

# HA particles can be released from well-fixed HA-coated stems

## Histopathology of biopsies from 20 hips 2–8 years after implantation

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**ABSTRACT** – 20 hip arthroplasties with a Landos Corail Ti6Al4V stem entirely plasma-sprayed with a  $155 \pm 35 \mu\text{m}$  thick HA coating were reoperated on after median 6 (2–8) years because of polyethylene wear (10), acetabular loosening (7), instability (2), or infection (1). We took biopsies from the proximal femurs adjacent to the well-fixed stems. Undecalcified sections were prepared and examined with a light microscope.

The biopsies contained median 5 (1.3–16) mm metal interface with 54% HA, 32% bone, and 14% soft tissue. The median thickness of the remaining HA coating was  $137 (6\text{--}380) \mu\text{m}$ , and the HA-tissue interface included 89% bone and 11% soft tissue. All HA coatings showed partial degradation and replacement by soft tissue, osteoid-like tissue, or bone. 6 hips had tissue ingrowth between HA and metal consistent with delamination. 14 hips showed bone resorptive areas containing some HA particles and large amounts of polyethylene and metal particles, partly internalized in multinucleated giant cells and macrophages. Bone resorption was associated with metal and polyethylene particles, but not with HA particles. The HA coatings were undermined, resulting in release of large flakes of HA with free access to the articulation. We believe this mechanism may be responsible for third-body wear.

Hydroxyapatite (HA)-coated hip prostheses can give excellent pain relief and reliable radiographic fixation (Geesink and Hoefnagels 1995, Røkkum and Reigstad 1999, McNally et al. 2000, Tonino and Rahmy 2000). Fixation by direct bone-implant contact has been shown with light microscopy

of components retrieved at autopsy (Bauer et al. 1991, 1993, Hardy et al. 1994, Tonino et al. 1999, Coathup et al. 2001). Radiostereometric studies up to 3 years after surgery have demonstrated less early migration and no difference in polyethylene wear with HA-coated hip components, as compared to similar components without HA coating (Kärrholm et al. 1994, Moilanen et al. 1996, Thanner et al. 1999). At longer follow-up, complications with excessive polyethylene wear, osteolysis, and loosening have been reported with some HA-coated hips (Bloebaum et al. 1994, Morscher et al. 1998, Røkkum et al. 1999). The demonstration of HA particles embedded in the polyethylene articulating surface suggests third-body wear (Bloebaum et al. 1994, 1997, Lausmaa et al. 1998, Morscher et al. 1998). Therefore, the HA particles may increase polyethylene wear, and the abundance of polyethylene particles could cause osteolysis (Schmalzried et al. 1992, Kadoya et al. 1998). HA particles may be detached from the coating during insertion of the prosthesis. If degradation of the HA coating takes place with the prosthesis in situ, this may also lead to the liberation of HA particles.

We examined biopsies from the proximal femoral bone adjacent to well-fixed HA-coated stems to evaluate the coating near the artificial joint after years of implantation, especially concerning evidence of HA particle release.

### Patients and methods

We operated on 20 hips in 19 patients from

Table 1. Patient data

A	B	C	D	E	F	G	H	I	J	K	L	M
1	m	arthrosis	57	107	rev.	Parhofer	steel	2.0	ac. loosening	+	changed cup	–
2	m	arthrosis	75	86	rev.	Corail	steel	3.6	instability	+	changed PE/head	1.3
3	m	cong. disloc.	56	85	prim.	Corail	steel	4.2	PE wear	+	changed cup	2.8
4	f	arthrosis	61	87	prim.	Corail	steel	4.3	ac. loosening	+	changed cup	0.3
5	m	Legg-Calvé-Perthes	32	75	prim.	Corail	Al <sub>2</sub> O <sub>3</sub>	4.8	instability	+	changed cup	–
6	f	arthrosis	59	68	prim.	Corail	steel	5.2	PE wear	+	changed PE/head	2.9
7	f	arthrosis	66	65	prim.	Landos cem.	steel	5.3	ac. loosening	+	changed cup	–
8	f	cong. disloc.	57	57	prim.	Corail	steel	5.6	ac. loosening	+	changed cup	1.4
9	f	arthrosis	56	62	prim.	Corail	steel	5.7	PE wear	+	changed PE/head	1.7
10	f	arthrosis	55	70	prim.	Corail	steel	5.8	PE wear	+	changed cup	5.7
11	m	arthrosis	60	75	prim.	Corail	steel	5.9	PE wear	+	changed PE/head	2.5
12	f	arthrosis	54	85	prim.	Corail	Al <sub>2</sub> O <sub>3</sub>	5.9	ac. loosening	+	changed cup	0.8
13	f	dysplasia	47	52	rev.	Corail	steel	5.9	infection	+	removed prosthesis	1.6
14	f	arthrosis	63	69	prim.	Corail	steel	6.1	PE wear	–	changed PE/head	1.8
15	f	arthrosis	58	57	prim.	Corail	steel	6.2	ac. loosening	+	changed cup	1.0
16	f	arthrosis	55	55	prim.	Corail	steel	6.3	PE wear	+	changed PE/head	1.9
17	f	arthrosis	66	58	prim.	Corail	steel	6.3	ac. loosening	+	changed cup	1.6
18	f	arthrosis	58	68	prim.	Corail	steel	6.4	PE wear	–	changed PE/head	2.8
19	m	epiphyseolysis	36	87	prim.	Corail	Al <sub>2</sub> O <sub>3</sub>	6.8	PE wear	–	changed PE/head	2.2
20	f	arthrosis	54	73	prim.	Corail	Al <sub>2</sub> O <sub>3</sub>	7.5	PE wear	+	changed PE/head	2.9

