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CORROSION OF METAL HIP ARTHROPLASTIES AND ITS POSSIBLE ROLE IN LOOSENING

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Abstract

Tissue removed with human hip arthroplasties during revision surgery of 45 patients was evaluated by transmission electron microscopy and X-ray microanalysis (XRMA). The results show that microscopic and submicroscopic particles are abundantly present in the tissue at the tissue/implant interface. XRMA of individual particles shows that the chemical composition of a portion of the particles was in agreement with that of the retrieved implants. Regularly, particulates with a dissimilar chemical composition were found. Sometimes, these particles could be recognized as filler particles of the cements used. Other particles could partly or completely be composed of the chemical elements that were used to produce the implant, but the mutual proportion of these elements was different from that of the retrieved arthroplasties.

It is known that corrosion may provoke the selective release of metals from metal alloys in an ionic form. The corrosion weakens the implant and wear particles will easily be detached from the surface. These particles then contribute to a further abrasion of the implant surface. In addition, the particles will contribute to a foreign body reaction that will eventually lead to the aseptic loosening of the implant. The results of the present study, using XRMA to evaluate the chemical composition of many individual particles, confirm these assumptions.

Key Words: Transmission electron microscopy, X-ray microanalysis, human hip arthroplasties, corrosion, wear particles.

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Introduction

The evaluation of periprosthetic tissue around total hip arthroplasties that are removed during revision surgery, gives important information on the processes that occur at the tissue/implant interface. In turn, the understanding of these processes is important for a better knowledge of the conditions that induce loosening of the implant. Thus far the failure of hip arthroplasties has generally been ascribed to the release of wear particles from the ultra high molecular weight polyethylene cup (Evans *et al.*, 1974; Charnley, 1975; Schmalzried *et al.*, 1992). Other investigators have reported the presence of metal in tissue at the tissue/implant interface (Pazzaglia *et al.*, 1985; Huo *et al.*, 1992; Williams and McQueen, 1992). It has already been hypothesized that also the release of metal wear particles may be an important factor in the failure of human hip arthroplasties (Black *et al.*, 1990; Hirsch *et al.*, 1993; Merrit and Brown, 1995). The present study was performed to confirm these observations and to establish the exact nature of the metal wear particles by transmission electron microscopy (TEM) and X-ray microanalysis (XRMA) so that the mechanism of particle release can be better understood.

Materials and Methods

Tissue samples from patients undergoing revision of hip arthroplasties were collected in two orthopaedic departments during a period of two years. Soft tissue biopsies were taken from well defined places around the implant, including the superior, lateral, and inferior margins of the acetabulum and the femoral canal in locations corresponding to the middle and distal portions of the femoral component (Fig. 1). In total, seven different brands of hip arthroplasties were evaluated for this study (Table 1). The present paper concerns tissue samples from 45 patients: 19 cemented total hip arthroplasties, 12 cementless total hip arthroplasties, seven hybrid total hip arthroplasties (cemented femoral and cementless acetabular component), and seven cementless bipolar

Table 1. Overview of metals detected in individual wear particles around 45 human hip arthroplasties.

