



Consensus statement “Current Evidence on the Management of Metal-on-Metal Bearings”

April 16, 2012

The following recommendations are based on expert opinions of an international multidisciplinary panel endorsed by “European Federation of National Associations of Orthopaedics and Traumatology” (EFORT), “European Hip Society” (EHS), the German “Arbeitsgemeinschaft Endoprothetik” (AE) and the “Deutsche Arthrosehilfe” (DAH).

1. What is the current evidence on the benefits (effectiveness), risks and uncertainties of Metal-on-Metal (MoM) bearings

a. What are the benefits (effectiveness)?

- MoM is currently the only technique for surface replacement.
- There are no polyethylene particles in pure MoM bearings that may cause osteolysis.
- MoM bearings produce less volumetric wear compared to conventional polyethylene.
- There is a reduced risk of fracture in MoM bearings compared to ceramics.
- Large head Total Hip Replacement (THR) (36mm head size and larger) as well as hip resurfacing have a reduced risk of dislocation compared to small head THR (28-32mm head size). In large head THR range of motion increases with the head size (only up to 40mm).
- Hip resurfacing allows more preservation of bone stock on the femoral side when compared to conventional THR.

b. What are the known risks?

Local risks:

- Due to small wear particle size the joint capsule is exposed to a larger amount of particles compared with polyethylene.
- Small heads: Little additional risk of adverse reaction to metal debris (ARMD) when compared to conventional bearings.

- Large heads: Higher risk for ARMD compared to conventional bearings. Elevated risk of taper wear and rim loading.
- Resurfacing: Risk for ARMD esp. with decreasing size, female patients, and low coverage arc. Risk for femoral neck fracture. Potentially more bone consumption at acetabular side in primary cases and in revision cases.

Systemic risks:

- Distribution of metal products to nervous system and other organs through blood circulation.
- Accumulation of metal ions in patients with renal dysfunction with unknown consequences.

c. What are the uncertain issues?

- Long-term effects of metal products (i.e. particles, ions, metallo-organic compounds) including systemic effects (i.e. carcinogenicity, teratogenicity, and toxicity).
- Predictive value of metal ion blood levels for local and systemic adverse effects.

2. Safety assessment of patients after implantation of MoM bearings:

a. Is systematic follow-up recommended? If yes – for which implants and patients?

- YES, for all patients and all implants. For small MoM-heads in THR a systematic follow-up comparable to conventional THR is sufficient. For large MoM-heads and resurfacing closer follow-up is recommended.

b. How long and how frequently should asymptomatic patients be monitored?

For the life of the joint:

- Small heads: as frequent as conventional THR.
- Large heads: Annually.
- Resurfacing: Annually for the first five years, then according to local protocols for patients with conventional THR. If metal ion levels are normal at year one and two postoperatively, the frequency of further annual follow-up investigations may be changed to local protocols for conventional THR . In patients with risk factors such as small size (<50mm femoral component), female gender, and low coverage arc annually for the life of the joint.

c. Which imaging techniques should be applied during follow-up?

- X-rays in all patients.

- In case of clinical / radiographic abnormality additional imaging (ultrasound, CT-scan, and/or MARS-MRI [ordinary MRI without MARS-technique is ineffective]).
- In case of Co-values above a certain threshold (within the range of 2 to 7 µg/L; exact level still to be determined): ultrasound, CT-scan, and/or MARS-MRI.

d. How should monitoring of metal ions be performed: frequency, sources, (blood/serum), technique, reference values?

- Frequency: time of regular follow-up in asymptomatic patients; in all symptomatic patients additionally between regular follow-up.
- Source: Metal ion determination of body fluids can be performed in blood, serum and urine. At present measurement of whole blood is most practicable. Co should be monitored as reference substance.
- Technique: Metal ion measurement must be performed under the rules of internal/external quality control. GF-AAS and ICP-MS are considered as valid. The preferred reporting units should be micrograms/liter (=ppb).
- Reference values: Co-values without clinical concern are at the moment: < 2 micrograms/liter. The threshold value for clinical concern is expected to be within the range of 2 to 7 µg/L (exact levels have still to be determined within this range).
- In increased values above the threshold additional imaging even in asymptomatic patients is recommended.

Note: Recommendations are based on local effects; critical values for systemic effects have not yet been established for patients after MoM implantation.

3. What are the indications for revision of MoM implants for safety reason?

a. What is the appropriate management for local ARMD?

- In asymptomatic patients small fluid collection indicative of ARMD needs close monitoring (repeated imaging is recommended).
- In symptomatic patients and /or patients with progressive osteolysis, large or expanding pseudotumor, and/or progressive neck thinning, and/or Co-ions above threshold level revision may be considered.

b. What is the appropriate management for elevated metal ions in asymptomatic patients? (what is a critical level/cut-off level for clinically relevant complications?)

- Elevated levels at first detection should be confirmed through repeated measurement in asymptomatic patients.
- Above a threshold of 2 to 7 µg/L (exact level still to be determined) additional imaging and closer follow-up is recommended. In case of pathological results of additional imaging and/or further significant increase of Co-level, revision surgery

should be discussed with the patient, as significant metal accumulation with local ARMD is to be expected (especially in Co-values $>20 \mu\text{g/L}$).

