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The chemical form of metallic debris in tissues surrounding metal-on-metal hips with unexplained failure

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ABSTRACT

Implant-derived material from metal-on-metal (MOM) hip arthroplasties may be responsible for an unexplained tissue inflammatory response. The chemical form of the metal species in the tissues is predominantly chromium (Cr), but the currently used techniques have not been able to determine whether this is Cr(III) phosphate or Cr(III) oxide. The analytical challenge must overcome the fact that the metal in the tissues is at a relatively low concentration and tissue preparation or the microscopy beam used can affect the results. Microfocus X-ray spectroscopy using a synchrotron beam is useful in addressing both these issues. Using this technique we compared tissue from failed MOM hips with: (1) tissue from metal-on-polyethylene (MOP) hips; (2) chemical standards; (3) metal discs cut from MOM hips. The most abundant implant-related species in all MOM hip tissues contained Cr. Comparison with standards revealed the chemical form was Cr(III) phosphate, which did not vary with manufacturer type (four types analysed) or level of blood metal ions. Cobalt (Co) and molybdenum (Mo) were occasionally present in areas of high Cr. Co was normally found in a metallic state in the tissue, while Mo was found in an oxidized state. The variety of metallic species may have arisen from corrosion, wear or a combination of both. No evidence of Cr(VI) was seen in the tissues examined.

1. Introduction

Metal-on-metal (MOM) hip arthroplasty now represent 35% of all hip arthroplasties performed per annum in the USA [1]. Recent reports found unexplained periprosthetic soft tissue reactions [2] and systemic genotoxicity [3] in patients with MOM hips. The commonest mode of failure of MOM hips is unexplained (43% of failures) according to the UK National Joint Registry. This is in contrast to metal-on-polyethylene (MOP) hips, where the commonest mode of failure is aseptic loosening. MOM hip replacements have been shown to work well in the medium term [4], even for highly active patients. However, sometimes the device has to be removed due to poor biocompatibility, at a rate ranging between 1% and 10% [5,6] depending on the type of prosthesis. A better understanding of the mechanism of poor biocompatibility may help surgeons select the longest lasting device for each patient and engineers to design implants with improved human biocompatibility. Biocompatibility can de defined as the ability of a material to perform with an appropriate host response in a specific application [7]. In one type of MOM hip the inflammatory changes were so severe [8] that the device was withdrawn from the UK healthcare market by the Medicines and Healthcare Products Regulatory Agency [9].

Histological investigations have shown that irrespective of the failure mode there are commonly seen scattered fine black particles that are associated with macrophages in superficial and deep tissue [10]. However, there is confusion as to what these particles are; Mahendra et al. [10] referred to them as cobalt (Co)–chromium (Cr) metal particles and aggregates. The properties of wear and corrosion products from ASTM F75 Co–Cr–Mo orthopaedic implants have been studied for some years [11,12] and it has generally been found that the wear debris and corrosion products in the tissue are abundant in Cr, however, relatively few studies have investigated the metal speciation of the debris.

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Table 1
Reports of chemical characterization of implant-derived metallic species in tissue surrounding hip replacements.

Author & date	Hip type and number	Specimen type	Analysis technique	Findings
Huber (2009) [13]	11 MOM, Sikomet small diameter Ti stem and cup	Periprosthetic tissue	EDXA & FTIR	All showed chromium Phosphate
Catelas (2006) [28]	All MOM 15 current generation; 4 Mckee–Farrar	Digested periprosthetic tissue	EDXA	Cr oxide and Co–Cr–Mo metallic particles
Chassot (2004) [29]	5 MOP, 1 COP	Periprosthetic tissue	Van De Graf accelerator	Co, Cr, Fe, Ni but no speciation
Ektessabi (2001) [27]	1 MOP	Periprosthetic tissue	Synchrotron XRF and XANES	Cr species, but not chromium oxide or chromium metallic
Shahgaldi (1995) [11]	7 MOM, 2 MOP	Periprosthetic tissue	EDXA	Mainly Cr
Urban (1994) [10]	15 MOP	Periprosthetic tissue and scrapings from prosthesis	FTIR	Cr phosphate

There are six reports that investigated the chemical speciation of implant-derived metallic species in human periprosthetic tissues. These are summarized in Table 1. All of these studies used formalin-preserved tissue. Synchrotron analysis was used in only one of these reports, investigating tissue from a single MOP hip [13]. Only two of these studies investigated tissues from MOM hips and neither were able to match spectra from the tissue with metal controls. These two studies disagree with the speciation of the main metallic species found: Huber et al. found Cr phosphate [14] and Catelas et al. found Cr oxide [15]. Characterization of implant-derived metallic species that are present in the tissues surrounding these hips in humans is a logical first step in understanding their biocompatibility. This can be in terms of physical (i.e. particulate or soluble) and chemical (valence state and other atoms bound) forms.

