



**TITLE:** Metal on Metal Hip Resurfacing as an Alternative to Total Hip Arthroplasty

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**PUBLISHER:** California Technology Assessment Forum

**DATE OF PUBLICATION:** October 19, 2011

**PLACE OF PUBLICATION:** San Francisco, CA



## **METAL ON METAL HIP RESURFACING AS AN ALTERNATIVE TO TOTAL HIP ARTHROPLASTY**

*A Technology Assessment*

### **INTRODUCTION**

The California Technology Assessment Forum (CTAF) is requested to review the scientific evidence for metal on metal (MoM) hip resurfacing as an alternative to total hip arthroplasty. This is an update to the CTAF assessment done on this same topic in 2010<sup>1</sup>.

### **BACKGROUND**

Disease affecting the hip joint is usually caused by osteoarthritis (OA), the most common form of joint disease<sup>2</sup>. OA is chiefly a disease of aging; 90% of all people have radiographic features of OA in weight-bearing joints by age 40<sup>3</sup>. It is characterized by changes to the structure of the entire joint, particularly degeneration of cartilage and hypertrophy of bone at the articular margins<sup>4</sup>. The presenting symptom of osteoarthritis of the hip is generally pain, which may be associated with a limited range of motion; though pain in the hip may be referred from other regions of the body, referred to other structures (such as the knee) or may be confused with other etiologies such as trochanteric bursitis.

Hereditary and mechanical factors may be involved in the pathogenesis of OA. Obesity is a risk factor for knee osteoarthritis and probably for the hip. Participation in competitive contact sports increases risk as do jobs requiring frequent bending and carrying; for example, farming carries a significantly increased relative risk for OA<sup>5</sup>.

OA of the hip joint contributes to morbidity for the individual and costs to society. Overall, OA is the sixth leading contributor worldwide to total years lost to disability, or disability adjusted life years (DALYs)<sup>5</sup>. Individuals with hip OA may suffer from pain, stiffness and loss of function, adversely impacting their health related quality of life. The direct and indirect societal costs attributable to OA are enormous. For example, individuals with OA are more likely to reduce work hours or take early retirement. Older adults with symptomatic arthritis report greater medical utilization and health care

costs compared with people not reporting arthritis<sup>6</sup>.

Rheumatoid arthritis (RA), an inflammatory arthropathy, may also lead to degeneration of the hip joint, but because it is a systemic condition is unlikely to affect the hip joint alone. Involvement of the hip joint in RA occurs in ten percent to 40% of individuals<sup>2</sup>. Other conditions that can cause secondary OA are avascular necrosis, congenital dislocation, Paget's disease, ankylosing spondylitis and traumatic arthritis.

Treatment for degenerative disease of the hip includes pharmacological and non-pharmacological measures, including lifestyle interventions. Analgesics such as acetaminophen and narcotics can treat the pain associated with the disease and improve function; non-steroidal anti-inflammatory medications, such as ibuprofen, can also be used and are more effective in more advanced disease but are less safe. Corticosteroid injections are a mainstay of treatment for OA and RA, though injections into the hip joint often need to be done under radiographic guidance<sup>7</sup>. Lifestyle interventions used to prevent or ameliorate the progression of OA include weight loss, exercise and physical therapy. Surgical interventions include arthroscopy, MoM hip resurfacing arthroplasty (HRA) and total hip arthroplasty (THA). More than 168,000 total hip arthroplasties are performed annually in the United States<sup>8</sup>.

In the 1950's the concept of resurfacing the arthritic socket, as well as the femoral head, emerged, but the material used (first Teflon and then methacrylate cement) and design flaws led to numerous device failures and adverse events, such as avascular necrosis<sup>9</sup>. The third generation of hip resurfacing emerged in England in the 1990s, and while there are at least ten different commercially available hip resurfacing systems, to date only the Birmingham Hip Resurfacing (BHR), the Cormet 2000, and the Conserve Plus systems are FDA approved. All three of these systems use a MoM Cobalt-Chromium articulation, but they use different combinations of materials for the backing of the acetabular component. While there are differences in materials and design, all hip resurfacing devices consist of two parts: a cup shaped acetabular component and a cemented femoral cap with a stem that inserts into the femur.



The potential advantage of MoM hip resurfacing over THA is that it allows for most of the femoral head to be preserved and only replaces the surface of the joint; this maintains the femoral canal and can make revision surgery, if necessary, less complex<sup>10</sup>. Thus, MoM hip resurfacing has been promoted for younger patients with end-stage OA of the hip or RA, traumatic arthritis, hip dysplasia or avascular necrosis for whom conventional THA is not expected to last their lifetime. Other potential advantages of hip resurfacing over THA include earlier return to function and less restriction on function compared to THA. However, one expert points out that the posterior approach favored in resurfacing devascularizes the femoral head, possibly permanently, potentially leading to avascular necrosis over time<sup>11</sup>. Hip resurfacing is considered by most to be a more challenging operation for the surgeon than THA and requires specialized training and a significant learning curve<sup>12 13,14</sup>.

The 2007 CTAF assessment concluded that the peer-reviewed literature had not kept pace with changes in hip resurfacing technology; most of the published literature consisted of case series from single surgeons, and there were no randomized controlled trials of FDA approved hip resurfacing devices.<sup>1</sup> The 2010 assessment was conducted to review the peer-reviewed literature of the three FDA approved MoM hip resurfacing systems published since the 2007 assessment, with a particular focus on randomized controlled trials (RCT) and comparative study (level 1-4) evidence.

