The effect of the diameter of metal-on-metal bearings on systemic exposure to cobalt and chromium

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The recent resurgence in the use of metal-on-metal bearings has led to fresh concerns over metal wear and elevated systemic levels of metal ions.

In order to establish if bearing diameter influences the release of metal ions, we compared the whole blood levels of cobalt and chromium (at one year) and the urinary cobalt and chromium output (at one to three and four to six years) following either a 50 mm or 54 mm Birmingham hip resurfacing or a 28 mm Metasul total hip replacement. The whole blood concentrations and daily output of cobalt and chromium in these time periods for both bearings were in the same range and without significant difference.

The understanding that osteolysis, induced by particulate wear-debris is a limiting factor in the long-term success of an arthroplasty has led to the resurgence of metal-on-metal bearings. Wear rates for these second-generation devices are much lower compared with conventional metal-on-polyethylene designs.[1]

Metal wear and corrosion generate insoluble metal particles and soluble metal ions, the latter passing into the systemic circulation. Because they are essential elements in the body, there is an effective renal clearance mechanism for cobalt, chromium and molybdenum, the constituent elements of most modern all-metal hip devices. Blood levels represent a balance between the release of metal ions from the device and renal clearance. The systemic release rate can be estimated from a 12- or 24-hour urine collection. There are concerns about the long-term effects of high systemic levels.

Several factors affect bearing wear. *In vitro* and *in vivo* studies have shown that wear and metal ion release are higher in low-carbon cobalt-chrome alloys[2-4] and heat-treated alloys.[5-11] If all other factors are equal, there is no difference in the wear properties of cast components compared with wrought components.[4,12,13]

In vitro studies on the effect of bearing diameter on wear reveal a two-phase effect.[1] Smaller bearings such as those of 22 mm diameter have higher wear rates with increasing diameters, as expected in a bearing in boundary lubrication mode. In larger bearings of 28 mm and above, the wear rate decreases with increasing diameter, as expected from mixed or fluid-film lubrication.

However, the *in vitro* regimes used in controlled wear studies on hip simulators cannot be expected to replicate the wide and varied loading patterns of hips *in vivo*. Therefore, *in vivo* findings often do not correlate with *in vitro* results. It is not known whether larger diameter bearings generate less systemic metal ion release *in vivo*. Our study looked at this issue by comparing both the daily urinary levels (two and five years post-operatively) and whole blood levels (one year post-operatively) of metal ions in patients after larger diameter (50 mm and 54 mm) metal-on-metal hip resurfacing with smaller diameter (28 mm) metal-on-metal total hip replacement (THR) patients.

Patients and Methods

The group of patients in our study had either a well-functioning 50 mm or 54 mm bearing diameter Birmingham hip resurfacing (BHR; Midland Medical Technologies, Bromsgrove, United Kingdom), or a well-functioning 28 mm Metasul total hip replacement (THR Sulzer Orthopaedics, Winterthur, Switzerland). Both bearings are made of high-carbon cobalt-chrome alloy and are not subjected to heat treatment processes in the later stages of manufacturing, although the BHR is made of cast alloy and the Metasul THR is of the forged variety. The BHR has a hydroxyapatite-coated, porous, uncemented acetabular component and a cemented femoral component, both made of as-cast high-carbon cobalt-chrome alloy. The Metasul THR has a cementless, porous-ingrowth titanium acetabular component and either a cemented, polished, tapered

