Understanding the Reactivity of CoCrMo-implant Wear Particles

CoCrMo-based metal-on-metal hip implants were introduced, particularly for younger patients, due to their superior wear resistance and theoretical mechanical advantages over other hip implant materials (especially the most commonly used metal-on-polyethylene). However, these CoCrMo-based implants suffered an unexpectedly high failure rate[1] raising concerns over their safety, and leading to considerable attention in the literature on explaining the reasons behind their failure. Lawsuits against manufacturers have been filed in the USA; additionally, they are currently the subject of one of the largest product liability hearings in the UK.[2] Researchers from Imperial College London and SSRL, have been using a correlative spectro-microscopy approach to try to understand the behavior of these systems, along with collaborators at Diamond Light Source, Leeds University and University College London.

Hip simulator studies have shown that despite exhibiting lower volumetric wear compared to other implant materials, CoCrMo alloys lead to the release of smaller, but a significantly larger *number*, of wear particles; up to one trillion particles maybe released in one patient annually.[3] These wear particles elicit an immune inflammatory response which eventually leads to implant failure and revision surgery.[4] CoCrMo is nominally an extremely stable material with high Cr content providing passivity. However, despite the Co:Cr ratio in the original alloy being 2:1; chemical analyses of wear particles from periprosthetic tissue explanted from patients have found the particles to be composed predominately of Cr species, with only trace amounts of Co remaining.[5] The dissolution of these wear particles leads to potential release of the cytotoxic and genotoxic Co(II) and Cr(VI) ions.[6] The aim of this work was to elucidate the mechanism that gives rise to this unexpected level of dissolution of these particles through a correlative spectroscopy and microscopy approach. Studies were performed in simulated biological fluid which mimics the lysosomal environment inside the immune system's macrophage cells where wear particles are typically found *in vivo*. Additionally, an applied electrochemical potential was used to simulate the increasingly oxidizing environment characteristic of the human inflammatory response.

Firstly, to understand how Co:Cr ratio (at.%) varied as a function of simulated environment, CoCrMo particles were analyzed *ex situ* after exposure to different environments, using energy dispersive x-ray spectroscopy via a Transmission Electron Microscope. A considerable drop in the Co:Cr ratio was observed when particles were polarized in a simulated biological fluid (SBF) (measurements over 54 different particles). Whilst a drop in the Co:Cr ratio revealed the preferential dissolution of Co from the alloy, it only indicated the relative dissolution of the two elements, rather than the absolute dissolution of each. The latter was observed using *in situ* x-ray absorption spectroscopy (XAS) at Beam Line I20 at Diamond Lightsource (figure 1(a)). The results revealed that this non-stoichiometric dissolution behavior was particularly prominent at a critical polarization potential. Approximately a 22 % drop in Co compared to 6 % drop in Cr was observed after 0.8 V polarization in SBF over a large population of particles (ca. 2000 particles).

Dynamic morphological changes to the wear particles were observed *in situ* using transmission x-ray microscopy (TXM) at SSRL Beam Line 6-2c. The x-ray images were collected above the Co edge with a spatial resolution of 30 nm as a function of time and applied potential. A rapid egress of dissolving materials was observed in the images (figure 1(b-d)) around the critical potential seen in the bulk spectroscopy measurements. To our knowledge, this is the first time a TXM-based approach has been used to follow local dissolution behavior. To obtain further insight on the dissolution behavior, higher spatial

resolution was achieved with scanning and transmission electron microscopy (SEM, TEM) post TXM experiments revealing the development of a nanoporous structure in the polarized particles (figure 1(e- f)).

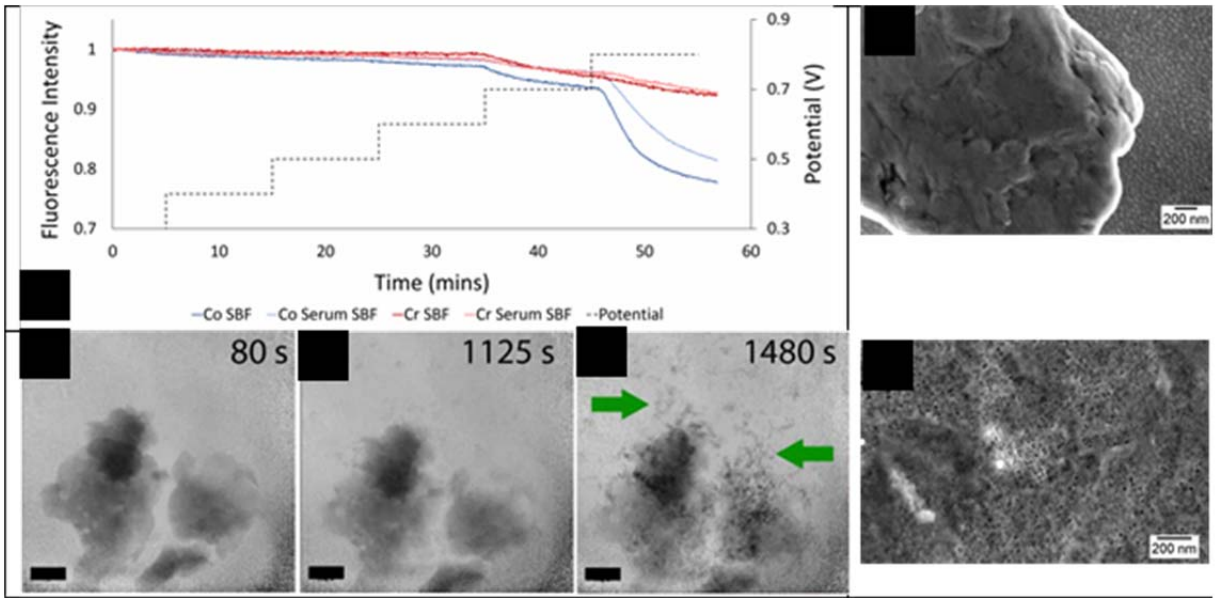

Figure 1: (a) Fluorescence intensity of Co (at 7757eV) and Cr (at 6009 eV) as a function of time and potential. The particles were held at OCP for the first five minutes before the potential was stepped from 0.4 to 0.8 V. A greater drop in the amount of Co compared to Cr is observed after the 0.7 V and 0.8 V steps. (b-d) A series of *in situ* TXM images of CoCrMo particle in SBF recorded during potential scan, revealing the onset of release of diffuse material, Scale bars = 3 µm. (e-f) Secondary electrons SEM images of (e) an as received CoCrMo particle (before exposure to biological environment), and (f) the surface of a CoCrMo particle after exposure to SBF at 0.8 V showing the development of a nano-porous surface

In conclusion, the complementary spectroscopy and microscopy approach was used to develop an understanding of the dissolution of the particles based on chemical and morphological changes. The data consistently show a significantly higher rate of dissolution of Co than Cr in oxidizing conditions used here to mimic inflammatory response *in vivo*. Furthermore, *in situ* TXM shows clear evidence of a rapid and inhomogeneous dissolution process, leading to the porous sponge-like structure observed *via* electron tomography. Taken together these data suggest that the particles undergo a dealloying-like process which was not evident in studies required for the clinical approval of materials. This approach provides valuable evidence on the likely behavior of particles *in vivo* and suggests that current methods for material assessment and approval are insufficiently discriminating.

The methodology developed will be beneficial to other systems where nanoscale, or early stage, dissolution phenomena are critical to behavior.

References

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