Heavy reading in heavy metal
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Chapter 1

Introduction
Osteoarthrosis (OA) of the hip, also known as osteoarthritis, coxarthrosis or coxarthritis is one of the leading causes of global disability and common in the elderly population with an age-standardised prevalence of 0.85% (95% UI 0.74% to 1.02%). The terminology OA is generally used for non-inflammatory degenerative hip joint pathology that has resulted in cartilage loss. Patients are confronted with pain in weight-bearing situations and OA also results in a decreased range of motion of the hip. Overall, this leads to a lower quality of life. The prevalence of OA is predicted to grow as a result of an ageing population that is getting more obese.

In general, surgical replacement of the hip joint with an artificial prosthesis, known as total hip arthroplasty (THA) or total hip replacement (THR), is the solution in cases where the normal anatomy of the hip is affected by a certain stage of OA leading to clinical problems that cannot be resolved by non-operative treatment. In the Netherlands, this procedure was performed in 2005 in 20,715 patients and according to demographic projections this will increase up to 31,731 patients in 2030. If trend projection is incorporated, this could even rise up to 51,680 patients in 2030.

When a conventional THA is implanted, the femoral head and the collum are surgically resected and a metal stem is placed in the femur and a polyethylene cup or a polyethylene liner in a metal shell is placed in the acetabulum (Fig.1).

Fig. 1. Anterior-posterior (AP) radiograph of a conventional total hip arthroplasty on the right side of the patient
Traditionally all components are cemented. Currently also uncemented (tight fit) components both acetabular and femoral are frequently used as well as (reversed) hybrid concepts.

A conventional THA has several distinctive components. The modular neck or taper is used to ensure that the specific size of the prosthetic head, which can be different in each patient due to the choice of the surgeon, can be placed on the stem. The various lengths, created by preferred head and taper of different lengths together, are used to mimic the initial natural situation in each individual patient. The prosthetic head articulates with the cup which inner diameter matches that of the head. This cup is always the first component that is placed and it is placed in the acetabulum of the patient.4

A conventional THA is characterized by a cemented all polyethylene cup. There are some common complications with the use of this type of THA. First of all, it is prone to wear, which can lead to an eccentric position of the head in the cup (Fig. 2).

A second complication is known as “particle disease”. Particle disease is a granulomatous inflammatory response to a foreign body. It can lead to bone loss which shows radiolucency's on conventional radiographs. These lucencies are visible at the metal bone interface or bone cement interface in respectively uncemented and cemented prosthetic components (Fig. 3).5
Infection, dislocations and component wear result in a limited life span of THAs.\textsuperscript{6}

The degenerative aetiology of OA leads to a peak age incidence in the 7\textsuperscript{th} decade of patients that have a sound indication for hip replacement.\textsuperscript{7,8} The combination of the increased life expectancy of patients and the limited life span of the conventional THA pose a problem for retaining mobility at older age. Moreover, younger patients with OA are also seen with increasing frequency.\textsuperscript{9} Young patients with higher activity levels experienced early failures with THA, whereas their longer life expectancy required that the THA lasts longer.

**MOM THA AND MOM HRA**

The bone resorption and component wear observed in conventional THA led 25 years ago to new concepts of hip replacements with longer survival rates. New materials and new components in THA were used such as metal-on-metal (MoM) THA and MoM hip resurfacing arthroplasties (HRA) with the assumption that these new arthroplasties could overcome the problems of limited life span in younger patients while being more suitable for the young and active patient with sufficient bone stock (Fig.4).\textsuperscript{10-13} The main difference between these THAs and conventional THAs is the articulation of the head and cup that is now by definition MoM instead of metal on polyethylene. The best indication for hip resurfacing seems to be the young and active patient with severe hip arthritis, good hip morphology and adequate bone quality.
The first person to use a MoM prosthesis on a regular basis was the English surgeon George McKee in 1953. It became unpopular in the 1970’s due to the observation of metal particles in cases of failure of the MoM THA that needed revision. With new designs, it gained some popularity in the beginning of the 21st century.\textsuperscript{14}

