junction i.e., the area inside the femoral head that receives the trunnion. A taper may either be the internal cone of the femoral head or of the sleeve adaptor inserted into the metal or ceramic femoral head to accommodate the prosthetic neck. The confined spaces (crevices) between taper and trunnion allow for an alteration of the chemical environment by trapping fluid, excluding oxygen and lowering the pH [42]. In addition, toxic corrosion products including metal oxides, chlorides and organometallic compounds, but also particles and third bodies may be trapped and accumulate. The low pH and degradation products form a highly toxic environment leading to rapid cell death, necrosis and tissue destruction even with low concentration of metal ions. Crevice corrosion is recognized as one of the failure mechanisms at the taper/trunnion modular connection of MoM THA with large diameter heads (Figure 8) [42,43].

Monitoring of metal ions is advocated as a screening tool for implant performance, in order to detect increased wear at an early stage, and, if necessary, perform a hip revision before extensive tissue destruction has occurred [19]. Furthermore, metal ion measurements are useful to prevent toxic local and systemic reactions which may result from continuous exposure to high levels of ions and particles, especially Co. Animal studies have identified  $\text{Co}^{2+}$  as the major element mediating mainly neurotoxicity but also cardiac and thyroid toxicity [44], whilst  $\text{Cr}^{3+}$  ions alone had no apparent clinical or histo-pathological adverse effects. According to the Mayo Medical Laboratories (Rochester, MN, USA),  $\text{Co} \geq 1 \mu\text{g/L}$  is indicative of Co exposure whilst dosages  $> 5 \mu\text{g/L}$  may be associated with adverse effects [45,46]. However, there is no established toxicity level in total joint arthroplasty (hips and knees). Systemic Co toxicity in relation with MoM hips has been referred to as arthroprosthetic cobaltism [47,48], including symptoms of hearing loss, visual impairment, vertigo, neurological disorders, cardiomyopathy, hypothyroidism, fatigue, cognitive disorders, behavioural and mood changes [23,47,48]. However, systemic Co toxicity is rare, is associated with high systemic Co levels  $>20 \mu\text{g/L}$  [19,23] to  $>100 \mu\text{g/L}$  [46] and is usually reversible after revision of the failing components with decrease of the Co levels [23,47–51]. Furthermore, there is no evidence of nephrotoxicity at 10 years [52].



**Figure 8.** Crevice corrosion inside taper of large diameter femoral head.

Co particles have also been shown *in vitro* to have a toxic effect on macrophages leading to apoptosis and necrosis [53]. In a review paper, Nine et al. tried to correlate biological findings with debris morphology and disintegration [54]. Smaller debris particles from any material (PE, metal, ceramic) are associated with higher inflammatory responses incl. cytokine release. Phagocytosis of particles by macrophages was shown to be size-dependent: nanosized particles from any material highly stimulate cells at high volumetric dosages whilst the size-dependent response rate weakens with lower doses [54]. Sansone et al. showed that CoCr particles may also have an adverse effect on bone by inhibiting osteoblastic functions whilst recruiting osteoclastic precursors, the combination of which may lead to osteolysis and aseptic component loosening [55].

Baskey et al. demonstrated that  $\text{Co}^{2+}$  and  $\text{Cr}^{3+}$  ions are capable of stimulating migration of T-lymphocytes, but not B-lymphocytes, which could explain the accumulation of T-cells in some of the ALTR [56]. These histological features were first characterised as ALVAL (Aseptic Lymphocytic Vasculitis Associated Lesions) by Willert et al. [14]. The term ALVAL is essentially a histological description and is often misused as diagnostic term. Attempts to classify the ALVAL features have led to several scores, which are mostly qualitative but unfortunately too inconsistent with each other to be compared [57,58]. Whether Baskey's findings can also be correlated with a possible delayed type IV hypersensitivity reaction remains to be elucidated. The incidence of failures of joint arthroplasties due to metal allergy is believed to be low, but the diagnosis is difficult as skin patch tests and lymphocyte transformation tests (LTT) are usually inconclusive [59], and the differentiation from a low grade infection often tricky. In a review of the Danish allergy register and the Danish Knee Register however, Munch et al. stated that metal allergy was probably underestimated as cause of failure of total joint arthroplasty, as multiple TKA revisions were more often associated with proven Cr or Co allergies [60].