In August, 2010, DePuy Orthopedics issued a voluntary recall of their ASR hip resurfacing systems after information from the UK National Joint Registry indicated that revision surgeries were higher than had previously been reported. The DePuy hip resurfacing system, was undergoing clinical trials in the U.S. and was being marketed overseas. On May 6, 2011, the FDA issued orders for post-market surveillance studies to manufacturers of metal on metal hip systems. CTAF is now reviewing the topic again in light of the Food and Drug Administration's (FDA) recent request that manufacturers of all metal hips undertake emergency studies of patients. We are again focusing on identifying any new randomized controlled trials or comparative studies, but in addition, including studies evaluating potential safety issues.



## TECHNOLOGY ASSESSMENT (TA)

**TA Criterion 1: The technology must have final approval from the appropriate government regulatory bodies.**

Metal on Metal Hip Resurfacing systems are categorized as Class 3 devices by the FDA and under the product code NXT. A search of the FDA database shows that the main product systems approved as of August 2011 include

- The Birmingham Hip Resurfacing (BHR) system (Smith & Nephew Inc., Memphis, TN, USA) which received FDA PMA approval in 2006.
- The Cormet 2000 Hip Resurfacing System (Corin USA, Tampa, FL, USA) which received FDA PMA approval in July 2007.
- Wright Medical Technologies (Arlington, TX, USA) CONSERVE Plus Hip System received FDA PMA approval in November 2009.

There are several other hip resurfacing devices which have been developed but which have not received FDA clearance at this time.

**TA Criterion 1 is met.**

**TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.**

The Medline, Embase, and Cochrane clinical trials database, Cochrane reviews database and the Database of Abstracts of Reviews of Effects (DARE) were searched for relevant references through July, 2011. At the time of the 2010 assessment, the majority of the search results were published case studies, there were four RCTs, two since the 2007 CTAF assessment and none of



which studied an FDA approved device<sup>15-18</sup>. One of these RCTs resulted in multiple publications<sup>18-22</sup>. There was a final publication which presented the study protocol for a planned RCT comparing MoM hip resurfacing to THA, but didn't state which MoM would be studied<sup>23</sup>. In addition, there were nine publications reporting on six non-randomized comparison studies<sup>24-32</sup>. Since the 2010 assessment, we have conducted a literature search in order to identify any new RCTs or safety related publications. We identified two new published RCTs, both reporting on intermediate outcomes<sup>33,34</sup> and new publications focusing on safety outcomes. We identified nine studies focusing on safety outcomes, five on rates of revision<sup>35-39</sup> and four on elevated ion levels in the blood and pseudotumors<sup>40-43</sup>.

Level of Evidence: 2, 3,4,5

**TA Criterion 2 is met.**

**TA Criterion 3: The technology must improve net health outcomes.**

#### Randomized Controlled Trials

In the 2010 review, we identified four published RCT's of MoM hip resurfacing compared with total hip arthroplasty, none of which studied an FDA approved device. As noted in the 2007 CTAF assessment, the first, by Howie et al, was stopped early due to early failures in the MoM hip resurfacing group<sup>17</sup>. The second, by Venditoli et al, found no difference in satisfaction or complication rates, but the MoM hip resurfacing group had better postoperative functional performance<sup>18</sup>. The third, by Garbuz et al, compared a non-FDA approved device to large diameter MoM total hip arthroplasty and while they found no difference in quality of life (QoL) outcomes, they noted increased serum cobalt and chromium ion levels in both groups, but highest in MoM large head total hip arthroplasty, demonstrating that circulating metal ions are a concern for all MoM hip devices<sup>16</sup>. The final trial, by Lavigne et al, compared a non-FDA approved device to large diameter THA and found no difference in gait speed, postural balance, and clinical scores; both groups achieved similar function to a healthy control group by three months<sup>15</sup>.

Since the 2010 assessment, we identified two additional published RCTs comparing MoM HRA to standard THA. In a study done in the Netherlands, 43 patients were randomized to either MoM HRA with ASR by DePuy (a non-FDA approved device) or THA. The main outcomes were recovery in mechanical muscle strength at one year. Patients who had THA had a slower recovery in maximal lower limb muscle strength than patients who underwent resurfacing. The impact of this on clinical outcomes was not assessed<sup>33</sup>. In the second study, 30 patients were randomized to either MoM HRA (Biomet hip resurfacing system: not currently FDA approved) or THA. The outcome was gait analysis at six and 12 weeks and was reported for 22 participants. There was no significant difference in gait outcomes between groups, but again the clinical significance of this outcome is not clear<sup>34</sup>.

#### Non-Randomized Comparative Studies

Again, as noted above, our search turned up nine publications reporting on six non-randomized comparison studies. (Table 1) All of these studies had small sample sizes and for many of them their comparator groups were either recruited selectively or were historical controls. Only one study (Brennan et al) reported on the BHR and they compared the weight of acetabular reamings for BHR patients compared to differentially selected un-cemented THA patients and found the weights to be similar; this is at best a surrogate marker for potential adverse outcome of a femoral neck fracture<sup>24</sup>.

Of the six publications reporting on the Conserve Plus hip resurfacing system, three reported slightly different comparisons and/or outcomes for overlapping patient populations<sup>27,28,32</sup>, and a fourth may well also be from an overlapping population given that the authors are also overlapping<sup>29</sup>. These were retrospective analyses comparing MoM HRA patients to historical control patients with 'conventional' THA from a separate registry; taken together they found no difference in Harris Hip Score – a measure of pain, function, and range of motion, satisfaction, or range of motion. There was a difference in activity level; however, activity level was different in the two groups at baseline and no adjustments were made for this, possibly because of the small sample sizes. A fifth study had similar findings and similar limitations<sup>25</sup>. The sixth study of Conserve Plus was a retrospective study in which patients acted as their own controls – they

assessed range of motion in those patients in their registry who had MoM HRA on one side and THA on the other, some of which were revisions from prior resurfacing procedures<sup>26</sup>. These authors found no difference by type of replacement, including no difference in the subset of patients with revisions and no difference when stratified by size of implant. Of note, the study was underpowered for these subanalyses.