Implant	Interval	A	B	C	D	E	F
1	38	1	1	1	63	3	Al,Ti
2	28	1	1	3	42	1	0
3	96	1	2	1	80	3	Co,Cr,Mo
4	81	1	3	1	64	3	Co,Cr,Mo
5	38	1	3	2	47	3	Cr,Fe,Mo,Ni
6	85	1	3	1	63	3	0
7	92	1	4	1	56	1	Co,Cr,Mo,Ti
8	171	1	2	1	68	3	Co,Cr,Mo
9	143	2	1	1	47	3	Ti
10	62	2	4	1	77	2	Ti
11	110	1	4	1	76	1	Al,Ti
12	105	1	2	1	70	3	Cr,Fe,Ni,Zr
13	38	2	5	1	81	3	Fe,Pt,Zr
14	48	1	6	1	88	3	Zr
15	158	2	6	1	86	2	Co,Cr.Mo,Zr
16	89	1	1	1	67	3	Co,Cr,Mo
17	54	2	5	1	63	1	Co,Cr,Mo,Zr
18	62	1	7	1	71	1	Al,Co,Cr,Ti
19	26	1	4	1	64	1	Co,Cr,Mo
20	98	1	7	1	46	1	Fe,Mg,Si,Ti
21	112	1	6	1	82	3	Co,Cr,Mo,Zr
22	92	1	4	1	68	1	Al,Ti,V
23	47	2	6	1	88	1	0
24	88	2	5	3	62	1	0
25	52	1	7	1	61	1	Al,Co,Cr,Ti
26	80	2	6	1	61	3	Ti
27	112	2	4	1	58	3	Co,Cr,Mo,Ti
28	74	2	6	1	86	3	Co,Cr,Mo
29	62	1	6	1	67	3	Co,Cr,Mo,Zr
30	149	1	4	1	61	1	Ti
31	80	1	7	1	74	1	Al,Cr,Ti

Table 1 continued. Overview of metals detected in individual wear particles around 45 human hip arthroplasties.

Implant	Interval	A	B	C	D	E	F
32	175	1	2	1	81	3	Zr
33	61	1	7	1	72	1	Co,Cr,Mo,Zr
34	72	1	6	1	86	1	Zr
35	94	1	6	1	59	1	Ti,Zr
36	173	1	6	1	87	1	Mo,Zr
37	204	1	6	1	71	1	0
38	110	1	4	1	67	1	0
39	173	1	7	1	66	1	Ti
40	140	1	1	1	66	3	Co,Cr,Fe,Mo
41	81	1	1	1	40	3	Ca,V
42	31	1	7	1	69	1	Al,Fe
43	66	1	4	1	63	1	Fe
44	181	1	2	1	60	3	Zr
45	95	1	1	1	44	3	Co,Cr,Mo

Interval: Interval (months) between primary operation and first revision or between revision and rerevision.

A: 1 = Woman; 2 = Man.

B: Type of primary arthroplasty:

1 = Uncemented Gerard double-cup arthroplasty (Co,Cr,Mo alloy)

2 = Cemented McKee-Arden total hip arthroplasty (Co,Cr,Mo alloy)

3 = Uncemented madreporic Lord total hip arthroplasty (Co,Cr,Mo alloy)

4 = Uncemented Mecring total hip arthroplasty (Ti,Al,V femoral stem and threaded cup) (Co,Cr,Mo modular femoral head)

5 = Cemented Muller Geradschaft total hip arthroplasty (Co,Cr,Mo alloy)

6 = Cemented Stanmore total hip arthroplasty (Co,Cr,Mo alloy)

7 = Hybrid total hip arthroplasty (Cemented Stanmore femoral component Co,Cr,Mo alloy) (Uncemented Mecring threaded cup, Ti,Al,V alloy)

C: 1 = First revision; 2 = Second revision; 3 = Third revision.

D: Age at time of revision (years).

E: 1 = revision of acetabular component; 2 = revision of femoral component; 3 = revision of both components

F: Chemical composition of intracellular particles obtained by XRMA. 0 = No elements detected.

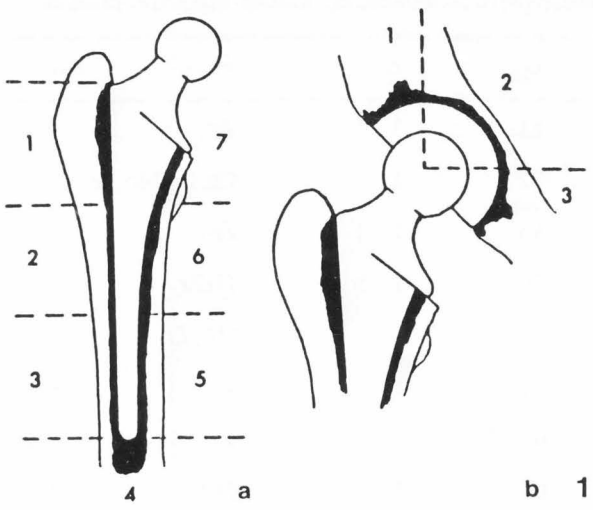

Figure 1. Schematic representation of the locations where the biopsies were taken. The biopsies examined in the present study derived from locations 1, 2, 6 and 7 of the femoral component (**1a**) and from the locations 1 and 3 of the acetabular component (**1b**).