However, already in 2008 alarming case reports on “pseudotumours” led to increased concerns about these MoM THA and MoM HRA.\textsuperscript{15-17} In 2009 Malviya A et al. reported the incidence of pseudotumours after hip resurfacing by a single surgeon over a 10-year period and in 2012 the disappointing ten-year survival of the Birmingham hip resurfacing (BHR) was presented by Murray DW and colleagues.\textsuperscript{18,19} A pathological capsular reaction due to metal particles released in the hip joint was believed to be the underlying cause of the initially radiologically detected large pseudotumours. These pseudotumours were defined as semi-solid or cystic periprosthetic mass of 2 cm in diameter or larger\textsuperscript{-semi-solid} or cystic periprosthetic mass of 2 cm in diameter or larger. By assessing the hip capsule, a pathological reaction of the hip capsule could be confirmed by means of biopsy of the hip capsule and rule out malignancy.\textsuperscript{20}

Additional case reports were published regarding metal ion deposits from the serum into the thyroid, heart and brain tissue anecdotally leading to cardiomyopathy and encephalopathy.\textsuperscript{21,22}
Initial retrospective studies reported that the incidence of pseudotumours after MoM THA was about 1%.\textsuperscript{15,18} However, these incidences were derived from symptomatic and revision cases and therefore most likely underestimated the true incidence. A prospective cohort study in our hospital (Isala hospital, Zwolle, the Netherlands) showed a substantially higher incidence of pseudotumour formation (39%) and subsequent revisions (12% of the total research population of 116 patients; 31% of patients diagnosed with a pseudotumour) in patients with Biomet M2a-Magnum/ReCap MoM THAs.\textsuperscript{20}

Alerts were sent out by orthopaedic societies and the Dutch orthopaedic association was the first to advice to stop with all (both THA and HRA) MoM large head hip arthroplasties.

**IMAGING OF PSEUDOTUMOURS**

In order to detect a pseudotumour one needs to use radiological imaging to assess the hip capsule. Ultrasound (US), Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) are applied for the detection. All these modalities have their pro’s and con’s.

**US**

No radiation, easy accessibility and the low cost of US make it an attractive surveillance tool, and it demonstrated a high degree of sensitivity in detecting the presence of adverse tissue reactions after MoM hip prostheses.\textsuperscript{23}

Disadvantages of US include that it is not able to assess all tissue surrounding the MoM. Comparison in follow-up is more difficult and it is less suitable for research purposes in quantifying encountered pathology. Its ability to accurately report synovial thicknesses and its sensitivity in detecting smaller, deep tissue deposits have not been investigated yet.\textsuperscript{24}

**MRI**

MRI is also used without potentially harmful radiation.\textsuperscript{25} However, the cost and time associated with the use of MRI as a surveillance tool remains a concern. MRI is unique in its ability to predict the severity of tissue destruction found at revision and the degree of tissue necrosis found at histologic evaluation.\textsuperscript{24}

The presence of metal is a problem especially if only conventional MRI sequences are applied but the presence of metal is of course also a problem with the use of CT and US. The use of specific, metal artifact reduction sequences (MARS) such as MA-VRIC (multiple acquisition variable-resonance image combination) and SEMAC (slice encoding for metal artifact correction) have increased the ability to both identify and characterize soft tissue lesions when compared with conventional MRI sequences.
Furthermore, in predictive models, the maximum synovial thickness and the presence of solid synovial deposits on MRI have greater sensitivity and specificity in detecting aseptic lymphocyte-dominant vasculitis-associated lesion (ALVAL) scores and quantifying intraoperative tissue damage than isolated serum ion levels.\textsuperscript{24}

In 2011 an MRI grading system was described which proved to be reliable for evaluating ALVAL in MoM prostheses using MRI but it was limited in differentiating mild disease from infection and it was not investigated whether this grading system correlated well with subsequent revision.\textsuperscript{26} In addition MRI does not detect acetabular osteolysis.\textsuperscript{27}

Overall, the main difficulty with MRI is that screening large cohorts of patients puts a lot of stress on already existing waiting lists for MRI in the radiology department and it is the most expensive modality.