Two papers reported on the Cormet 2000 hip resurfacing system in the same patient population<sup>30,31</sup>. The earlier report concludes that the resurfacing patients had equal overall clinical success with the ceramic-on-ceramic THA patients in terms of a composite score including Harris Hip Score, 'radiographic evidence of success', absence of device related complications and absence of revision; however, in the later study, MoM HRA group had substantially more revisions (7.1% vs. 1.9%) in a shorter follow-up time frame<sup>31</sup>. Revisions were primarily due to femoral neck fractures and femoral component loosening. The THA group were historical controls. The later report assessed the Harris Hip Score at specific time-points over two-year follow-up in the same two groups of patients, concluding that while there were differences early on, with the THA group doing better at six weeks and the MoM HRA group doing better at six months, there was no difference at 12 or 24 months with >90% of both groups scoring in the excellent range<sup>30</sup>.

**Table 1:** Non-randomized comparison studies of MoM hip resurfacing and total hip arthroplasty

Study	Hip Resurfacing Device	Comparison Groups	Methods	Outcomes	Results	Comments
<b>Brennan et al 2009<sup>24</sup></b>	Birmingham (BHR)	N=31 BHR patients  N=31 uncemented THA patients	Prospective Differential group assignment: obesity, older women, large subchondral pseudocysts, history of AVN to uncemented THA group	Weight of acetabular reamings in two groups adjusted for acetabular size	No significant difference in weight of acetabular reamings.	Differential assignment makes comparison difficult. Outcome is surrogate marker for clinical outcome/complication risk.
<b>Fowble et al 2009<sup>32</sup></b>	Conserve Plus	N=50 Conserve Plus patients  N=35 THA patients	Prospective 2-4 year follow-up Single site, single surgeon	Harris hip score Range of motion Complete relief of pain. SF-12 physical activity scores UCLA activity scores	No significant difference in Harris hip score for resurfacing group compared to controls (97 vs. 96; p=.4) or for range of motion post-operatively.  Resurfacing group with more marked pain pre-op (94% vs. 58%; p=.0001); fewer in resurfacing group had complete relief of pain than in THA group post-operatively (48% vs. 80%; p=.007).  Higher functioning (SF-	No adjustment for baseline clinical characteristics, including baseline measurements of pain and activity scores which differed across groups.



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Study	Hip Resurfacing Device	Comparison Groups	Methods	Outcomes	Results	Comments
					12 physical score, UCLA activity score) at baseline and post-operatively in resurfacing group.	
<b>Le Duff et al 2009<sup>26</sup></b>	Conserve Plus	35 patients bilateral hip replacements, one side resurfacing, one side THA	Retrospective Mean follow-up 7 years Patients act as own controls All resurfacing procedures were primary; 14 THA were revisions (12/14 from resurfacing to THA)	Range of motion	No difference in range of motion. No difference for subset of patients with revisions. No difference when stratified by size of implant.	Strength to have patients as own controls. Still likely underpowered to see a difference. Heterogeneity in which surgery was done first, time of follow-up, whether primary or revision surgery. Time between surgeries not reported.
<b>McGrath et al 2009<sup>27</sup> (same patients as Mont 2009<sup>28</sup>)</b>	Conserve Plus	N=34 Conserve Plus patients requiring conversions to THA (21 with total hip resurfacing; 13 with hemi-resurfacing)  N= matched group of 34 patients with 'conventional' THA	Retrospective Single surgeon for all procedures. Cases subset of cohort of 510 total hip resurfacing and 602 hemi-resurfacing arthroplasties. Matched with parallel cohort of THA during same time period on diagnosis, gender,	Harris hip score Range of motion	No significant difference in Harris hip score (92 vs. 94 points; p=.25), or mean range of motion scores (4.9 vs. 4.8; p=.69) for conversion vs. primary THA patients.	Comparison between those with conversion to THA vs. primary THA; better comparison may be to patients requiring revision of their primary THA since theoretical advantage of hip resurfacing is in great ease of conversion to THA due to bone preservation.



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Study	Hip Resurfacing Device	Comparison Groups	Methods	Outcomes	Results	Comments
			age, BMI, pre-operative Harris hip score, length of follow-up.			
<b>Mont et al 2009<sup>28</sup></b> <b>(same patients as McGrath 2009<sup>27</sup>)</b>	Conserve Plus	N=54 Conserve Plus patients  N= matched group of 54 patients with 'conventional' THA	Retrospective Drawn from same cohorts as McGrath et al 2009 paper; single surgeon. Controls matched to cases during same time period on diagnosis, gender, age, BMI, pre-operative Harris hip score, length of follow-up. 3-year average follow-up (2-5 year range)	Harris hip score Satisfaction Activity score	No significant difference in Harris hip score (90 vs. 91; p=.77), satisfaction score (9.2 vs. 8.8; p=.40) for resurfacing compared to THA.  Larger increase in activity score for resurfacing group (p=.0004); baseline activity scores in resurfacing group also higher (p=.01).	Matching done retrospectively; cases are a subgroup of large cohort – unclear how cases chosen or why studies only a small number.
<b>Zywiell et al 2009<sup>32</sup></b> <b>(same patients as McGrath 2009<sup>27</sup>)</b>	Conserve Plus	N=33 Conserve Plus patients  N= matched group of 33 patients with 'conventional' THA	Retrospective Drawn from same cohorts as McGrath et al 2009 and Mont et al 2009 papers. Matched with parallel cohort of THA during same time period on	Activity score Harris hip score Satisfaction Pain	Mean activity score higher for resurfacing group than for THA group (10.0 vs. 5.3; p<.001).  No difference for Harris hip score, satisfaction or	Matching done retrospectively; cases are a subgroup of large cohort – unclear how cases chosen or why studies only a small number. Attempted to match 54 patients, but