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double-cup hip arthroplasties. From the 45 patients under study, 10 were male and 35 female. The mean age at revision was 67 years (range 40-88 years). The mean interval between the primary operation and revision was 94 months (range 26-204 months). There were 42 first revisions, one second (case 5), and two third revisions (cases 2 and 24). The revision in 21 cases involved both components, and in 22 cases only the acetabular component was revised. The majority of the acetabular components were threaded Mecring cups (Mecron, Berlin, Germany). In two patients, only the femoral component was revised. All biopsies presented in this paper were obtained from the remnant soft tissue covering the femoral component at locations 1, 2, 6 and 7 in Figure 1a, and soft tissue from between the acetabular component and bone at locations 1 and 3 in Figure 1b. Sometimes, the biopsies were visibly dark-colored. In other cases, the presence of wear debris could not be suspected from the macroscopical appearance of the biopsies. After retrieval, the biopsies were prepared for TEM and XRMA evaluation. Detected particles were analysed and the chemical elements were recorded. We did not register the elements per individual particle.

Specimen preparation

All biological material was prepared according to our routine method (Koerten *et al.*, 1990b). In short, the biopsies were pre-fixed during 2 hours at 4°C in 1.5% glutaraldehyde in 0.14 M sodium-cacodylate buffer (pH 7.3, 350 mOsmol). After pre-fixation, the tissue samples were cut into small blocks of approximately 1 mm^3 and post fixed in 1% osmium tetroxide. After fixation, the specimens were dehydrated in a graded series of ethanol and embedded in epoxy resin (LX 112, LADD Research Industries Inc., Burlington, VT). The plastic was allowed to polymerize during 48 hours at 60°C. Ultrathin sections were made with a diamond knife on a Reichert OM U3 ultratome (C. Reichert Optische Werke AG, Wien, Austria).

Transmission electron microscopy

Material, that was fixed, embedded and sectioned according to the method described above was examined by TEM. The sections, approximately 70 nm thick, were collected on copper grids. A portion of the sections was contrasted with uranyl acetate and lead hydroxide, and used for morphological evaluation. The sections were examined in a Philips EM 400 T (Philips Electron Optics, Eindhoven, The Netherlands) transmission electron microscope {equipped with a scanning transmission electron microscopy (STEM) unit} operated at an accelerating voltage of 80 kV. Another part of the section was studied without the use of contrasting agents, to allow an undisturbed establishment of the chemical composition by XRMA.

X-ray microanalysis

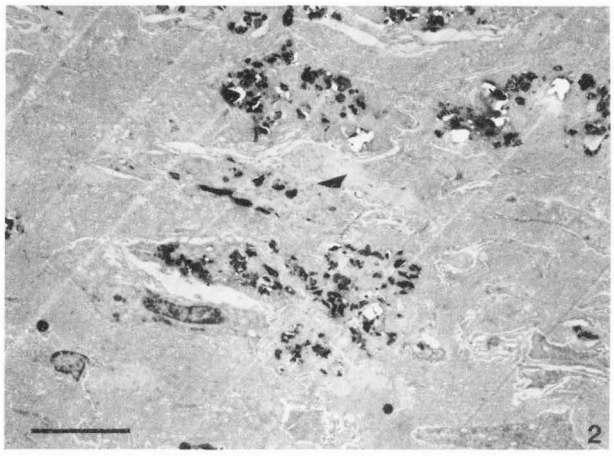
XRMA was performed in the same Philips EM 400 T, using a Tracor Northern TN 2000 X-ray Microanalysis system (Tracor Northern, Middleton, WI). For XRMA measurements, the specimen holder was tilted at an angle of 108° relative to the electron beam, to allow optimal collection of the X-rays. The XRMA measurements were performed at an accelerating voltage of 80 kV and a spot size of 40 nm. Peak identification was performed using the commercially supplied software of the XRMA system.