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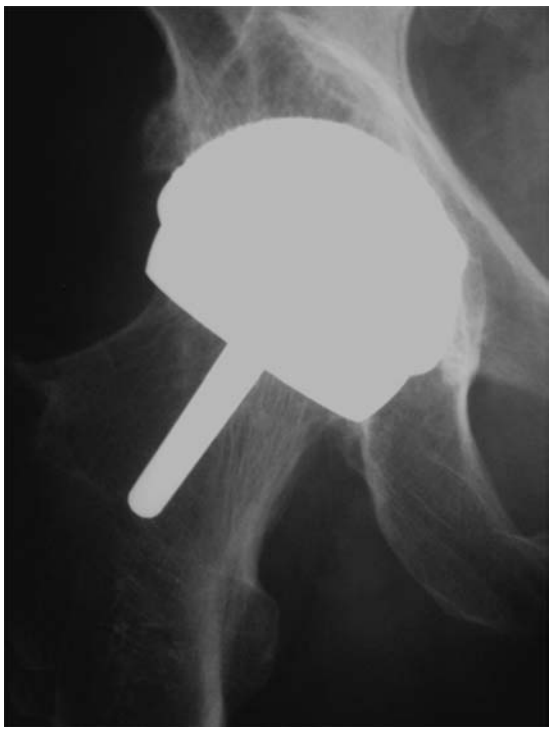

Fig. 1a

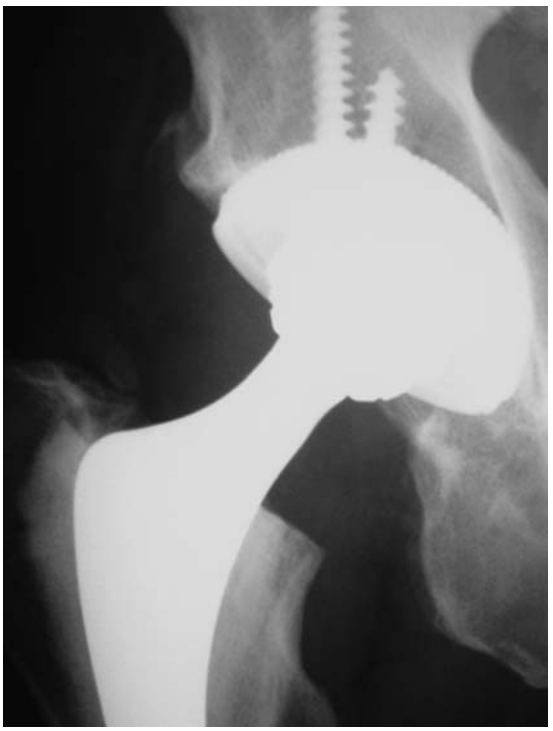

Fig. 1b

A radiograph, taken at five-year follow-up, of, a) a patient with a 54 mm Birmingham hip resurfacing and b) a patient with a 28 mm Metasul total hip replacement.

stainless steel femoral component or a cementless, porous-ingrowth titanium alloy femoral component (Fig. 1).

We recruited 26 consecutive patients, who were at the two-year post-operative stage after unilateral BHR. Only those with a femoral component of 50 mm or 54 mm were included. We chose two femoral sizes to keep the group uniform. The mean age of these patients at operation was 52.9 years (28.7 to 67.1).

We compared these patients with a further 28 who had undergone a unilateral Metasul THR a mean of two years previously. Each had a 28 mm high-carbon wrought cobalt-chrome bearing. Their mean age at operation was 56.6 years (39.0 to 62.8).

There were a further two groups of patients, one of 58 patients with a mean age of 52 years (28.3 to 74.4) at operation who had undergone unilateral BHR five years previously and one of 23 patients with a mean age of 59.7 years (45 to 67) who had undergone unilateral Metasul THR using a 28 mm bearing at a mean of five years previously.

Patients who were operated on for diagnoses other than osteoarthritis and those with renal impairment or with other metal devices in the body were excluded. All patients gave informed consent. We obtained 12-hour urine collections from all patients in each group.

Because there were fewer patients with a Metasul THR than with a BHR available for investigation, we extended the range of the follow-up period. One- to three-year patients with Metasul THR were compared with two-year BHR patients while patients four to six years after THR were compared with those five years after BHR.