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Study	Hip Resurfacing Device	Comparison Groups	Methods	Outcomes	Results	Comments
			diagnosis, gender, age, BMI, pre-operative activity level.		pain.	couldn't find match for 21 cases. Unclear why matching different in this study than in Mont 2009 study as apparently same cases.
<b>Stulberg et al 2009<sup>30</sup> (same patients as Stulberg 2008<sup>31</sup>)</b>	Cornet 2000	N= 337 Cornet 2000 patients with unilateral hip resurfacing and minimum 2 year follow-up  N= 266 THA patients (ceramic on ceramic) historical controls with unilateral hip arthroplasty	Multicenter Comparison to historical controls. Examined results at similar time points post-operatively up to 2-years.	Harris hip score at 6 weeks, 6 months, 12 months, and 24 months.	At six weeks, THA group with higher scores (p=.01); at 6 months, resurfacing group with higher scores (p<.001); at 12 months no difference between groups (p=.10); at 24 months both groups with >90% with scores in 90-100 range (p=.93).	Historical controls. Only 2 year follow-up.
<b>Stulberg et al 2008<sup>31</sup> (same patients as Stulberg 2009<sup>30</sup>)</b>	Cornet 2000	N= 337 Cornet 2000 patients with unilateral hip resurfacing and minimum 2 year follow-up  N= 266 THA patients (ceramic on ceramic)	Multicenter Comparison to historical controls Non-inferiority study	Harris hip score  Composite clinical success score used for non-inferiority test with 4 components: 1. Harris hip score $\geq$ 80 2. radiographic evidence of success	No difference in Harris hip score at 24 months or at >24 months.  Composite clinical success score difference between two groups = -.015.  More revisions in the	Historical controls. Non-inferiority test was 1-sided test.  Non-inferiority based on composite clinical summary score, but clearly more revisions necessary in the resurfacing group



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Study	Hip Resurfacing Device	Comparison Groups	Methods	Outcomes	Results	Comments
		historical controls with unilateral hip arthroplasty.		3. absence of device-related complications 4. absence of revision  Revision rate  Outcomes examined at 2 –years	resurfacing group (24/7.1% vs. 5/1.9%; no p-value given) at time of publication (16 pre-24 months and 8 in follow-up; 3 pre-24 months and 2 in follow-up).	primarily due to femoral neck fracture and femoral component loosening
<b>Mont et al 2007<sup>29</sup></b>	Conserve Plus	N=15 Conserve Plus patients  N=15 THA patients  N=10 patients with hip osteoarthritis	Retrospective from registry of resurfacing patients and parallel registry of THA patients. Unclear if OA patients recruited prospectively. Used normative database of 30 subjects without disease for gold standard.	Gait speed Hip abductor and extensor moments	Walk speed greater for resurfacing group than for either THA or OA groups, but not greater for THA group compared to OA group.  No difference between resurfacing and THA groups in abductor or extensor moment.	Very small study. Retrospective. No adjustment for baseline differences.

### Studies focused on adverse outcomes or side effects

There have been an increasing number of publications since the past several years focusing on adverse events associated with FDA approved hip resurfacing device systems. The two main types of adverse outcomes are 1) early failure and revision rates and 2) elevated levels of metal ions in the blood.

**Revision rates:** The literature search for the 2010 CTAF update search found four publications since the 2007 CTAF assessment which specifically focus on early failure<sup>44-47</sup>. Of the four studies focused on early failure and revision rates, three were case series and one was a meta-analysis<sup>47</sup>. The case series with the longest follow-up period (mean five years) included patients with varying MoM hip resurfacing devices in place, but most were BHR, and reported a 5.2% failure rate with pain being the predominant reason for revision and loosening of the femoral component the next most common cause<sup>44</sup>. The other study of BHR had a much lower revision rate (2.8%) with a shorter mean follow-up time of 3.5 years, and pain was also the predominant cause, followed by femoral neck fracture<sup>46</sup>. At time of revision, these authors found evidence of metallosis (immune reaction to metal) and necrosis. The meta-analysis included multiple devices for both MoM HRA and the comparator THA patients, although all of the THA had cementless femoral components, and all of the included studies had a young patient population (mean age <55)<sup>47</sup>. These authors found a higher overall failure rate for THA when failure was defined as all reasons, including after revision and asymptomatic radiographic failure. The THA patients had approximately double the follow-up time as the HRA patients (8.5 years vs. 3.9 years). When the authors defined failure more narrowly to focus on the greatest risk with MoM HRA as 'femoral failure due to mechanical failure', the HRA group had about double the rate of failure.

Since the 2010 CTAF review, we identified five additional studies that focused on risk for revision with HRA<sup>35-39</sup>. The first, a single surgeon series of 144 procedures in 130 patients with 10 year follow up, showed that 10 out of 130 patients needed revisions, but there was no THA comparator group<sup>36</sup>. The second, was a case control study which compared 39 HRA recipients with 39 ceramic on polyethylene recipients. They found that over 12-14 years, there were no revisions in the MoM resurfacing group and 13 in the ceramic on polyethylene group.