Results

Macroscopic observations

All implants were removed because of clinical and roentgenographic mechanical loosening. Cases of septic loosening were excluded by bacteriological tests. The alloys of the arthroplasties under study contained one or more of the elements Ti, Al, V, Co, Cr and/or Mo (see Table 1).

In case of revision of a resurfacing hip arthroplasty, remnant tissue covering the femoral component and tissue from between the acetabular component and bone were obtained. Sometimes, the biopsies had a dark-stained appearance. In other cases, the presence of wear debris could not be suspected from the macroscopic appearance of the biopsies.



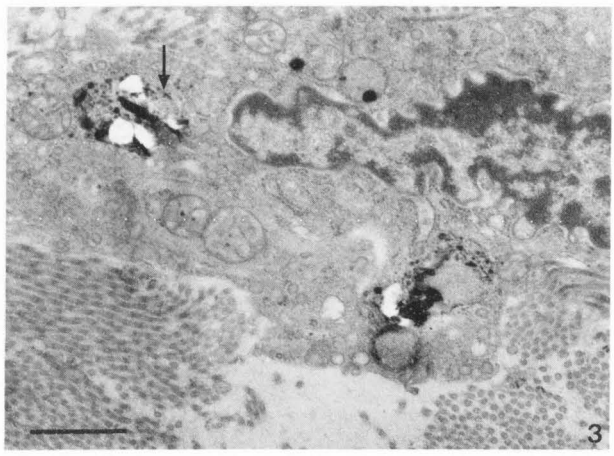


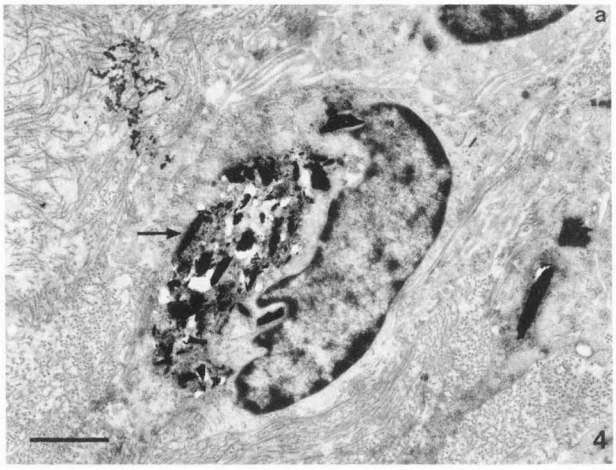
Figure 2 (at left). Transmission electron micrograph of tissue, derived from the interface of the femoral component (location 7) of implant number 4. Numerous dark inclusions can be seen in the cytoplasm of the cells. The variation in the size and form of the particles is clear. Bar = 7 μm.

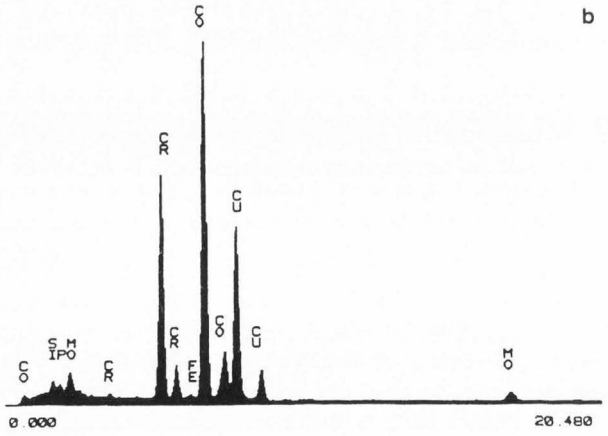
Figure 3 (at right). Transmission electron micrograph of a cell in the same location as Figure 2, showing endocytosed particles, some of which have been removed during sectioning. Nevertheless, the limiting membrane of the inclusion bodies containing the remaining particles is intact (arrow). Bar = 1 μm.

