The Relationship between Cobalt/Chromium Ratios and the High Prevalence of Head-Stem Junction Corrosion in Metal-on-Metal Total Hip Arthroplasty

Harry S. Hothi, BEng, MSc, PhD
Reshid Berber, BSc, MBBS, MRCS (Eng)
Robert K. Whittaker, BSc
Gordon W. Blunn, BSc, PhD
John A. Skinner, MBBS, FRCS (Eng), FRCS (Orth)
Alister J. Hart, MA, MD, FRCS (Orth)

1. Institute of Orthopaedics and Musculoskeletal Science, University College London and the Royal National Orthopaedic Hospital, Stanmore, United Kingdom, HA74LP

Corresponding Author:
Harry S. Hothi
Institute of Orthopaedics and Musculoskeletal Science (University College London)
Royal National Orthopaedic Hospital
Brockley Hill
Stanmore, Middlesex
HA7 4LP
United Kingdom
Phone: +44 (0) 208 909 5825
Fax: +44 (0) 208 954 8560
Email: h.hothi@ucl.ac.uk
Abstract

Background: The size of the clinical impact of corrosion of the taper junction of metal-on-metal total hip replacements (MOM-THRs) is unclear. Examination of a large number of retrieved MOM resurfacing and total hip replacements can help us understand the role of taper corrosion in metal ion release.

Methods: We graded the severity of corrosion at the taper junction of 395 MOM-THRs and compared the pre-revision whole blood metal ion levels of these hips with 529 failed MOM hip resurfacings.

Results: Virtually all MOM-THR hips (n=388) had evidence of corrosion of the head-stem taper junction and graded as severe in 31% (n=124). The median Co/Cr ratio was 1.58 (0.01-13.82) and 1.08 (0-4.86) for MOM-THR and MOM hip resurfacing respectively; this difference was significant (p<0.001). THR hips with severely corroded tapers had the highest median Co/Cr ratio of 1.86 (0.01-10).

Conclusions: This study demonstrates the high prevalence of severe taper corrosion, which may be related to an elevated Co/Cr ratio prior to revision.

Keywords: Taper, Corrosion, Metal-on-Metal, Retrieval, Cobalt, Chromium
Introduction

The size of the clinical impact of metal ions released from the taper junctions of metal-on-metal total hip replacements (MOM-THR) is unknown. Numerous studies have reported on the wide range of volumetric material loss that has been measured at the surface of the femoral head taper [1-3] and it is largely accepted that the mechanism of material loss may be due to mechanical wear, corrosion or a combination of both.

The volume of material loss at the taper has been shown to be significantly moderately correlated with a well-published visual scoring scale for the severity of corrosion [4, 5]. It was found that virtually all tapers that had evidence of no, mild or moderate corrosion had volumetric material loss of less than 5mm$^3$, however tapers that were visually severely corroded (score 4) revealed a large variation in material loss of between 1mm$^3$ and over 25mm$^3$.

The black surface deposits associated with severe taper corrosion have been shown to be rich in chromium (Cr) with comparatively fewer cobalt (Co) ions [5]. It is speculated that as the severity of corrosion increases, an increase will also be detected in the whole blood Co/Cr ratio as more chromium will be retained on the taper surface whilst a greater concentration of cobalt ions will be released into the blood.

It is proposed therefore that a greater focus on the analysis of severely corroded tapers may be key in understanding the role of the taper junction in implant failure. The magnitude of the clinical frequency of severe taper corrosion however is unclear. Recent studies that have reported on corrosion of failed contemporary hips have examined a relatively low number of components, ranging from 12 to 150 [4, 5, 6-12]. Goldberg et al. [5] reported evidence of
severe corrosion in 10% of 221 tapers however these were of hips explanted over a decade ago. It remains unclear to what extent severe taper corrosion is present in a wider cohort of failed modern MOM hips.

