Microscopical analysis of synovial fluid wear debris from failing CoCr hip prostheses

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Abstract. Metal on metal hip joint prostheses are now commonly implanted in patients with hip problems. Although hip replacements largely go ahead problem free, some complications can arise such as infection immediately after surgery and aseptic necrosis caused by vascular complications due to surgery. A recent observation that has been made at Manchester is that some Cobalt Chromium (CoCr) implants are causing chronic pain, with the source being as yet unidentified. This form of replacement failure is independent of surgeon or hospital and so some underlying body/implant interface process is thought to be the problem. When the synovial fluid from a failed joint is examined particles of metal (wear debris) can be found. Transmission Electron Microscopy (TEM) has been used to look at fixed and sectioned samples of the synovial fluid and this has identified fine (< 100 nm) metal and metal oxide particles within the fluid. TEM EDX and Electron Energy Loss Spectroscopy (EELS) have been employed to examine the composition of the particles, showing them to be chromium rich. This gives rise to concern that the failure mechanism may be associated with the debris.

1. Introduction

The materials used in commercially available hip prostheses have undergone significant developments since their integration into routine surgery. When a hip implant is necessary, the replacement should mimic the natural predecessor as closely as possible. The choice of material is important as it should have little or no impact on the biological environment it is used in. If the material impacts on the health of the patient, maintenance or even replacement of the part may need to be carried out, causing them stress and discomfort. Metal on polymer prostheses have been shown to have high wear rates [1], thus generating significant amounts of wear debris which can lead to osteolysis [2]. Ceramic on ceramic prostheses are also available, but these are prone to damage due to the materials brittle nature [3]. In more recent years, metal on metal hip replacements produced using cobalt-chromium (CoCr) alloys with extremely low wear rates have become popular. It has been shown that wear rates are low compared to metal on polymer replacements [1], and gross wear debris is not as significant in these types of prostheses and so osteolysis is a less common problem.
However, a recent observation at Manchester in metal on metal CoCr hip prostheses is failure through an as yet unidentified mechanism. The primary symptom of this mode of failure is chronic pain in the patient, and in cases it can lead to replacement of the synovial fluid or even of the hip itself. It has already been established that fine wear debris particles are still produced in this type of prostheses [4], and the presence of such fine particles in the body and their impact on health is a matter of concern. In addition, the presence of chromium deserves some attention, as in certain chemical states the element can have an impact on biological systems [5]. This report describes an investigation into the nature of these wear particles using Transmission Electron Microscopy (TEM). Parallel Electron Energy Loss Spectroscopy (EELS) has proved a useful technique, giving information on the chemical nature as well as the composition of the wear particles.

2. Experimental techniques
TEM specimens were prepared by fixing the synovial fluid with glutaraldehyde before dehydrating, embedding in resin and cutting microtome sections. These sections were then lifted onto formvar coated copper grids (Agar Scientific) suitable for TEM. Prior to examination in the microscope, specimens were carbon coated with a < 5 nm layer to minimise charging. Samples used to measure standard Cr \( L_{2,3} \)-edges for different oxidation states were prepared using Cr(II)F\(_2\), Cr(III)Cl\(_3\), Cr(III)\(_2\)O\(_3\) and Cr(IV)O\(_2\) powders (Sigma-Aldrich). These were crushed using a pestle and mortar in acetone, and then the mixture was drop cast onto a holey carbon coated copper grid (Agar Scientific). Onto the same grids, TiO\(_2\) (anatase) powder (Sigma-Aldrich) prepared in the same way was drop cast, so each of the grids contained a mixture of both the chromium based powders and TiO\(_2\) (the O EELS K-edge from TiO\(_2\) was used to calibrate the spectra).

Samples were examined using a Philips CM200 FEGTEM operated at 197kV, fitted with an Oxford Instruments UTW EDX detector and a Gatan GIF 200 imaging filter. Spectra were collected onto a 1024 pixel CCD camera, at a dispersion of 0.1 eV per pixel. An approximate energy resolution of 0.8 eV was recorded. For EELS, the microscope was operated in diffraction mode (image coupled) with a collection semi-angle of 6 mrad and a convergence semi-angle of approximately 1 mrad. Energy calibrations were carried out on the standard samples using the distinctive O K-edge for TiO\(_2\).

Figure 1 Examples of three typical particles found within the synovial fluid. Below the images are associated EDX spectra collected for the particles. Particle A has a similar composition to the bulk material (cobalt, chromium and molybdenum) and is crystalline, but particle B is richer in chromium and molybdenum and the particles shown in C appear to be composed predominantly of chromium and oxygen. Particles B and C were both amorphous.
Energy calibrations were carried out on the sectioned samples using the zero loss peak and relying on the accuracy of the applied drift tube voltage.