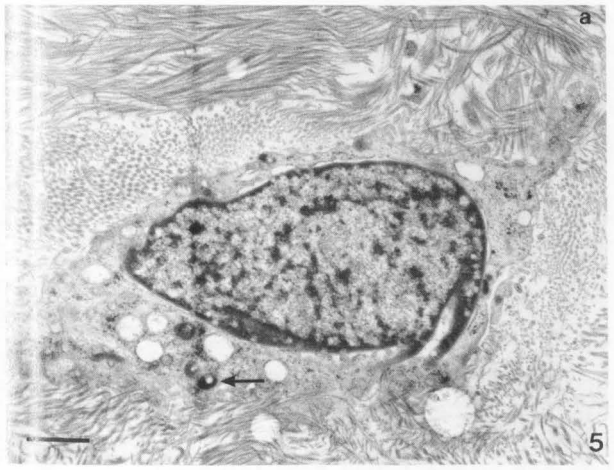
Transmission electron microscopy and X-ray microanalysis

TEM of the interface tissue showed a typical foreign body reaction, characterized by the massive amount of connective tissue. Large areas of collagen and many fibroblasts were observed in the sections. Macrophages and multinucleated giant cells were frequently present. Electron-dense particles were found to be endocytosed by macrophages and to a lesser extent also by fibroblasts. The size of the detected particles varied from < 0.1 μm to 10 μm (Fig. 2). As Figure 2 shows, also the form of the particles varied. Sometimes sharp-edged particles were seen, but more frequently such inclusions were rounded off. Regularly, most probably due to their physical hardness, the particles were removed from their original position during sectioning and had shifted to other places in the sections. If this happened, characteristic sectioning artifacts and clearly dislocated particles were visible. At other places, however, particles were still in their original position, i.e., contained in inclusion bodies with the limiting membrane still intact (Fig. 3). Cells characteristic for an acute inflammatory reaction, i.e., neutrophil granulocytes and monocytes were not detected in any of the cases.

XRMA was used to determine the chemical composition of the small electron-dense inclusions. The results of these measurements, as summarized in Table 1, showed in general peaks that represent the metals that were used to manufacture the implants (Fig. 4). It appeared, however, that the spectra were not always in agreement with the chemical compositions as given in the manufacturers documentation of the compounds used to produce the implants. Sometimes, one or two of the composing elements were absent (Fig. 5) or, in cases that all elements were present, the ratios between the peak heights could be different from those found generally for implants of that specific brand. In other cases, elements that were completely different from those in the implant alloy were detected. We could demonstrate the presence of Ni, Fe, Pt, Mg, Si and Zr. Especially, the number of particles that gave spectra with peaks for the latter element was relatively large (Fig. 6). For cements applied for implantation of the prostheses that were evaluated in the present study, the radiopaque labelling used consisted of Zr only. In cases where Ba is used as a radiopaque label, this element can be demonstrated as frequently as Zr (results not included). Incidently, relatively large electron dense structures (> 10 μm) were seen (Fig. 7). XRMA of these particles gave spectra without specific elemental peaks, meaning that the measured structures were composed of elements with an atomic number below 11; hence the measured structures were of an organic (polymeric) nature. Such particles were found exclusively in biopsies from double-cup hip-arthroplasties containing high molecular weight polyethylene.