The purpose of this study therefore was to: (1) report on the prevalence and severity of corrosion in the largest study of retrieved MOM-THR hips of current designs (n=395) and (2) determine whether this damage mechanism can be detected prior to revision by comparing corrosion scores with pre-revision blood metal ion levels of the 395 MOM-THRs and a series of 529 failed MOM hip resurfacings.
**Methods**

This was a retrospective cohort study involving a consecutive series of 395 failed MOM-THR hip implants received at our retrieval centre that had an unobstructed female head taper surface which could be visually assessed. Implants were collected from over 38 contributing hospitals during the period July 2009 to April 2014. Pre-revision cobalt and chromium blood metal ion levels were collected, together with patient demographic data relating to gender, age at primary surgery and time to revision, Table 1. The hip designs consisted of the Adept (27), ASR XL (68), BHR (66), Conserve (10), Cormet (35), Magnum (50), Metasul (42), Mitch (10), Pinnacle (66), Ultima (6) and others (15), with a median head diameter of 45mm (28-60); these consisted of 19 small heads (<36mm) and 376 large heads (≥36mm).

The implants were retrieved from 162 male and 233 female patients with a median age of 61 years (23-83) and a median time to revision of 50 months (7-200). Median whole blood cobalt (Co) and chromium (Cr) levels pre-revision were 7.02 ppb (0.47-212.4) and 3.93 ppb (0.2-111) respectively. The Co/Cr ratio was calculated individually for each patient; the median ratio was 1.58 (0.01-13.82).

In order to assess the clinical significance of corrosion at the modular junctions of the MOM-THRs, we also considered in this study pre-revision whole blood metal ion levels of a series of 529 retrieved MOM resurfacing hips previously collected at our centre, Table 1. Median cobalt and chromium levels were 5.83 ppb (0-273.8) and 5.92 ppb (0.3-343) respectively; the median Co/Cr ratio was 1.08 (0-4.86). These implants had been retrieved from 216 male and 313 female patients with a median age of 55 years (16-74) and a median time to revision of 59 months (8-178). The median head diameter was 46mm (38-58).
Corrosion Assessment

Each head taper surface was inspected macroscopically and with the aid of a Leica M50 light microscope [Leica Microsystems, Germany] at up to x40 magnification. A well-published corrosion classification method [5] was used to grade each surface with a score of 1 (no corrosion), 2 (mild corrosion), 3 (moderate corrosion) or 4 (severe corrosion), with increasing evidence of black debris, pitting and etching indicating greater corrosion. This method has previously been demonstrated as being both repeatable and reproducible [4]. The statistical significance of any differences between the corrosion scores in relation to (1) time to revision; (2) head size; (3) Co and Cr blood metal ion levels; (4) age at primary were examined. Following this the statistical significance of any differences in the Co/Cr ratios between: (1) all resurfacing hips, (2) all THRs and (3) THR hips in each of the four corrosion score categories was investigated. We also tested to see if there was a significant association between time to revision and Co/Cr ratios for both the resurfacing and total hips.

The Shapiro-Wilk test for normality revealed that all the parameters under investigation were not normally distributed. Therefore Kruskal-Wallis non-parametric ANOVA tests were initially performed to detect the presence of significant differences and post-hoc analysis using Mann Whitney testing was used to identify which specific differences were significant.

Source of Funding

Two authors received funding from the British Orthopaedic Association through an industry consortium of nine manufacturers: DePuy International Ltd (Leeds, UK), Zimmer GmbH (Winterthur, Switzerland), Smith & Nephew UK Ltd (Warwick, UK), Biomet UK Ltd (Bridgend, South Wales, UK), JRI Ltd (London, UK), Finsbury Orthopaedics Ltd
(Leatherhead, UK), Corin Group PLC (Cirencester, UK), Mathys Orthopaedics Ltd (Alton, UK), and Stryker UK Ltd (Newbury, UK). This did not play a direct role in this investigation.

**Results**

We found that that 98% (n=388) of retrieved head tapers showed evidence of corrosion and 31% (n=124) of tapers were severely corroded (Figure 1).