\textbf{CT}

Until 2010 CT was not routinely used as the first-choice modality. This was probably mainly due to radiation burden and lack of visualization of the soft tissue around the hips. The main difficulty of CT in the MoM HA population was also the metal artefacts from the very large MoM implants that obscured the readability of acquired CT scans of the hips.\textsuperscript{28}

Relative low cost, the accessibility of CT, the possibility to assess different component orientations, evaluation of osteolysis in the acetabulum, all in combination with new dedicated CT metal artefact reduction techniques improving readability, paved the way for the use of CT as a primary tool for radiological evaluation of the MoM hip arthroplasty population.

\textbf{CT AND BONE MINERAL DENSITY MEASUREMENTS}

In cases where MoM THA has led to a significant pathological capsule reaction, the metal cup needs to be replaced by a conventional polyethylene cup, all polyethylene or as a polyethylene liner in a metal shell. Resection of the metal cup in the MoM-configuration often damages the native remnants of the acetabulum in such a way that before a new cup can be placed, additional hardware needs to be installed to keep the cup in the correct position (Fig. 5). If there is not enough surrounding bone or the surrounding bone present is not strong enough, additional hardware cannot be placed unless augmentation with bone graft is used routinely with homogeneous cancellous bone impacted in the deficient acetabulum. Thus, it is important for the orthopaedic surgeon to be aware of the bone status, more specific the bone mineral density (BMD), of the acetabulum before the start of the revision procedure.
Assessment of the BMD around the prosthesis components is not possible in the case of metal artefacts, due to disturbance of the radiation extinction defined by Hounsfield Units, but the acetabular bone at zone I according to De Lee and Charnley is free of metal artefacts.\(^\text{29}\) With the daily reality of a high amount of surgical revisions of MoM THA it could be useful if CT would be able to not only detect pseudotumours, evaluate component orientation, but in addition could also detect and quantify osteolysis in the acetabulum all in a single scan. With this approach, different causes for revision could be addressed in one scan.

**CT AND O-MAR**

Until the release of dedicated metal artefact reduction techniques, the pelvis in case of an inserted THA could be considered “no man’s land” due to severe metal artefacts. It was very difficult to read the soft tissues in the pelvis that were obscured by these metal artefacts. An experienced eye was capable of looking through, past, or behind the metal artefacts but with the introduction of orthopaedic metal artefact reduction software (O-MAR) this became much easier for every reader. Using O-MAR the reader is able to actually see the tissues in the pelvis between THA on both sides such as the posterior wall of the bladder, the pelvic floor muscles and delineation of the recto
sigmoid (Fig. 6). Although O-MAR was designed for large metal implants, there was actually no evaluation of O-MAR in patients with THA.\(^{30}\)

The high incidence of pseudotumours after MoM THA and HRA and subsequent revisions warranted a screening program in our hospital (Isala hospital, Zwolle, the Netherlands) which was later adopted in the Netherlands. All patients involved were invited for intensive follow up consisting of an outpatient intake, quantification of serum metal ion levels and radiological evaluation by means of conventional radiographs and computed tomography (CT).

Because of the necessity to screen a large cohort of patients (>700) and to subsequently reduce pressure on the logistic capacity of the radiology department and associated costs, we decided to use CT as a primary screening tool. In addition, the advantage of CT is that it offers the possibility to measure the orientation of different components in THA and it can be used to assess BMD which is essential and meaningful in the indication procedure for revision surgery. During the follow up program an unusual amount of revisions had to be performed.