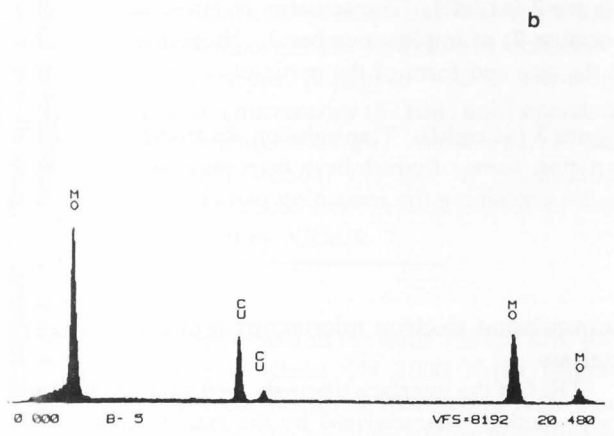


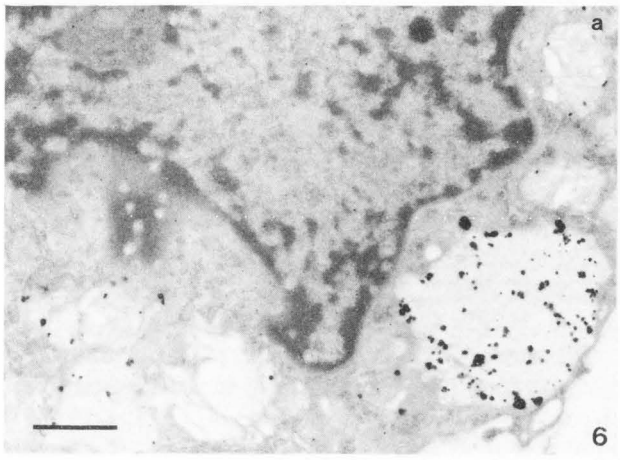
Figure 4 (at left). (a). Transmission electron micrograph of a biopsy from location 7 in the femoral component of implant number 3. A cell containing numerous electron dense inclusions is clearly visible. Bar = 1 μm. (b). XRMA spectrum of the particle (indicated in Fig. 4a; arrow) showed the presence of the characteristic elements Co, Cr and Mo.

Figure 5 (at right). (a). Transmission electron micrograph of a biopsy from location 7 in the femoral component of implant number 19. Some small electron dense inclusions are present. Bar = 1 μm. (b). XRMA spectrum of the particle (indicated in Fig. 5a; arrow) showed the presence of Mo only.

Discussion

Thus far, many researchers have investigated the loosening of cemented and non-cemented total hip arthroplasties in humans, but there is still no consensus about the clinical background of aseptic loosening. It has been postulated that the occurrence of sterile chronic inflammatory reactions at the tissue/material interface is an important factor in the aseptic loosening of implants. Focal osteolysis occurs frequently around loose cemented components (Harris *et al.*, 1976; Willard and Semlitsch, 1977; Carlsson *et al.*, 1983; Lennox *et al.*, 1987; Tallroth *et al.*, 1989; Maloney *et al.*, 1990) and cementless components (Maloney *et al.*, 1990; Santavirta *et al.*, 1991) of total hip arthroplasties. Such osteolytic activity is thought to be induced by factors that are released during inflammatory and foreign body reactions.

The present study was performed to establish the nature of particles in tissue around revised hip arthroplasties. For that purpose, individual electron-dense particles were detected with TEM and then evaluated by XRMA. It was found in this part of the study that numerous submicron particles can be present in the cytoplasm of macrophages and giant cells, and even in fibroblasts. XRMA showed that the majority of the particles derived from bone cements, in which they are used as