Genotoxicity of Co and Cr ions has been a concern. *In vitro* studies and studies of cells retrieved from synovial fluid recovered at MoM hip revisions demonstrated chromosomal changes/DNA damage associated with  $\text{Cr}^{3+/6+}$  and  $\text{Co}^{2+}$  ions [61]. These findings do not imply a greater risk for cancer, however. In young female patients with an MoM hip who became pregnant, ion transfer via the placenta amounted to about 50% of the whole blood levels [62]. However, to date, there has not been any evidence of teratogenicity or fetal toxicity. Co ions have also been found in the sperm of men with MoM hips [63], but an effect on paternal fertility comparable to the decreased fertility of stainless steel welders exposed to  $\text{Cr}^{6+}$  [64] has not been demonstrated.

In order to assess possible carcinogenesis of MoM hip replacements, epidemiological studies have been undertaken. Mäkelä et al. matched the Finnish Hip registry and the Finnish Cancer Registry from 2001 to 2010 to compare the overall cancer and death risk of 10,728 MoM hips and 18,235 conventional THA and concluded that the risk was not increased with MoM [65]. Similarly, Smith et al. investigated the National joint Registry of England and Wales and showed that there was no evidence that MoM was associated with an increased risk of cancer [66].

Individual series and hip registries are now publishing excellent long-term (15 to 20 years) survivorship results of MoM THA with the Metasul® bearing and of certain MoM HRA including BHR, CONSERVE PLUS (Microport Orthopaedics, Boston, MA, USA) and RECAP (Biomet Inc., Warsaw, IN, USA) [67–69]. A paper reporting short-term results from the Finnish registry put the BHR forward as the best hip replacement option [70]. Important factors of success were male gender and surgical volume and experience [27]. The latest reports of the Australian Registry show excellent survivorship of the BHR, ADEPT (Matortho, Leatherhead, UK) and MITCH (Stryker, Kalamazoo, MI, USA), with better results than conventional THA in patients younger than 50 at surgery [25]. Functional results including gait analysis and activity assessments are also more favourable for hip resurfacing [70,71]. Most remarkable were the papers demonstrating a significantly lower 10 year cumulative patient mortality rates for MoM hip resurfacing (2.6%) compared to non-cemented (3.2%) and especially cemented THA (7.3%) after adjustment for age, gender, comorbidity, rurality and social deprivation [72,73]. The reasons for these mortality findings have not been elucidated.

For all the aforementioned reasons, MoM bearings have become controversial. Despite the fact that an estimated 1 million current generation MoM hip replacements have been performed over the last 20 years with good to excellent results from experienced surgeons even on the long term, especially in the case of Metasul® THA and BHR HRA [25,67,74], the reports of revisions for unexplained pain and soft tissue reactions have alerted the orthopaedic community, the health authorities and the patients. Advisory organs such as the SCENIHR (Scientific Committees on Emerging and Newly Identified Health risks) of the European Commission [75] and Health authorities such as the Food and Drug Administration (FDA) in the USA [76] and the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK [77] have issued repetitive alerts and recommendations regarding the use of MoM hip arthroplasty and the management of patients. MoM THA with BFH > 36 mm are not to be used anymore except for unusual revision cases. MoM HRA is still acceptable, but implantation in females and in patients with small head sizes is advised against. Patients with an MoM hip replacement are to be followed closely and regular metal ion measurements are advocated. In case of unexplained pain or elevated ion levels, additional cross-sectional imaging with Magnetic Resonance Imaging (MRI) or ultrasound is advised; if ALTR is diagnosed, revision of the MoM hip to a THA with an alternative bearing couple is advocated. Certain countries have banned MoM hips altogether including hip resurfacing (the Netherlands, Sweden, Denmark), and well-functioning and asymptomatic MoM hips are being revised under the pretense that they would be poisonous. In 2015, Smith&Nephew decided to withdraw the BHR smaller sizes from the market [78] and Zimmer-Biomet is ending the 30 year-long Metasul story in December 2017.

Unfortunately, due to all the negative publicity around MoM, there is a major lack of interest and funding for fundamental research to finally elucidate the pathogenesis of the ALTR and investigate individual patient susceptibility. In the meantime, the new problem of trunnionosis or taperosis and associated destructive ALTR described above has become a cause for increasing concern regarding CoCrMo and TiAlV taper-trunnion connections, and also with MoP and ceramic bearings and < 40 mm head sizes [79].

Even though the long-term survivorship and functional results of MoM HRA are excellent and better than THA in the young and active patients group, the future of MoM hip replacement looks gloomy and new bearing couples for hip resurfacing are likely to take over soon.

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