The BHR was specifically designed for younger patients and is regularly performed for younger age groups than the THR, so we did not attempt to match the patients by age because we felt this would be an artificial process. Furthermore, younger patients who are suitable for a BHR may be more active. Therefore, we did not attempt to match patients by activity, as there is no validated activity score available to make a meaningful match. For the blood levels of metal ions, samples were taken one year post-operatively in the 26 patients who had undergone unilateral BHR and in another group of 20 consecutive patients (mean age 63.3 years; 55 to 74.7) who had undergone a unilateral Metasul THR one year before.

Specimen collection. We sent patients a 2.7 l container by courier, as well as clear instructions for a 12-hour collection of urine. On completion, the container was returned. All precautions for the safe transport of body fluids were observed. Once a collection was received in our laboratory, its volume was recorded and samples were decanted into two 10 ml urine specimen bottles (Sarstedt Ltd, Leicester, United Kingdom) and frozen at -18°C. One was stored as a reserve. The other was kept frozen, batched and sent to the

Table I. Standard operating conditions for spectrometry analysis in our study (Finnigan MAT Element high-resolution ICP*-mass spectrometry)

Forward power (W)	1150
Resolution	3000 (10% valley definition)
Argon coolant gas flow rate (l/min)	14
Argon auxillary gas flow rate (l/min)	1.0
Argon nebuliser gas flow rate (l/min)	1.0
Nebuliser	Babbington's type†
Nebuliser uptake (ml/min)	1
Samples per peak	20
Setting time (ms)	5
Number of replicates	3 x 20
Mass window	100%
Integration window	80%

* ICP, inductively-coupled plasma

† Finnigan Mat Element, Thermo Electron Corporation, Bremen, Germany

Laboratory of Government Chemists (LGC) Laboratories (Teddington, Middlesex, United Kingdom) for metal ion analysis. The concentration of ions was then multiplied by the overall 12-hour volume in order to obtain the 12-hour excretion. This was doubled to obtain the 24-hour output. Two of the 12-hour collection containers and the specimen bottles from each batch were filled with deionised water and sent to LGC laboratories to ensure that both were free from trace metals.

For the sample of whole blood, 5 ml to 6 ml of blood was drawn into each of two 6 ml lithium-heparin blood sample Vacutainer tubes (Becton Dickinson Vacutainer, Plymouth, United Kingdom) and stored at -18°C. One tube was kept frozen as a reserve and the other was batched and forwarded frozen to LGC Laboratories for analysis. We used the same batch of needles and tubes throughout. Deionised water was flushed through two unused needles and tubes from each batch, which were analysed to ensure that there was no trace metal contamination.

Instrumentation. All metal ion analyses were performed using a Finnigan MAT (Thermo Electron Corporation, Bremen, Germany) Element high-resolution inductively-coupled plasma mass spectrometer. The element has an argon plasma source coupled to a magnetic sector mass spectrometer. A differential entrance slit with three resolutions permits greater separation of mass peaks. Table I lists standard operating conditions for urine analysis by this method.

Analytical grade Ultrex II acids (MallincKrodt Baker BV, Deventer, The Netherlands) were used throughout and were diluted with deionised water taken from an Elga Maxima water purification unit (Elga, Marlow, United Kingdom). The effects of signal suppression and instrumental drift were corrected using a ^{103}Rh internal standard, added on-line via a T-piece mixing line. Calibration standards were prepared from concentrated stock solutions (Alfa, Aesar, Karlsrhue, Germany) and were diluted to produce a range of five standards which spanned the concentrations of the samples. A linear regression of the calibrations produced a value for $R^2 > 0.99$. Urine samples were diluted in a 1% HNO_3 solution. All standards were prepared in the same acid. A reagent containing 0.01 M ammonia, 0.0002 M EDTA and 1% Triton X-100 was used as the stock diluent for whole blood samples.