Two large registry studies compared outcomes in HRA recipients compared with HRA recipients<sup>37,38</sup>. Together these studies included over 12,000 patients with HRA and over 300,000 patients with total hip arthroplasty (THA). ..One study followed patients for up to two years<sup>37</sup> and one followed patients for up to eight years<sup>38</sup>. Both found that revision rates were higher in patients who underwent HRA than in those who underwent THA. In addition, both found that these revision rates were higher in women. Men actually had a lower risk for earlier revision. Smaller femoral head size was found to be a risk for revision in some studies, but not in others.

Finally, a meta-analysis of randomized and controlled trials compared revision rates for young patients undergoing MoM HRA vs THA<sup>35</sup>. They found that revision rates were higher in the HRA group than in the THA group and also found that component loosening was higher in the HRA group<sup>35</sup>.

**Elevated levels of metal ions in the blood:** There has been increasing concern in the literature about blood metal ion levels as a result of wear from MoM hip replacements, in both HRA and THA. While there is no safe or toxic level of chromium and cobalt in the blood, the concern about increased levels ranges from local tissue toxicity, to chromosomal damage and malignant cellular transformation<sup>48-51</sup>. In addition, metal induced hypersensitivity may be a component of aseptic lymphocyte dominated vasculitis associated lesions (ALVAL) which has frequently been seen in association with failed HRA. In addition, there has been concern about the development of soft tissue reactions (pseudotumors) associated with these ion levels.

The literature search for the 2010 CTAF review found four studies reporting on blood metal ion levels<sup>52-55</sup>. The four publications identified during the 2010 review of this topic studied patients with BHR. One found that both HRA and MoM THA patients with small diameter (28mm) heads had similar chromium and cobalt levels, both higher than healthy controls without metal implants<sup>55</sup>. Another study compared unilateral MoM BHR, bilateral MoM BHR with metal-on-polyethylene THA and ceramic-on-ceramic THA<sup>52</sup>. They report the highest chromium and cobalt ion levels with both types of MoM hip replacement, smaller elevation for the metal-on-polyethylene group, and



negligible levels for the ceramic-on-ceramic group. A third study again reported increased ion levels for patients with MoM hip resurfacing implants; however, they found that as the femoral component size increased, ion levels decreased, implying that with less friction and wear there is less release of ions<sup>54</sup>. The fourth study found enhanced lymphocyte activity for nickel, but not for chromium and cobalt; there was no difference for patients with and without pseudotumors (a cystic or solid mass relating to resurfaced hip), although the pseudotumor group was very small (n=10)<sup>53</sup>. Since the 2010 CTAF review, we identified two additional studies focusing on elevated metal ions and two other studies focusing on the development of pseudotumors<sup>40-43</sup>. One study showed an elevation in ion levels in patients with HRA that fluctuated over time<sup>40</sup>, whereas the other study showed no increase with HRA<sup>41</sup>. Pseudotumors were found to be relatively rare in one study (prevalence of 0.10%) but were associated with elevated chromium and cobalt levels<sup>42,43</sup>.

Summary: Although HRA may have some benefits, particularly in younger active individuals, there are also potential risks. Revision rates appear to be higher in patients receiving HRA procedures than in those receiving THA, which is of particular importance since the HRA procedure targets young people. This risk may be particularly high in women. In addition, the elevated levels of metal ions are concerning. Although the clinical significance of these elevated ion levels is still uncertain, they are implicated in the development of ALVAL, often seen in aseptic failure of HRA. Pseudotumors appear to be a more severe manifestation of ALVAL. There is clearly no evidence that the potential benefits outweigh the potential risks.

**TA Criterion 3 is not met.**

**Table 2:** Studies of MoM hip resurfacing focusing on adverse outcomes

Study	Device	Methods	Adverse Events	Comments
<b>Eswaramoorthy et al 2009<sup>44</sup></b>	Birmingham (BHR) Cormet 2000 Conserve Plus McMinn	Multisurgeon case series of 504 patients over 10 years, mean follow-up 5years (range 1.7-11.7)	<u>29 revisions (5.2%) for failure</u> – 23 BHR, 4 Mc Minn, 1 Cormet 2000, 1 Conserve Plus <i>Causes:</i> 11 pain, 7 loosening of femoral component, 4 femoral neck fracture, 3 loosening of femoral and acetabular component, 2 loosening of acetabular component, 1 infection, 1 groin mass <i>Mean time to revision</i> 42 months (range 4-102)	No deaths; no loss to follow-up.
<b>Kim et al 2008<sup>45</sup></b>	Conserve Plus	Multicenter case series of 200 patients, mean follow-up 31 months (range 12-54)	<u>14 revisions (7.0%) for failure</u> <i>Causes:</i> 10 loosening of acetabular component, 2 femoral neck fracture, 1 loosening of femoral component, 1 pain <i>Mean time to revision</i> 19.5 months (range 3-47) <u>Association with failure:</u> Younger age Higher BMI Smaller femoral component	No loss to follow-up.  4/5 surgeons with limited experience with resurfacing prior to study (range 5-30 cases); 5 <sup>th</sup> surgeon had done 80 cases and had no failures in study.  Authors conclude that since most failures due to loosening of acetabular component, likely related to learning curve
<b>Ollivere et al 2009<sup>46</sup></b>	Birmingham (BHR)	Multisurgeon case series of 463 patients over 6 years, mean follow-up 43 months (range 6-90)	<u>13 revisions (2.8%) for failure</u> <i>Causes:</i> 7 pain, 3 femoral neck fracture, 2 dislocation, 1 infection 9 had evidence of <i>metallosis</i> (immune reaction to metal resulting in inflammation & scarring) and necrosis <u>Association with failure:</u> Female Higher BMI Smaller femoral component	2 patients died of 'unrelated causes' and 3 lost to follow-up.  Too few outcomes (failure) to draw firm conclusions about predictive factors, and with observational study cannot draw conclusions about causality.
<b>Springer et al</b>	Multiple for	Meta-analysis: failure	<u>Hip resurfacing:</u> 15 studies, 3002 patients, mean age 46.6	THA studies with considerably