These previous analyses relied on combinations of techniques, such as energy dispersive X-ray spectroscopy (EDX) and Fourier transform infrared spectroscopy. These can give either stoichiometric or chemical information, but not both simultaneously or unambiguous chemical species determination. To determine the speciation of these particles we used microfocus X-ray spectroscopy. This is a method that can determine both the valence state and the chemical structure of nano- and microscale materials within tissue specimens. It uses a high intensity X-ray beam that is produced by a synchrotron. This technique neither requires invasive sample preparation, such as staining, nor any special conditions, such as a vacuum. Thus, the sample can be looked at in as near to the "in vivo" state as possible. Hence, the aim of this study was to definitively identify the chemical form of the main metal-containing species in the periprosthetic tissues of current generation MOM hips using a direct method. We have previously reported data from two patients in a preliminary report [16], where we showed that the effect of fixation did not apparently affect the amount of Cr and Co seen and in those two patients that most of the metal-containing debris was Cr phosphate. Here we report the results of the full study on seven MOM patients and have examined the state of Cr- and Co-containing particles.

2. Patients and methods

2.1. Patients and controls

The research ethics committee approved the study on 25 February 2008 and all patients consented to the use of their tissue. In order to check that there was no influence of the hip type, we analysed tissue from seven patients with current generation MOM hips (three ASR, two BHR, one Biomet and one Cormet). The median age of the patients was 49 years at primary implantation and the median number of months between primary and revision operations was 26.5. We chose to examine capsular tissue from patients where the mode of failure was unexplained following clinical examination and assessment by plain radiographic, microbiological and intra-operative methods.

As control samples we used tissue from two patients with failed MOP hips. These hips failed due to aseptic loosening. Comparison was also made with Cr standards [16] and Co(II) acetate, Co(II) phtalocyanine, Co metal and metal discs cut from two MOM hips, an ASR (DePuy International, Leeds, UK) and a Durom (Zimmer GmbH, Winterthur, Switzerland). These hips were manufactured from CoCrMo ASTM F75.

2.2. Preparation of patient hip tissue

Hip capsule tissue from nine patients with two types of failed hips (MOM and MOP) was analysed. The results are summarized in Table 2. We used three methods of tissue preparation to examine the effect of preparation on the chemical species present in the tissue: formalin fixed; fresh frozen; metal contamination avoidance (MCA). The formalin fixed tissue was processed in paraffin wax, 3–4 μm thick sections were cut and stained with haematoxylin and eosin (H&E). This enabled histological examination of the tissue so that the joint surface edge could be found and cell features identified. This also enabled the architecture of the section to be determined so that we could reliably chose the area to be mapped by the synchrotron beam (because unstained sections were aligned in the beam before analysis). For synchroton analysis we used sequential 10 μm sections to increase any potential signal. The sections were dewaxed by immersion in xylene. We used quartz slides to reduce the signal from the variable iron background in many regular glass slides.

There were concerns that the process of fixing and sectioning could contaminate the tissue or alter the distribution and chemistry of the implant-derived wear debris, so a MCA procedure was adapted from the work of Collingwood et al. [17], who investigated metal-based particles in brain tissue. This involved sectioning with polytetrafluroethylene-coated blades, spreading epoxy glue around the sections on the slides and covering with 25 μm thick Kapton (a polyamide film, Du Pont, Stevenage, UK), cut to size using plastic scissors.

In addition, the MCA procedure was used to prepare snap frozen sections from two patients. One section was cut at 5 μm thickness for H&E staining and sequential sections cut at 10 μms were picked up onto silica slides and brought to room temperature. The cryostat and blade were cleaned with absolute alcohol between specimens.

2.3. Synchrotron methods

The synchrotron work was conducted in the microfocus spectroscopy beamline (I18) at the Diamond Light Source (Harwell Science and Innovation Campus, UK) [18]. Two types of experiments were performed: X-ray Fluorescence (XRF) mapping of the sample