3. Results and Discussion

3.1. Morphology and composition of wear debris particles
Sections of the synovial fluid showed a distribution of fine particles of varying size, morphology and structure. TEM Energy Dispersive X-ray (EDX) analysis of the particles showed the larger particles to be closer to the bulk composition of the metal hip component (cobalt, chromium, molybdenum) and crystalline, whereas the smaller particles were more commonly chromium rich and amorphous. It may be that the top surface of the joint is chromium rich and amorphous, and this is why the smaller particles that were identified were of this composition/structure. Figure 1 shows three different particles that were typical of the sample along with EDX spectra collected from them. Particle C is actually composed of many particles, ranging in size from 50 nm down to < 5 nm. That they are clustered together is of interest, they may have been generated together, or may have become clustered while inside the fluid.

3.2. Cr standards used for EELS
The standards were chosen to give Cr L\text{2,3}\text{-}edges for Cr(II), Cr(III) and Cr(IV). A comparison of the edges (figure 2) shows an increasing energy loss value (measured from the L$_3$ peak) with increasing oxidation state. As well as changes in position, a distinctive change in shape of the L$_3$ peak can be observed in the spectra. The Cr(II) L$_3$ peak is intensity-weighted to the lower energy loss side, whereas the Cr(IV) L$_3$ peak is weighted to the higher energy loss side.

Table 1: Material L$_3$ peak position / eV

| Material        | $L_3$ peak position / eV |
|-----------------|--------------------------|
| Cr(II)$_2$F$_2$ | 576.0                    |
| Cr(III)Cl$_3$   | 576.9                    |
| Cr(III)$_2$O$_3$| 577.8                    |
| Cr(IV)O$_2$     | 578.6                    |

3.3. EELS from wear debris particles
The chromium L$_{2,3}$-edge was collected for the three particles shown in figure 1. The low loss spectrum was also collected from each for calibration. A comparison of the spectra can be seen in figure 3.

The positions of the L$_3$ peaks in each of the spectra lie between 575.4 and 576.1 eV energy loss. The oxidation state that these edges most closely resembles (with respect to energy loss) is Cr(II). However, the shape of the L$_3$ peak better matches that of Cr(III). It is probable that the particles studied are composed of Cr(III), as the shape of the Cr(II) L$_3$ peak is quite distinctive (and not evident here). An exception may be the spectrum for particle C. Although it is very noisy, there is some evidence for weighting of the L$_3$ peak to the high energy loss side. This would match Cr(IV) from figure 2, and may suggest that the particle is composed wholly or partially of Cr(IV). This would agree with the difference in composition measured by EDX. In this instance, peak shape rather than position is probably a better method for giving a qualitative indication of oxidation state, as the calibration method used differed from that of the standards. Using an internal calibration (as was done.

![Figure 2](image-url) EEL spectra collected from standard samples. An increase in energy loss of the edge can be observed with increasing oxidation state, along with a distinctive change in shape of the $L_3$ peak.

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with the standards, using the TiO$_2$ O K-edge) is a more accurate method of calibration than using the zero loss peak. It is feasible that some energy drift could have occurred when switching from the low loss to the core loss region when measuring the spectra from the particles, and that could explain the peak positions not matching those of Cr(III)/Cr(IV).

**Figure 3** A comparison of the three spectra collected from particles A, B and C (shown in figure 1). The positions of the $L_3$ peak in each have slightly lower value than those from the standard samples (figure 2), though this may be a result of a different energy calibration method (i.e. using the zero loss peak). Regarding their shape, they most closely resemble those of the Cr(III) materials measured, although particle C may exhibit a shape close to that of Cr(IV).

### 4. Conclusions

This study has shown that transmission electron microscopy can be used effectively to examine wear debris from metal on metal joint replacements. If the CoCr bulk material forms a passivating chromium oxide layer (as stainless steel does), and this layer is amorphous, then this would explain the observation that the smaller particles were chromium rich and amorphous (and originated from wear at the top surface). Examination of a cross section of the hip replacement will resolve this.

EELS gave even more information about the composition of the particles that were observed. Using reference spectra collected from standards, the particles could be best described as being in the oxidation state Cr(III), with the exception of the smallest particles measured (particle C) which may be either a mixture of Cr(III) and Cr(IV) or wholly Cr(IV). The most reliable indicator as to oxidation state is thought to be the shape of the $L_3$ peak, as a distinctive difference in peak shape for Cr(II), Cr(III) and Cr(IV) has been shown (figure 2). Errors must be taken into account when performing peak position analysis, unless a thorough and reliable energy calibration method is used.

Although no direct evidence for the mode of failure was found, identification and thorough analysis was carried out on a number of wear particles. It is suggested that the failure mode may well be associated with the fine wear debris. Further TEM and EELS work will try to reinforce this proposal.

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