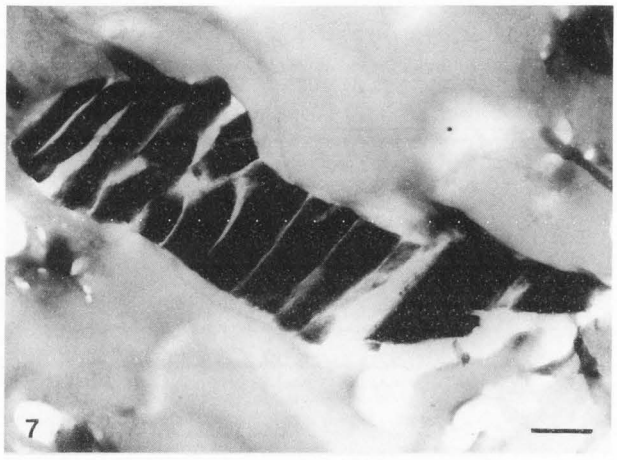


Figure 7. Transmission electron micrograph of a biopsy from location 2 in the acetabular component of implant number 22. The large particle gave no detectable signal when measured using XRMA, indicating that elements with an elemental number above 10 were absent. We assume that this particle concerns ultrahigh molecular weight polyethylene. Bar = 0.5 μm.

b

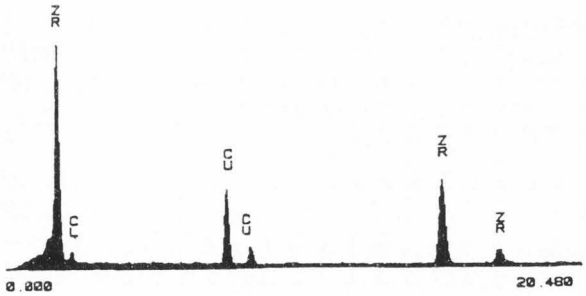


Figure 6. (**a**). Transmission electron micrograph of a biopsy from location 6 in the femoral component of implant number 13. (**b**). Numerous small inclusions can be observed. XRMA of the particles showed the presence of Zr without exception.

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radiopaque filler particles, and from the articulating surfaces of the implants. We hypothesize that these particles are therefore important in the induction of chronic inflammatory effects, whose seriousness is related to size and quantity of the wear debris. Indeed, a relation between the size of these particulates and their effect on inflammation has been shown in a previous study performed by our group (van der Meulen and Koerten, 1994). In that study, it was demonstrated by the introduction of latex spheres into the mouse peritoneal cavity that the size of the particles is inversely proportional to the severeness of the inflammatory reaction. On the basis of this previous study, it is hypothesized that especially the small to very small particles are responsible for the initiation of inflammatory effects. These particles may, therefore, play an important role in the loosening of total hip arthroplasties. The fact that such

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small particles were without exception present in tissue derived from loose implants in the present study is suggestive of a relation between the inflammatory effect and nature of the particles. Future observations on biopsies from non-failed implants, for instance obtained from amputation surgery or from autopsy material, are required to test this hypothesis.

The chemical composition of a large proportion of the particles generally related to the composition of the implants. However, in many cases, this composition did not match with that from the manufacturers' documentation. A part of these divergent particles can be explained: Ba and Zr are known to be used in bone cements as radiopaque markers. Si may be remnant from the polishing procedure of the implant. Fe, although also present in low concentrations in some of the implant types, may also represent the normal iron metabolism of macrophages. Indeed, we observed in former studies where macrophages dealt with poorly dissolvable material in a mouse peritoneal model that macrophages are well capable to accumulate iron as hemosiderin in residual bodies or inclusion bodies (Koerten *et al.*, 1990a). The origin of platinum in implant 13 remains unclear. We hypothesize that these particles may be derived from instruments used during surgery; Ca is an element that is present in bone as the mineral component, but Ca can also be present due to pathological calcification of connective tissue. It is our opinion that the difference in chemical composition between particles that are with certainty

derived from the implant and the implant itself relates to a process of selective corrosion. Indeed, corrosion of metallic implants has been reported (Ferguson *et al.*, 1960; Meldrum *et al.*, 1993). In their paper, Ferguson *et al.* (1960) reported experimental evidence for the ionization of metals in tissues around implants in rabbits. We believe that selective corrosion of electrochemically active phases or other microstructural constituents will result in slow release from the implant alloy. After such electrochemical corrosion, the alloy will have lower resistance to wear, and secondary phase particulates may be released from the surface. The presence of impurities in the alloys of which implants are made, may accelerate this process, due to the formation of additional secondary microstructural phases that are susceptible to corrosion. We have indications that such metallic impurities are present in brand new human hip arthroplasties already and further investigations directed towards the occurrence of these impurities have already been started.