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Study	Device	Methods	Adverse Events	Comments
2009 <sup>47</sup>	both hip resurfacing (including BHR, Cormet 2000 and Conserve Plus) and THA.	rates for young patients undergoing hip resurfacing vs. total hip arthroplasty (THA) with cementless femoral components. Studies through March 31, 2008 including young adults (mean age <55) undergoing TA with modern	<p>(34.2-57.8), mean follow-up 3.9 years (0.6-8.7).</p> <p><u>THA: 22 studies, 5907 patients, mean age 41.4 (32-55.4), mean follow-up 8.5 years (4.8-13.5).</u></p> <p><i>Overall failure rate for any reason (including revision and radiographic failure)</i></p> <p>Hip Resurfacing 3.7 (2.0-6.5) THA 11.6 (7.5-17.4) (Random effects model)</p> <p><i>Femoral failure due to mechanical failure requiring revision surgery</i></p> <p>Hip Resurfacing 2.6 (2.0-3.4) THA 1.3 (1.0-1.7) (Fixed effects model)</p> <p>Hip Resurfacing 2.4 (1.5-3.8) THA 1.3 (1.0-1.7) (Random effects model)</p>	<p>longer follow-up than resurfacing studies.</p> <p>Overall failure rates higher for THA – these results include failure for any reason including after revision &amp; radiographic failure.</p> <p>Authors argue that concern with hip resurfacing greatest for mechanical femoral failure and so focus on this result as providing evidence that ‘modern’ cementless THA in young patients may be just as good or perhaps better than hip resurfacing, negating primary reason for hip resurfacing.</p> <p>Includes devices which are not FDA approved</p>
Jiang, 2011 <sup>35</sup>	Multiple including Cormet, Conserve and Durom	Meta-analysis: Rate of revision for young patients undergoing MoM vs THA . Studies through June, 2009 including adults <65 years old with at least 12 month follow-up	<p><u>4 trials met criteria (N=9680)</u></p> <p><u>Revision rates: Higher incidence of revision in the MoM group than in the THA group (RR 2.60; 95% C.I. 1.31-5.15)</u></p> <p><u>Dislocation: nonsignificantly higher in the THA group</u></p> <p><u>Femoral neck fracture: Incidence may be higher in MoM group but heterogeneity between groups</u></p>	<p>Authors conclude that there is insufficient evidence to determine whether modern MMHRA offers clinical advantages over standard THA for treatment of hip disease in active young patients</p>



Study	Device	Methods	Adverse Events	Comments
			<p><u>Component loosening: Higher incidence in MoM HRA than THA (RR 4.96: 95% C.I. 1.82, 13.50)</u></p> <p><u>Hip functioning scores similar between the two groups but higher activity levels in resurfacing group</u></p>	
<b>Treacy, 2011<sup>36</sup></b>	Birmingham (BHR)	Single surgeon series of 144 consecutive BHR procedures in 130 patients at 10 year follow up	<p><u>Cumulative survival of the BHR: 93.5%</u></p> <p><u>Number of revisions: 10 (out of 130 patients)</u></p>	<p>Hard to interpret without comparative data for THA</p> <p>Relatively few women (26) so hard to compare between genders</p>
<b>Migaud, 2011<sup>39</sup></b>	Metasul, Zimmer	Case control study 39 patients with HRA compared with 39 ceramic on polyethylene with 12-14 year follow-up	Revisions: 0 in MoM group and 13 in ceramic on polyethylene group	Authors conclude that for young active patients, MoM implants have better survival than THA in active young patients
<b>Johanson, 2010<sup>37</sup></b>	Multiple types of hip resurfacing implants including BHR, Durom, ASR and Cormet	3 national joint replacement registry databases of Denmark, Norway and Sweden comparing hip resurfacing outcomes with THA outcomes at two year follow up (N=1,638 HRA and N=172,554 THA)	<p><u>Revision: HRA had an increased risk of revision compared with THA (RR=2.7, 95% C.I. 1.9-3.7) . Greater for women, especially when compared with cemented THA (RR=4.7, C.I. 2.6-8.5) and for HRA vs cemented THA (RR =7.4 (95% C.I. 3.7-150) )</u></p> <p><u>Early revision: risk lower in males (RR=0.5; Femoral head size had no effect on revision rate</u></p>	Authors conclude that these results do not support continued use of HRA
<b>Prosser, 2010<sup>38</sup></b>	Multiple types of hip resurfacing implants including ASR,	Australian national joint replacement registry comparing HRA outcomes with THA outcomes with 8 year	<u>Revision rates: at 8 years, cumulative percent revision of HRA was 5.3% (4.6-6.2) vs 4.0% (3.8, 4.2) for THA. Females had a higher revision rate than males, but after adjusting for head size, rates were similar.</u>	<u>Risk factors for revision of resurfacing: older age (&gt;55 years), smaller femoral head size, patients with developmental dysplasia and</u>