We maintained quality assurance throughout the analysis through repeated measurement of the calibration standards. The calculated recovery values were all within SD 5% of the known value. In addition, some samples were 'spiked' with additional trace elements and a recovery value calculated, relative to the unspiked samples. Typical recovery values were SD 5%. The raw data (i.e. peak integrals) from the instrument were then exported to Microsoft Excel. Here the raw data were processed and the concentrations determined for each element in each sample. The limits of detection for cobalt and chromium were 0.02 μg/l in the urine study, while the reporting limit was three times this value (i.e. 0.06 μg/l). The reporting limits in the whole blood study were 0.2 μg/l, the limits of detection being 0.067 μg/l). Two methods of statistical significance were used (Microsoft Excel, Microsoft, Redmond, Washington), 95% confidence intervals are displayed in Figures 2 to 5 and *t*-test for unpaired groups (Medical Software, Broekstraat Mariakerke, Belgium) were also used. A p value ≤ 0.05 was considered significant.

Results

The results of our studies are shown in Figures 2 to 5. Urinary cobalt and chromium output (Figs 2 and 3) in patients with a BHR are in the same range as the output in patients with a 28 mm Metasul THR at the equivalent two-year period. By the equivalent five-year period, the mean chromium output was higher in the BHR (7.0 μg/day) compared with the 28 mm Metasul THRs (4.1 μg/day). This trend was reversed for cobalt output (BHRs 13.6 μg/day, Metasul THRs 14.2 μg/day). The differences between the cobalt levels in patients with Metasul THRs when compared with those with BHRs were not statistically significant either at the two-year period ($p = 0.88$), nor at the five-year period ($p = 0.9$). The differences for chromium were also not significant ($p = 0.33$ for the mean difference at two years and $p = 0.08$ at five years). Both the mean difference between whole blood cobalt levels in the Metasul and BHR groups (difference 0.4 μg/l; $p = 0.28$) and the difference between chromium levels in the two groups (difference = 0.69 μg/l; $p = 0.055$) were insignificant at the one-year follow-up period (Figs 4 and 5).

Discussion

A metal-on-metal bearing does not lend itself to the traditional methods of *in vivo* wear measurements which are used for a conventional polyethylene-containing bearing. Indeed, Jacobs et al[14] suggested that *in vivo* wear of metal-on-metal bearings can conceivably be assessed by blood, serum, erythrocyte, and/or urine metal levels, although this has not as yet been proven. It is known from animal studies that there is a good time-dependent relationship between

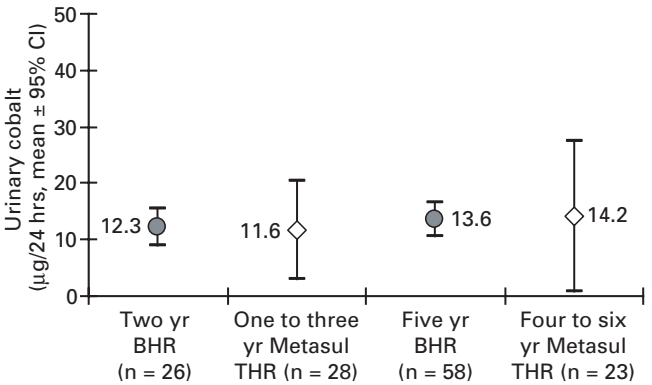

Fig. 2

Daily urinary output of cobalt in patients with Birmingham hip resurfacing compared with 28 mm Metasul total hip replacements (95% CI, 95% confidence interval; BHR, Birmingham hip resurfacing; THR, total hip replacement).

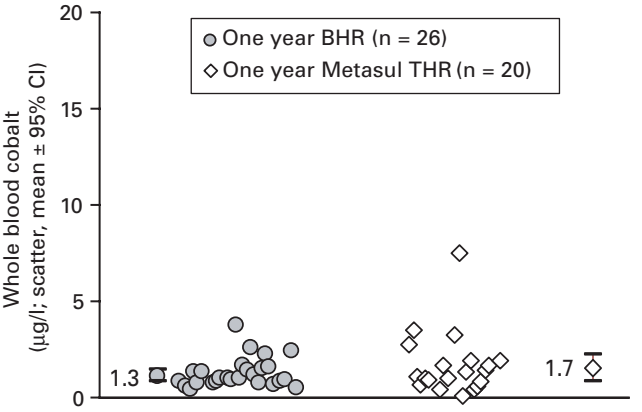

Fig. 4

Whole blood cobalt concentrations in patients with Birmingham hip resurfacing at the one-year post-operative stage compared with 28 mm Metasul total hip replacements at the same stage (95% CI, 95% confidence interval; BHR, Birmingham hip resurfacing; THR, total hip replacement).