- In case of excessive elevation (Co approximately $20 \mu\text{g/L}$ or above), because of potential osteolysis, tissue necrosis, and long-term health effects, revision surgery should be discussed with the patient.
- The individual risk-benefit-ratio should be considered before intervention.

c. Is routine monitoring of metal ions necessary after removal?

- Routine monitoring of metal ions after removal of MoM bearings is not recommended, as no effective interventions can currently be recommended in case of increased metal ions.

4. Appropriate communication/distribution of recommendations to stakeholders

a. What is the best approach to patients?

- Before intended surgery with MoM bearing implants every patient must be informed comprehensively in written and oral form about the benefits, risks, uncertainties, and recommended monitoring concerning MoM bearings. There should be a dialogue between the patient and the surgeon.
- Patients with already implanted large head MoM THR and hip resurfacing should be informed that a higher frequency of monitoring is recommended compared to conventional MoM bearings.
- Risks and benefits should be expressed by patient-relevant outcomes such as morbidity, health-related quality of life, and risk of adverse events. Absolute risk estimations are preferable to relative risk estimations. It should be highlighted that a complete (100%) prediction of positive or adverse outcomes is not possible. Uncertainties concerning both, risks and benefits, should be made explicit.
- Ideally, the patient information should be based on a systematic and comprehensive literature review.
- The information should allow patients informed decision making concerning the implantation of MoM bearings as well as indication for revision in problem-cases with implanted MoM.
- Different stakeholders including but not necessarily limited to patient organizations, orthopedic surgeons, toxicologists, and epidemiologists should be involved in the development of the patient information. Any potential conflicts of interest of persons involved in the development of the patient information should be declared.
- The access to the information should be possible for free without any barrier. Communication of information may be disseminated in different formats, through different media, and/or organizations, but should be identical in content.

b. How should surgeons be addressed?

Information of surgeons should

- cover comprehensively and understandably the benefits, risks, uncertainties, and recommended monitoring concerning MoM bearings including product-related as well as implantation-related aspects.
- include the advice to assess and consider the patient's individual benefit-to-risk-ratio prior to surgery.
- include the recommendations as described above concerning safety assessment of patients after implantation of MoM bearings as well as indication for revision surgery.
- be based on a systematic and comprehensive literature review. The information should highlight the evidence-level of any recommendation (i.e. expert opinion, single RCT, single non-RCT, meta-analysis of randomized / non-randomized studies).
- include a declaration of potential conflicts of interest of persons involved in the development of the information.
- be disseminated in different formats, through different media, and/or organizations, but should be identical in content.
- be provided to other medical disciplines (i.e. neurologists, cardiologists, oncologists) as patients with MoM implants may seek their advice.

5. Unmet medical needs for future research?

a. Pre-clinical research:

It is necessary, to

- investigate the influence of relevant parameters on wear and corrosion of taper connections (taper size, diameter and length), material, texture, head diameter, joint articulation friction, assembly forces and direction. Wear products from taper interfaces and joint articulation should be differentiated, if possible.
- determine the mechanisms creating particles / ions / metallo-organic compounds or aggregates in large ($\geq 36\text{mm}$) and small ($<36\text{mm}$) MoM bearings functioning under ideal and suboptimal conditions. The distribution of nano-particles should be determined.
- determine the potential impact of additional metal ions (i.e. titanium).
- investigate the interaction between wear and corrosion of MoM interfaces and to develop appropriate pre-clinical testing methods; means (by design or metallurgy) to avoid synergistic corrosion effects should be identified.
- establish in-vitro models to investigate local and systemic consequences of metal debris (i.e. 3-d scaffolds).

b. Clinical research

It is necessary, to

- perform comparative tests to identify reproducibility of metal ion measurements among different labs.
- investigate urine as screening tool.
- determine metal ion levels after the implantation of any kind of artificial implant (i.e. knee arthroplasty, spine implants and osteosynthesis devices) and to investigate associations with clinical symptoms.
- establish joint registries with better documentation of revision reasons.
- examine correlations between the presence of wear / corrosion at taper connections and the presence / extent of adverse local tissue reactions (i.e. necrosis, pseudotumor).
- determine true incidence as well as clinical relevance of ARMD in all MoM implants. Adverse reactions from small / large head MoM THR should be compared to that of hip resurfacing.
- determine the local and systemic distribution and pathological effects of particles / ions / metallo-organic compounds produced in MoM bearings.
- investigate effects of long-term exposure to metal ion concentrations between 2 and 7 µg/L by determining the change in circulating T and B cells in patients with varying levels of metal ions.
- determine the incidence and clinical relevance of potential systemic effects of metal products including organ toxicity, carcinogenicity and teratogenicity.

Appendix: Currently, a systematic review on the concentration and distribution of metal ions after implantation of MoM bearings is being undertaken by members of the expert panel. A second systematic review concerning the risk of local and systemic adverse reactions after implantation of MoM bearings including appropriate surgical strategies for revision appears to be necessary to strengthen or modify the present recommendations.

Expert Panel

The following twenty one experts (10 orthopaedic surgeons, 1 allergologist, 2 biomechanic scientists, 2 biomonitoring experts, 2 epidemiologists, 2 basic science/pathology experts, 1 patient organization representative, 1 regulatory authority representative) from 8 countries participated at the consensus conference and contributed to the recommendations:

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