Study	Device	Methods	Adverse Events	Comments
	BHR, Durom, Cormet, conserve Plus	follow up (N= 10.489 patients for HRA and N=129,992 patients for THA)		<u>certain implant designs.</u>
<b>Blood metal ion    Theoretical concern with increased ion levels: local tissue toxicity, inflammation, bone loss, renal insufficiency, immune modulation, hypersensitivity, chromosomal damage, malignant cellular transformation</b>				
<b>Moroni et al 2008<sup>55</sup></b>	Birmingham (BHR)	Non-randomized, prospective comparison of ion levels (chromium, cobalt) from 1) 20 HRA patients with large diameter MoM heads (average 48mm) 2) 26 THA patients with 28mm MoM heads 3) 'healthy subjects'	Median follow up for HRA 24 months Median follow up for THA 25 months  HRA and THA groups both had elevated serum levels of chromium and cobalt compared to healthy controls. There was no statistically significant difference between the operative groups in either ion level.	Unclear how 'selected' patients. Nothing reported about the health controls' baseline characteristics.  Trend toward higher levels of chromium with hip resurfacing, but not statistically significant. Study underpowered.
<b>Hart et al 2009<sup>52</sup></b>	Birmingham (BHR)	Cross-sectional study assessing levels of chromium and cobalt ions and absolute number of circulating lymphocytes in patients with 1) unilateral MoM HRA, 2) bilateral MoM HRA, 3) metal on polyethylene THA, and 4) ceramic on ceramic THA	Both Chromium and cobalt ion levels the highest for both MoM groups (unilateral and bilateral) and the lowest for the ceramic-on-ceramic group. The metal-on-polyethylene group had minimally elevated levels.  MoM unilateral  CD8+ lymphocytes counts were significantly reduced in both MoM hip resurfacing groups.	Safe or toxic level of chromium and cobalt not know. Unclear clinical implications of lowered T-cells under these circumstances.



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Study	Device	Methods	Adverse Events	Comments
<b>Langton et al 2009<sup>54</sup></b>	Birmingham (BHR) (ASR results not reported here; not FDA approved device)	Cross-sectional assessment of relationship of femoral size and acetabular component orientation with circulating metal ion levels in 70 patients with Birmingham hip resurfacing.	Both cobalt and chromium ions were elevated in patients with Birmingham hip resurfacing devices in place.  As the femoral component size increased, the serum ion levels decreased (correlation $-.265$ ; $p=.04$ ).  Acetabular orientation was not correlated with ion levels for those patients with the largest femoral components; however, for those with smaller femoral components, as acetabular anteversion increased, so did ion levels.	Size and positioning of MoM devices impacts serum metal ion levels; it remains unclear what level is safe or toxic.
<b>Kwon et al 2010<sup>53</sup></b>	Birmingham (BHR)	Cross-sectional assessment in 92 patients of relationship between MoM HRA with and without pseudotumor and systemic metal hypersensitivity.  Three groups: 1) BHR and pseudotumor (cystic or solid mass relating to resurfaced hip) N=10 2) BHR and no pseudotumor N=60 3) age-matched controls without metal implant or known metal allergy N=22	Level of enhanced lymphocyte activity only increased for nickel & not for chromium and cobalt in patients with BHR compared with controls.  No significant difference for patients with pseudotumor compared to those without pseudotumor.	Authors conclude that systemic hypersensitivity type IV reactions may not be dominant etiology of soft tissue pseudotumors related to MoM hip resurfacing implant.
<b>deSouza, 2010<sup>40</sup></b>	Corin Cormet	Single surgeon cases series (N=56)	Both cobalt and chromium ions were increased during the first 18 months Levels decline slowly for 5 years and then start rising again up	In contrast to other studies, no differences in circulating ion levels between men and women



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Study	Device	Methods	Adverse Events	Comments
			to 10 years	
<b>Beaule, 2011<sup>41</sup></b>	Conserve Plus	Matched pair analysis THR patients (n=26) matched with MoM patients ((n=26) for gender, femoral hesize and BMI	Chromium: no significant differences between groups at 6, 12 and 24 months  Cobalt: Higher in the THR group than the MoM group at 6, 12 and 24 months  No association between chromium or cobalt and age, gender, head size or cup inclination	Use of a differential hardness bearing with a large head metal on metal THR does not have an advantage with respect to metal ion release
<b>Adverse Local Tissue Reactions</b>				
<b>Canadian hip Resurfacing Study Group, 2011<sup>42</sup></b>	BHR DUROM ASR Conserve Plus Comet 2000 Mitch	Multi-Center survey	A total of 3,432 HRA Follow up for a mean of 3.4 years Pseudotumor in 4/3442 arthroplastids : prevalence 0.10%	Pseudotumors relatively uncommon Associated clinical factors remain to be determined
<b>Kwon, 2011<sup>43</sup></b>		Retrospective studies of patients having MoM HRA at least 3 years ago in single institution (N=201 hips in 158 patients)	Pseudotumors in 7 patients (4%) Pseudotumors were associated with higher cobalt and chromium levels and lower functional scores	Pseudotumors may be associated with increased wear generated from MoM articulations



**TA Criterion 4:           The technology must be as beneficial as any established alternatives.**

Because TA criterion 3 was not met, by definition TA criterion 4 cannot be met. The primary established alternative is THA. While the comparison studies cited above all report results showing equivalent functional results after MoM HRA and THA, these are all small trials with historical controls or differentially selected controls. There are no RCTs of the FDA approved hip resurfacing devices comparing to current conventional THA devices. In addition, the promise in HRA is that it is a temporizing measure for early treatment of hip disease in young adults who will likely need more than one replacement and subsequent revision to THA will be easier than from one THA to another. Yet recent studies have shown an increased risk of failure with HRA, requiring revision after MoM HRA. In addition, there is increasing concern about the effects of the elevated blood levels of cobalt and chromium seen with HRA and their potential clinical consequences. An RCT comparing HRA with THA which has long term follow-up is needed so that the potential benefits and potential risks of each procedure can be appropriately weighted. . In addition, even if MoM hip resurfacing is ultimately shown to be equally beneficial to THA, the long-term health effects remain unclear and while THA can be performed without using a MoM system, other materials have not been successful for hip resurfacing.