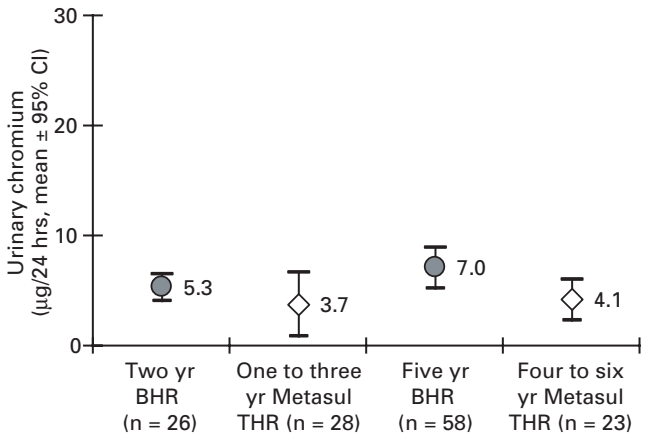

Fig. 3

Daily urinary output of chromium in patients with Birmingham hip resurfacing compared with 28 mm Metasul total hip replacements (95% CI, 95% confidence interval; BHR, Birmingham hip resurfacing; THR, total hip replacement).

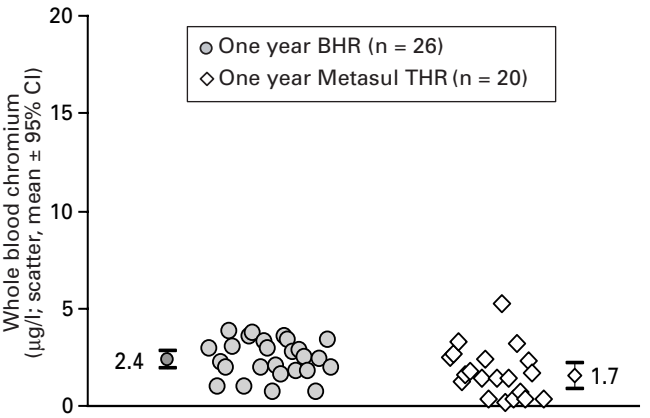

Fig. 5

Whole blood chromium concentrations in patients with Birmingham hip resurfacing at the one-year post-operative stage, compared with 28 mm Metasul total hip replacements at the same stage (95% CI, 95% confidence interval; BHR, Birmingham hip resurfacing; THR, total hip replacement).

the systemic release of metal ions, especially cobalt, and their renal excretion.[15] Almost an entire bolus of released cobalt can be obtained from the urine within 48 hours of its release.

There is a wide variation of chromium in plasma or serum, so it is necessary to assess whole blood levels rather than levels in plasma serum, or red blood cells alone.[16] In addition, chromium tends to accumulate in red blood cells, so plasma or serum levels do not show the whole picture. Consequently, whole blood analysis provides a better estimation of systemic metal ion exposure than an analysis of plasma or serum in isolation.

Estimation of the concentration of metal ions in urine does not take into account the confounding factor of urinary dilution. There is wide individual variation in the volume of urine produced over a given period of time, dependent on several factors, including fluid intake, ambient temperature, and metabolic activity. As a result, an assessment of the daily (24-hour) output, or timed excretion, is of more value than an assessment of concentration alone. For young patients, it has been observed that compliance for a 24-hour collection is much less than for a shorter timed excretion.[17,18] The output of urinary metal ions based on a timed excretion is therefore, a useful measure of

metal ion release from an implanted device. High-resolution inductively coupled plasma mass spectrometry has been shown to be far more accurate and reliable than both conventional mass spectrometry and graphite furnace atomic absorption spectrophotometry (GFAAS). It offers many improvements in performance,[19] including lower limits of detection, increased sensitivity and reliability and a reduced risk of contamination.