The large-scale use of CT put us in a special position since other investigators used ultrasound (US) and/or magnetic resonance imaging (MRI) for the evaluation of cohorts of these specific patients. Moreover, it gave us the opportunity to investigate dedicated MARS in CT.

(a) (b)

Fig. 6. Axial CT images of the pelvis in bilateral total hip arthroplasty with large head metal on metal without (a) and with O-MAR (b)
OUTLINE OF THE THESIS

In this thesis, we described 5 years of investigating the value of CT-imaging for the stratification and prevalence of pseudotumours in several screening cohorts that had been treated with a MoM THA or MoM HRA. In addition, the biological behaviour of acetabular bone, which is important when a revision is indicated, was investigated. Finally, the capacity of an orthopaedic metal artefact reduction (O-MAR) software tool to actually reduce metal artefacts in imaging was assessed.

Chapter 2

The use of CT for the pre-operative evaluation of the hip joint and planning of a hip resurfacing is reviewed. We describe a robust, easy-to-use five-point grading system (I to V) for morphology of the hip capsule based solely on morphological changes to the hip capsule observed in MoM THA.

Research question:
1. What is the spectrum of capsular disease in a screening population of patients with MoM THA?

Chapter 3

The description of the spectrum of pathology that can be seen by the radiologist in CT scans from MoM THA patients in a screening population, needs to be clear and meaningful for the orthopaedic surgeon.

A refined more comprehensive CT classification than described in chapter 2 is presented that shows clinical correlation with revision and is therefore of use for communication between radiologists and orthopaedic surgeons.

Research questions:
1. How reliable is the designed CT classification between observers?
2. How does the CT classification relate to surgical revision?

Chapter 4

We investigated the prevalence of pseudotumours and analysed whether we could identify risk factors for pseudotumour formation after MoM HRA with a BHR. The BHR is the result of a significant different prosthesis design of MoM THA that leaves the collum femor is relatively intact and only resurfaces the femoral head with metal that articulates with a metal cup. MoM orthopedic implants thus differ in design and therefore it is possible that patient populations differ in presented pathology. In this chapter, we discuss the prevalence of capsular reactions in MoM HRA with a BHR.
Chapter 1

Research question:
1. What is the prevalence of pathological capsular reactions in MoM HRA?

Chapter 5

Density measurements in CT depend on intrinsic patient variables. Therefore, we scanned a small cohort of patients with an external phantom during the first follow-up in order to be able to correlate Hounsfield Unit (HU) measurements with the external phantom. We compared both phantom based CT density measurements with Phantom Less Based Bone Mineral Density measurements (PLBMD) to investigate whether the use of an internal reference standard for fat and muscle could serve as a replacement for the external reference standard with a phantom.

Research question:
1. Can we measure BMD without the use of a phantom on non-iodine CT-scans of the pelvis?

Chapter 6

After the introduction of the PLBMD method in the pelvis we investigated whether MoM THA results in bone loss of the acetabulum over the course of time. In addition, we investigated whether the inflammatory environment in case of a pathological capsular reaction of the hip capsule leads to more bone loss of the acetabulum by using the contralateral hip in which no surgery was performed as internal reference.

Research questions:
1. Does the MoM THA result in bone loss of the acetabulum over the course of time?
2. Does the inflammatory environment in cases of pathological capsular reaction of the hip capsule lead to more bone loss of the acetabulum?

Chapter 7

In general, metal artefacts impede reading soft tissue and bone in CT-imaging. Post-processing tools may contribute to creating better images. Because of the large patient population in our hospital that received a metal implant, we used a special dedicated O-MAR add on for our 64-slice system. We aimed to optimize the CT image of the hips in our 64-slice scanner, by dealing with metal artefacts, to quantify the strength of this visually beneficial post processing software tool and to investigate whether the produced images also reflected in vivo or in vitro reality.
Research question:
1. Can we quantify the observed improved image quality in CT by use of the dedicated metal artefact reduction post-processing tool O-MAR?
REFERENCES