There was a significant difference in the time to revision (months) between the corrosion scores (p<0.001). Post hoc analysis confirmed that the time to revision for hips with corrosion score 3 was significantly greater than score 2 (p<0.05) and the time to revision for score 4 was significantly greater than scores 2 and 3 (p<0.05). There was no association between head size and corrosion scores (p=0.141) and there was no statistically significant difference between the corrosion scores of small (<36mm) and large (≥36mm) diameter heads (p=0.685). We also examined the effect of categorising 36mm heads as small diameter; there was again no significant difference in corrosions scores between heads ≤36mm and >36mm (p=0.4106). Corrosion scores were not affected by patient age (p=0.998) and no significant association was found with cobalt (p=0.286) or chromium (p=0.115) blood metal ion levels.

Figure 2 plots the distribution of Co/Cr ratios of the resurfacing and THR hips and also the subgroups of the THRs categorised by corrosion score. The data for hips with a corrosion score of 1 were omitted in the graph and subsequent statistical analysis due to their low numbers (n=7). The Kruskal-Wallis test revealed that there was a highly significant difference in the Co/Cr ratios between the groups (p<0.001). Post-hoc analysis showed that the median Co/Cr ratio of 1.58 (0.01-13.82) for the THR group was significantly greater than
the resurfacing group, which had a median ratio of 1.08 (0-4.86) (p<0.001). The median CoCr ratios for the THR hips with corrosion scores 2, 3 and 4 were 1.30 (0.03-8.94), 1.67 (0.29-13.82) and 1.86 (0.01-10) respectively (Table 2); all three groups had significantly greater CoCr ratios than the resurfacing hips (p<0.05). Comparison of median Co/Cr ratios for THR with different corrosion scores suggested that there was a trend towards greater corrosion being associated with higher Co/Cr ratios. Statistical analysis showed that ratios for corrosion scores 3 and 4 were significantly greater than for corrosion score 2 (p<0.05) however no significant differences were found between corrosion scores 3 and 4 (p=0.461), Table 3. We did not find any significant associations between the time to revision and Co/Cr ratios for the resurfacings (p=0.721) or total hips (p=0.808).
Discussion

In a recent commentary by Jacobs and Wimmer [13], the importance of implant retrieval analysis by centres with access to large retrieval cohorts was emphasised as significant in understanding mechanisms of failure and also for developing future preclinical testing models. In this study we have presented the results of retrieval analysis of the largest number of failed MOM-THRs to date; we report findings on the corrosion of the taper junction of almost 400 MOM-THRs and have compared blood metal ion ratios of these hips with ratios of over 500 failed MOM hip resurfacings.

We found that virtually all retrieved head tapers (98%) displayed visual evidence of corrosion, with a statistically significant trend towards increasing severity with longer time to revision. Surprisingly almost one-third of all tapers were severely corroded with considerable evidence of black debris and in many cases clear imprinting of the thread of the stem trunnion. Analysis of Co/Cr ratios revealed that these were significantly greater for THRs than resurfacings. When the THR hips were subdivided in relation to their taper corrosion scores, comparisons of median ratios appeared to suggest that greater corrosion was correlated with higher ratios; statistical analysis however only found a significant difference between the Co/Cr ratios of mildly corroded hips and moderately/severely corroded hips. Whilst significance was not detected, the severely corroded group of THRs had the highest median Co/Cr ratio of 1.86.

The National Joint Registry of England, Wales and Northern Ireland [14] reports that revisions rate of MOM-THRs are approximately 50% greater than their equivalent resurfacing counterparts, which are absent of a taper junction. Our study demonstrates the
high prevalence of severe corrosion at this junction, which may help to explain these
accelerated failure rates due to a greater release of metal debris.

Additionally, material may be lost at the taper junction through mechanical means such as
fretting or toggling of the implant due to incomplete engagement or differences in stem-
trunnion tolerances [15]. Assessment of fretting was not performed in the current study as it
has previously been shown that visual scoring of this damage mechanism is an unreliable
method and is difficult to quantify accurately [4]. Increased modularity, such as with a neck-
stem junction or the use of modular cups with interchangeable liners and shells, has been
shown to introduce additional regions of corrosion which are likely to contribute to elevated
blood metal ions [7, 9, 10]. Another source of metal ions may be from the corrosion of
cemented stems; Bryant et al. [16] reported on considerable evidence of surface changes and
chromium rich black debris at the stem-cement interface of a series of retrieved CoCr stems.