**TA Criterion 4 is not met.**

**TA Criterion 5:           The improvement must be attainable outside of the investigational setting.**

Although MoM HRA has been used broadly outside of investigational settings, because TA criterion 3 and 4 were not met, TA criterion 5 cannot be met. Improvement in the investigational setting has not been proven.

**TA Criterion 5 is not met.**



## **CONCLUSION**

The 2007 CTAF assessment stated that “It is not possible to conclude from the current peer reviewed literature that the currently approved hip resurfacing systems in the United States improve health outcomes comparably with the current standard of care, total hip arthroplasty”.

In 2010, when CTAF reviewed this topic, several questions which were of concern during the 2007 assessment remained and we reiterate them here: What is the long term durability of the resurfaced hip compared with THA? What will be the short and long term results when this generation of younger patients who have undergone hip resurfacing are eventually converted to THA? Will there be unforeseen long term complications that will make this revision more problematic than anticipated? What are the long term health consequences of increased low levels of circulating metal ions produced by MoM hip resurfacing?

Now at the time of this assessment, the same questions remain unanswered. Particularly in light of the registry evidence showing an increased revision rate with HRA compared with THA and increasing concerns about elevated metal ion levels, it is incumbent upon the hip resurfacing community to prove the efficacy and safety of MoM hip resurfacing in randomized clinical trials, rather than subjecting young patients to significant potential harm over their lifetimes.

## **RECOMMENDATION**

It is recommended that metal on metal hip resurfacing using the BHR, Cormet 2000, or Conserve Plus devices does not meet CTAF criteria 3-5 for safety, efficacy and improvement in health outcomes for patients as an alternative to total hip arthroplasty.

*The CTAF Panel voted unanimously to accept the recommendation.*

October 19, 2011

This is the third assessment of this technology.



## **RECOMMENDATIONS OF OTHERS**

### **Blue Cross Blue Shield Association (BCBSA)**

A June 2007 assessment by the BCBSA Technology Evaluation Center found that “use of an FDA-approved metal-on-metal total hip resurfacing device as an alternative to THA in patients who are likely to outlive the 10 years or more functional lifespan of a traditional MoM prosthesis meets the TEC criteria.”

### **Centers for Medicare and Medicaid Services (CMS)**

Neither a National Coverage Decision nor a Local Coverage Decision was found through a search of the CMS Coverage database.

### **California Orthopaedic Association (COA)**

The COA was invited to have a representative attend the meeting and to provide an opinion on this technology. COA did not provide an opinion nor send a representative to the meeting.

### **Alliance for Orthopedic Solutions**

The Alliance for Orthopedic Solutions was invited to have a representative attend the meeting and to provide an opinion on this technology. The Alliance for Orthopedic Solutions did not send an opinion nor send a representative to the meeting.

### **National Institute for Health and Clinical Excellence (NICE)**

In August 2011, NICE announced that they will reassessing guidance provided on TA2: Hip disease – replacement prostheses for clinical and cost effectiveness. The announcement can be found at <http://guidance.nice.org.uk/TA2/ReviewDecision/ReviewDecisionAppendix/pdf/English>

### **Canadian Coordinating Office for Health Technology Assessment (CCOHTA)**

In March 2005 the CCOHTA published a document on Minimally Invasive Hip Resurfacing. The CCOHTA notes: “Outcome-based research and long-term follow-up are necessary to assess the clinical and economic impact of a minimally invasive approach to hip resurfacing. There is also a need for defined criteria to determine which patients might benefit from this surgical approach”. In



March 2008, CCOHTA performed a Health Technology Inquiry Service (HTIS) titled: Elevated Blood Ion Levels from Metal on Metal Hip Implants – Biological and Adverse Effects. CCOHTA stated: “Separating theoretical from real risks will be complex and require long term followup, for example, the latency period associated with metal-induced cancers. In the short term, policy/decision makers may be limited to mitigating the potential risks for certain patient groups by researching and identifying possible contraindications s.a. child-bearing potential and impaired renal function.”

### **American Academy of Orthopedic Surgeons (AAOS)**

AAOS is in the process of developing a technology assessment on metal on metal hip systems. Expected completion of the technology assessment is December 2011 after which they will be better able to objectively provide evidence- based answers, share research results, and provide a position. AAOS did not send a representative to the meeting.



## **ABBREVIATIONS USED IN THIS REVIEW**

CTAF	California Technology Assessment Forum
MoM	Metal on metal
OA	Osteoarthritis
DALYs	Disability adjusted life years
RA	Rheumatoid arthritis
HRA	Hip resurfacing arthroplasty
THA	Total hip arthroplasty
BHR	Birmingham Hip Resurfacing
RCT	Randomized controlled trial
DARE	Database of Abstracts of Reviews of Effects
QOL	Quality of life
THR	Total hip resurfacing

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