Metal-on-metal bearings are known to have an early running-in phase. *In vivo* assessments[20] in young patients have shown this to occur approximately six months after operation. Thereafter, the metal ion levels are reported to enter a lower steady-state phase.[20] It was for this reason that we chose to study the blood concentrations and daily output in all groups of patients during this steady-state phase.

At the two-year stage, the output of metal ions in patients with a BHR was in the same range as those with a 28 mm Metasul THR. There is only one other study[21,22] where the daily output of metal ions has been assessed using high-resolution inductively-coupled plasma mass spectrometry. In that study, the mean daily output of cobalt after a 28 mm metal-on-metal THR was 50.6 μg/day two years post-operatively. This is four times the mean cobalt output at the same interval of time after BHR in our study (12.3 μg/day). In addition, at five years post-operatively, the daily urinary output of cobalt and chromium in patients with a BHR compares well with the output in those with a Metasul THR and these differences were too small to be statistically significant.

Our results suggest that bearing diameter does not make a difference to the daily urinary output of metal ions. It should be noted that in both the high-carbon devices studied, there was no steady increase in metal ion generation over the years, unlike other 28 mm metal-on-metal bearings.[23,24]

There have been several studies, which have investigated systemic metal ion levels in patients with hip resurfacings and replacements. The results have shown widely varying ranges because of the variation in the specimens studied (serum, whole blood, red blood cells) and the analytical techniques used.

One recent study by Clarke et al[25] suggested that plasma metal ion levels were higher in larger, rather than smaller, diameter bearings. In that study, plasma analysis was performed, an inadequate measure when compared with whole blood analysis. In addition, a further confounding factor appeared in that study because two types of resurfacings were combined. One was the double heat-treated Cormet 2000 (Corin Group PLC, Cirencester, United Kingdom) (carbide volume fraction 2.3%) and the other, the as-cast BHR (carbide volume fraction 5%). From the data presented in that study, the median plasma cobalt and chromium values for the Cormet 2000 were 44% and 60%, respectively higher than for the BHR. The fact that this difference was not significant may have been because of the small numbers of individual types of bearing investigated (16 BHR, six Cormet), leading to a possible statistical beta error.

It has been shown by Pfister et al,[3] who also analysed whole blood cobalt and chromium with high-resolution inductively-coupled plasma mass spectrometry, that the levels of these ions were significantly higher in patients with low- rather than high-carbon devices. Heat treatment has been shown to lead to carbide depletion and can lead to higher wear rates *in vitro*[5-10] and a higher incidence of osteolysis-related failures *in vivo*.[11] In trying to look at the effect of one variable, such as bearing diameter, it is important to keep the other variables constant and therefore, to compare components which have identical or similar wear characteristics.

In our study, the 28 mm THRs and the BHRs were two distinct, but homogeneous groups. Different types of component were not combined in either group. Both devices were made of high-carbon alloy and were not subjected to later heat treatments, although one device was as-cast and the other was forged.

The one-year mean whole blood cobalt level for the BHR (1.3 μg/l) and the Metasul THR (1.7 μg/l) in our study compares well with the cobalt levels in patients with a high-carbon 28 mm THR reported by Pfister et al[3] (2.6 μg/l at a follow-up of one to 5.9 years). Both studies used the same specimens (i.e. whole blood samples) and analytical methods. Importantly, we found no significant difference in cobalt and chromium levels when BHRs with bearing diameters of 50 mm and 54 mm were compared with Metasul THRs with a bearing diameter of 28 mm. Our results suggest that bearing diameter does not influence the whole blood levels of metal ions.

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