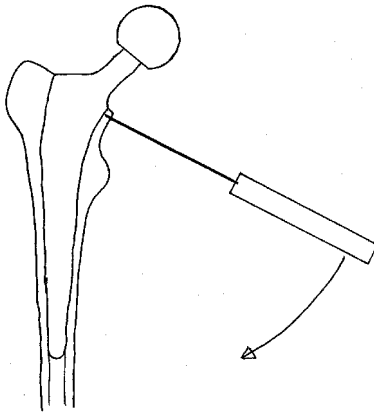
  

A Hip no.	H Femoral head
B Gender	I Implantation time, yr
C Diagnosis	J Reason for reoperation
D Age at stem insertion, yr	K Hip pain
E Weight, kg	L Reoperation
F Primary stem or revision	M Eccentricity, mm
G Cup type	

December 1988 to September 1992 with insertion of an HA-coated stem. There were 14 female and 6 male hips. Their median age at operation was 57 (32–75) years, and median weight 70 (52–107) kg. The diagnoses were arthrosis (15), congenital hip dislocation (2), epiphyseolysis (1), dysplasia (1), and Legg-Calvé-Perthes (1). 17 primary stem implantations and 3 stem revisions due to aseptic loosening were performed (Table 1).

The Ti6Al4V stem was entirely plasma-sprayed with a  $155 \pm 35 \mu\text{m}$  layer of HA, having a purity greater than 98%, a density between 1.2 and 1.6 g/mL, and a crystallinity between 50% and 70%, according to the manufacturer (Landos Corail, Landanger, Chaumont, France). The bonding strength was reported from 20 to 30 MPa, and the surface roughness was characterized as having an Ra value of about 10  $\mu\text{m}$  and an Rt value between 60 and 65  $\mu\text{m}$ . We used 18 HA-coated Landos Corail hemispherical cups with self-tapering threads, one cementless uncoated Parhofer screw cup and one cemented Landos polyethylene cup as well as 16 steel and 4 alumina ceramic 32 mm femoral heads.

No patient suffered from thigh pain, and on radiographs, the stems showed bone apposition without diaphyseal lines. Prior to reoperation, pain had developed in 17 hips. Standardized antero-posterior radiographs of the pelvis and femurs centered over the pubis and lateral views of the femurs were taken before reoperation. We defined osteolysis as any focal area of bone loss adjacent to the prosthesis; it had been present in all hips, starting from 2 years postoperatively. We found 2 acetabular osteolytic lesions in region A and 2 in regions A and B (DeLee and Charnley 1976). Periprosthetic double lines (Amstutz et al. 1989) were classified as linear osteolysis when the lucency exceeded 1 mm (Zicat et al. 1995). Femoral linear osteolysis was seen in regions 1 and 8 (Gruen et al. 1979, Johnston et al. 1990) in 14 hips. Scalloping in region 7 (calcar) was found in 12 hips and 2 osteolytic lesions were located in the greater trochanter. No lesion extended into the diaphysis. Increased eccentricity of the femoral head in the acetabulum was measured in hips with available standardized radiographs (Røkkum and Reigstad



**Figure 1. Biopsy harvesting.**

A thin slice of bone was chiseled out, approaching the stem without hitting it. By tilting off the slice, using the remaining femoral bone as hypomocion, the biopsy loosened from the stem, leaving only a metallic surface without visible HA.

1998), using postoperative radiographs after the index operation as reference (Table 1).

The hips were reoperated on after median 6 (2–8) years because of polyethylene wear (10), acetabular loosening (7), instability (2), and infection (1). The indications for reoperation of a hip with polyethylene wear were pain or threatening wear-through of the polyethylene, occasionally manifested as a sudden rapid increase in eccentricity. Some hips had a minimum polyethylene thickness of just 3 mm. 7 of the 10 hips that were reoperated on because of polyethylene wear had developed pain (Table 1). Osteolysis alone was not considered an indication for reoperation.

The reoperations, done via a direct lateral approach (Hardinge 1982), included replacements of the acetabular cup (10), of the polyethylene liner and femoral head (9), and complete removal of the prosthesis (1). The back of the polyethylene inserts removed were smooth and slightly depressed, except for the areas below the holes in the backing where the markers of machining could still be seen. As a part of the procedure, 1–3 biopsies were taken from each hip, including bone and soft tissue from the proximal femur adjacent to the medial or anterior aspect of the stem (Figure 1).