The trend between longer time to revision and increasing corrosion scores are to be expected
and are in agreement with previous work [5]. This re-emphasises the importance of
considering the effect of implantation time when interpreting data related to damage of the
taper junction. There was however no association between time to revision and the Co/Cr
ratio for either of the two hip groups; this may be due to metal ions being continuously
excreted from the body rather than accumulating over time.

It has been suggested that higher frictional torques due to increasing femoral head size can
lead to greater corrosion at the taper junction [6, 17]. There is some debate over the
classification of 36mm bearings as being of ‘large’ or ‘small’ diameter, however the majority
of retrieval studies suggest that it should be considered as large head, with Dyrkacz et al. [6]
reporting significantly higher corrosion in 36mm heads in comparison to 28mm heads. We
found that there was no significant difference in corrosion scores between large and small heads regardless of if 36mm was categorised as large or small diameter. Whilst these findings do not add to the debate of the classification of 36mm bearings, it does highlight that severe corrosion can occur in all hip designs and sizes.

The absence of significant correlations between corrosion scores and either cobalt or chromium blood metal ion levels are perhaps not surprising when considering the differences in material loss between the taper and bearing surfaces that have previously been reported. Matthies et al. [1] showed that up to 228mm$^3$ and 194mm$^3$ of volumetric material loss was measured at the head and cup bearing surfaces respectively, whilst a maximum of 25mm$^3$ was lost at the corresponding head taper surface. The considerably greater amount of metal ions released from the bearing surface are likely to mask the individual effect of the taper junction on increasing cobalt or chromium levels in the blood.

Our findings in relation to Co/Cr ratios are however clinically significant. We have shown that the Co/Cr ratios of the MOM-THRs were significantly greater than that of the resurfacings, Figure 2. Whilst the bearing bulk alloy has a Co/Cr ratio of approximately 2, the resurfacing hips had a median whole blood Co/Cr ratio closer to 1. This may be explained by considering that Co ions are more soluble and readily excreted whereas Cr ions tend to be retained in surrounding soft tissue, Figure 3. The increase in the median Co/Cr ratio for the MOM-THRs by approximately 50% must therefore be due to corrosion at the modular junctions; a damage mechanism which results in much of the chromium ions being retained in the black corrosive surface debris whilst much of the cobalt ions are released into the blood, Figure 4. These findings are in agreement with the study by Cooper et al. [7] who reported elevated Co/Cr ratios in modular neck hips with non-MOM bearings and evidence of
severe corrosion at the modular junctions. Hart et al. [18] also found evidence of considerably more Co than Cr in their analysis of periprosthetic tissue of patients with problematic MOM-THRs that were found, after retrieval, to be substantially corroded. We acknowledge however that some of the differences in the ratios may be explained by the finding that the resurfaced hips have comparatively higher Cr levels than the total hips.

We observed a clear positive trend between increasing taper corrosion score and increasing median Co/Cr ratios, such that hips with severely corroded tapers had the highest median ratio (almost 2) in comparison to all other groups. There was a significant difference between the Co/Cr ratio for hips with corrosion score 2 (mild) and those with a score of 3 (moderate) or 4 (severe). This may be explained by the fact that tapers were scored as being mildly corroded if there were signs of discolouration or surface dullness but if there was evidence of black corrosive debris, these tapers were classed as moderately or severely corroded, according to Goldberg’s scoring system [5]. Whilst hips with severely corroded tapers had a higher median Co/Cr ratio than those with moderately corroded tapers, this difference was not significant. As discussed earlier, it is possible that high wear of the MOM bearing surfaces may obscure the contribution of metal ions released from the taper, thus making it difficult to distinguish between moderate and severe corrosion pre-revision. Indeed it has been speculated that increased bearing surface wear and edge wearing of the cup are associated with greater material loss at the head taper. Nevertheless we have shown that the severity of corrosion increases over time, therefore the Co/Cr ratio could be used as a biomarker for monitoring the increase in taper junction corrosion over the course of regular clinical follow ups.
Limitations

We have reported metal ion data based on the last available blood test prior to revision; we acknowledge that the time between blood test and revision may not be consistent for all hips in this study. As metal ions are continuously excreted from the body, differences in the time of blood test may have influenced the ratios measured.