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Discussion with Reviewers

Reviewer I: Could the authors briefly summarize possible explanations for the discrepancies of elemental composition between particles and the manufactured implants?

Authors: As mentioned in **Discussion**, we believe that the formation of a galvanic element and the subsequent

galvanic corrosion may induce the selective release of ions from the implant surface. In addition impurities in the compounds have been reported. Wear particles derived from corroded or impure areas in the surface will have a deviating chemical composition. Furthermore, it cannot be excluded that particles are derived from other sources, i.e., instruments used during surgery.

Reviewer I: Have the authors found any relationships between the type of prothesis and their findings? What is the role of implantation period for the observed findings?
Authors: During the course of the experiments performed for this paper, we had no indications that the occurrence of particles with a deviating chemical composition could especially be ascribed to a certain implant brand. However, impurities were already seen in the surface of new implants (see last paragraph of **Discussion**). In evaluations that we are performing presently, observations have been made that point to type related imperfections. The number of released particles in relation to implantation time was not evaluated in the present study. We assume, however, that the amount of wear will increase with the duration of implantation.

W.A. Brantley: Could the authors provide references to information about the composition of implant alloys and bone cements?
Authors: It is very difficult to obtain information from implant manufacturers about the accurate composition of their products. We did not succeed to get this information from them. To the best of our knowledge there is also not something like a report that gives this information. The data given in Table 1, column B are obtained from the surgeons that performed the revision operations. From XRMA measurements in SEM on the surface of intact implants, we know that certain other elements can be present.

G.M. Roomans: The authors have found that there were differences between the manufacturers' data on the alloys used in the implant and the composition of metal particles as seen by X-ray microanalysis. The authors suggest that this is due to (a) leakage of elements by corrosion, (b) the presence of metal impurities. On the basis of their data, can the authors indicate which elements appeared to have leaked out most frequently, and which elements could be considered as impurities?
Authors: We did not investigate the "leaking" of elements within the scope of the present paper. It was found that, in areas of corrosion on the implants itself, the signal for Co is low, relative to the surrounding non-affected areas when X-ray maps are recorded. Cr and Mo are in the same maps present in much higher concentrations as was deduced from the intensity of the signal in these maps. The results of this latter study are in relation to one specific type of implant and currently being prepared for publication.

G.M. Roomans: Was the dark color of the biopsies connected with a higher metal content or the presence of specific elements? Could it be due to hemorrhaging?
Authors: The dark color of the biological tissue is definitely derived from the presence of metal residue from the implants. As shown in Figure 2, for instance, the concentration of particles in the biopsies can be very high. It can indeed not be excluded that Fe originating from hemorrhage will be present in the cells surrounding the implants.

P. Thomsen: Could the authors comment on the spatial distribution of particles and elements (possible differences between locations and possible gradients in relation to the surface of the prosthesis?
Authors: As we took the tissue biopsies from the implant after revision, and because we used remnant tissue at the interface only, it is not possible to give information on the distance where particles could still be found or about the possibility that a gradient in particle concentration is present. We know, however, from the macroscopical observations by the surgeons, that tissue next to the implant could sometimes have a black appearance, suggestive for large amounts of particles millimeters distant from the implant surface.

P. Thomsen: Could authors comment on the possible role of impurities for the pathophysiology of inflammation, fibrous repair and loosening?
Authors: Referring to our paper (van der Meulen and Koerten, 1994), we know that the presence of particles will induce an inflammatory effect. The smaller the particles, the stronger the inflammation. The fact that cells in inflamed areas can release osteolytic factors is well known (see references indicated in **Discussion**). Therefore, it can be expected that the persistent presence of inflammatory agents will maintain the osteolytic effect and ultimately result in the loosening of the implant.