Future Work

Future work continuing from this study will involve quantifying volumetric material loss at the bearing (cup and head) and taper junction surfaces of hips identified in the current work as having severely corroded tapers. The comparatively higher wear rates of the bearing surfaces may mask the true extent of the impact of taper damage; we will therefore seek to isolate and further examine cases that have: (1) elevated metal ion levels or ratios, (2) severe taper corrosion and (3) low bearing surface wear rates. It will also be of great interest to investigate differences observed from cross-sectional imaging between cases with elevated Co/Cr ratios and those with comparatively lower ratios. A number of recent studies have reported on the corrosion of modular neck junctions in THR$s [7, 19, 20]. Future work from our centre will also investigate the clinical impact of this increased modularity in the stem-neck junction relative to the neck-head junction.

Conclusions

This was the largest retrieval study to date to report on the corrosion of failed contemporary MOM-THR$s. Almost all head tapers showed signs of corrosion and one-third were severely corroded. The greater Co/Cr ratios in the MOM-THR$s in comparison to the MOM resurfacings support a mechanism of corrosion at the taper junction, which retains chromium on the surface and releases more cobalt into the blood. The results of our study suggest that
an elevated blood metal ion ratio could be used as a biomarker for detecting corrosion at the modular junctions of MOM-THRs. However this may be masked by high bearing surface wear, meaning that the absence of an elevated Co/Cr ratio may not necessarily mean the absence of corrosion at the modular junction.
References


Figure 4

Click here to download high resolution image
Figure Legends

Figure 1: Distribution of corrosion scores of the THR head tapers

Figure 2: Distribution of Co/Cr ratios between the resurfacing and all THR groups and the subgroups for THRs with a taper corrosion score of 2, 3 and 4 (THR Cr 4)

Figure 3: Schematic explanation of the Co/Cr ratio observed for resurfacing hips

Figure 4: Schematic explanation of the Co/Cr ratio observed for modular hips
<table>
<thead>
<tr>
<th>THR Bearing Design</th>
<th>Number</th>
<th>THR Median (Range)</th>
<th>Resurfacing Median (Range)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Male : Female)</td>
<td>162 : 233</td>
<td>216:313</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Age at Primary Surgery (years)</td>
<td>61(23-83)</td>
<td>55 (16-74)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Time to Revision (months)</td>
<td>50 (7-200)</td>
<td>59 (8-178)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Femoral Head Diameter (mm)</td>
<td>45 (28-60)</td>
<td>46 (38-58)</td>
<td>0.184</td>
<td></td>
</tr>
<tr>
<td>Whole Blood Cobalt (ppb)</td>
<td>7.02 (0.47-212.4)</td>
<td>5.83 (0-273.8)</td>
<td>0.144</td>
<td></td>
</tr>
<tr>
<td>Whole Blood Chromium (ppb)</td>
<td>3.93 (0.2-111)</td>
<td>5.92 (0.3-343)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Cobalt/Chromium Ratio</td>
<td>1.58 (0.01-13.82)</td>
<td>1.08 (0-4.86)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Biomet Magnum</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Corin Cormet</td>
<td>35</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DePuy ASR XL</td>
<td>68</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DePuy Pinnacle</td>
<td>66</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Finsbury Adept</td>
<td>27</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S&amp;N BHR</td>
<td>66</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Stryker Mitch</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wright Conserve</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Zimmer Metasul</td>
<td>42</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Others</td>
<td>21</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Resurfacing Bearing Design</td>
<td>Corin Cormet</td>
<td>98</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DePuy ASR</td>
<td>35</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Finsbury Adept</td>
<td>29</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>S&amp;N BHR</td>
<td>304</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Stryker Mitch</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wright Conserve</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Zimmer Durom</td>
<td>17</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Others</td>
<td>24</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1: Patient and implant data for the MOM-THRs and MOM Resurfacings
<table>
<thead>
<tr>
<th>Hip Type</th>
<th>Number of Hips</th>
<th>CoCr Ratio - median (range)</th>
<th>Absolute Co - median (range)</th>
<th>Absolute Cr - median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resurfacing</td>
<td>529</td>
<td>1.08 (0 - 4.86)</td>
<td>5.83 (0-273)</td>
<td>5.92 (0.3-343)</td>
</tr>
<tr>
<td>All THRs</td>
<td>395</td>
<td>1.58 (0.01 - 13.82)</td>
<td>7.02 (0.12-212)</td>
<td>3.93 (0.2-111)</td>
</tr>
<tr>
<td>THR Corrosion 1</td>
<td>7</td>
<td>1.58 (0.53-2.01)</td>
<td>27.67 (7.4-26.1)</td>
<td>15.1 (4.1-29.8)</td>
</tr>
<tr>
<td>THR Corrosion 2</td>
<td>116</td>
<td>1.30 (0.03 - 8.94)</td>
<td>6.5 (0.5-167)</td>
<td>4.1 (0.4-76)</td>
</tr>
<tr>
<td>THR Corrosion 3</td>
<td>148</td>
<td>1.67 (0.29 - 13.82)</td>
<td>7.3 (0.12-153)</td>
<td>4.1 (0.4-111)</td>
</tr>
<tr>
<td>THR Corrosion 4</td>
<td>124</td>
<td>1.86 (0.01 - 10)</td>
<td>6.8 (0.46-212)</td>
<td>3.7 (0.22-109)</td>
</tr>
</tbody>
</table>

*Table 2: Median (range) values for Co and Cr and Co/Cr ratios found for each group*
<table>
<thead>
<tr>
<th>Mann Whitney Comparison Test</th>
<th>Significant Difference in Co/Cr Ratio?</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resurfacing vs All THRs</td>
<td>Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resurfacing vs THR Cr 2</td>
<td>Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resurfacing vs THR Cr 3</td>
<td>Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resurfacing vs THR Cr 4</td>
<td>Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All THRs vs THR Cr 2</td>
<td>No</td>
<td>0.1247</td>
</tr>
<tr>
<td>All THRs vs THR Cr 3</td>
<td>No</td>
<td>0.4121</td>
</tr>
<tr>
<td>All THRs vs THR Cr 4</td>
<td>No</td>
<td>0.5227</td>
</tr>
<tr>
<td>THR Cr 4 vs THR Cr 3</td>
<td>No</td>
<td>0.9224</td>
</tr>
<tr>
<td>THR Cr 4 vs THR Cr 2</td>
<td>Yes</td>
<td>0.0434</td>
</tr>
<tr>
<td>THR Cr 3 vs THR Cr 2</td>
<td>Yes</td>
<td>0.0495</td>
</tr>
</tbody>
</table>

Table 3: Summary of statistical analysis of differences in Co/Cr ratios
Acknowledgements

We are grateful for the support of Gwynneth Lloyd, Charlotte Page and Elizabeth Ellis for their coordination of the retrieval centre. Two authors received funding from the British Orthopaedic Association through an industry consortium of nine manufacturers: DePuy International Ltd (Leeds, UK), Zimmer GmbH (Winterthur, Switzerland), Smith & Nephew UK Ltd (Warwick, UK), Biomet UK Ltd (Bridgend, South Wales, UK), JRI Ltd (London, UK), Finsbury Orthopaedics Ltd (Leatherhead, UK), Corin Group PLC (Cirencester, UK), Mathys Orthopaedics Ltd (Alton, UK), and Stryker UK Ltd (Newbury, UK).