The bone removed with adherent soft tissue was oriented and marked, fixed by immersion in 4% neutrally-buffered formaldehyde, dehydrated in graded series of ethanol, and finally embedded in

light-curing resin (Technovit 7200 VLC, Kultzer & Co., Germany). The cutting direction was perpendicular to the bone surface that had been in contact with the prosthesis, which also included the attached soft tissue. Cutting and grinding were done in an Exakt sawing machine and grinding equipment, using the method described by Donath (1993). The undecalcified sections were ground to a thickness of about 10  $\mu\text{m}$  before routine histological staining in 1% toluidine blue in 1% borax solution mixed in a 4:1 proportion with pyronin-G solution. This staining method makes it possible to identify various structures of the tissue stained in different ways with a light microscope: old bone stains pale purple, new bone dark purple, osteoid grey-bluish, and soft tissue blue.

The histomorphometric evaluation was done with a light microscope, using a mouse connected to Leitz Microvid equipment coupled to a PC computer. Distinctively demarcated and smoothly-shaped biopsy surfaces corresponding to the implant were assumed to represent the metal interface. We examined the metal and HA-tissue interfaces and measured the lengths and the distribution of soft tissue, bone, and HA. The thickness of HA and bone layers was measured perpendicular to the metal interface at 150  $\mu\text{m}$  intervals. HA degradation and replacement were recorded, as well as the distribution of HA and metal particles. Polyethylene particles were identified using polarizing filters. We also did a qualitative evaluation of the specimens.

The study was approved by the local ethics committee, and informed consent was obtained from every patient in the trial.

### Statistics

Comparison of categorical data was done with the two-tailed Fisher's exact test, and statistical significance was set at  $p < 0.05$ .

### Results

The stems were well-fixed, although we found osteolysis between the proximal femoral bone and the stem in all hips. Emptying of the osteolytic lesions showed disappearance of the HA coating from the surfaces of the stems that were not cov-

Table 2. Results

Hip no.	Biopsies (n)	Metal interface				HA-tissue interface			HA thickness ( $\mu\text{m}$ , median, range)	Bone resorption	Particles			
		Total (mm)	HA (%)	Bone (%)	Soft tissue (%)	Bone (%)	Soft tissue (%)	HA			Metal	PE		
1	3	10.4	64	8	28	97	3	130 (128–138)	n	y	n	n		
2	2	10.0	81	9	10	92	8	158 (143–227)	n	y	n	n		
3	3	3.4	82	18	0	100	0	170 (159–193)	y	y	y	y		
4	2	5.1	89	8	3	85	15	152 (123–171)	y	y	y	y		
5	2	15.6	9	80	11	100	0	63 (47–76)	n	y	n	n		
6	3	3.8	100	0	0	85	15	182 (146–213)	y	y	y	y		
7	1	5.2	79	12	9	94	6	92 (83–130)	y	y	y	y		
8	3	–	–	–	–	–	–	–	y	y	y	y		
9	1	7.6	0	83	17	–	–	–	y	n	y	y		
10	3	11.5	12	54	34	16	84	163 (121–170)	y	y	y	y		
11	2	2.4	100	0	0	95	5	127 (96–128)	y	y	y	y		
12	2	–	–	–	–	–	–	–	y	n	n	y		
13	2	2.3	0	84	16	–	–	94 (58–130)	y	y	y	y		
14	2	–	–	–	–	–	–	–	y	y	y	y		
15	2	5.2	92	0	8	67	33	109 (77–146)	y	y	y	y		
16	1	4.0	100	0	0	100	0	241 (233–280)	y	y	y	y		
17	3	1.6	100	0	0	81	19	128 (116–141)	y	y	y	y		
18	1	–	–	–	–	–	–	–	n	y	n	n		
19	2	1.9	76	0	24	88	12	277 (194–340)	n	y	n	y		
20	2	4.3	100	0	0	95	5	197 (131–221)	n	y	n	n		

n no, y yes

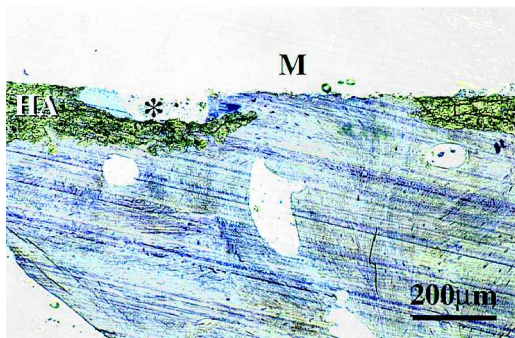


Figure 2. Hip 7 (5.3 years).

Smooth and slightly curved surface consistent with the shape of the stem. The HA layer is interrupted by bone. A limited zone of soft tissue (\*) between HA and previous metal (M) is seen on the left side. Osteoid-like tissue on each side of the soft tissue is becoming bone on right.

ered with bone; patchy in the earliest reoperations and almost complete at longer follow-up.

Biopsies from 16 hips showed median 5 (1.3–16) mm long, smoothly-shaped surfaces interpreted as the metal interface, containing together 54% HA, 32% bone, and 14% soft tissue (Table 2, Figure 2). We found no smoothly-shaped surface in the biopsies from the remaining 4 hips, which had to

be excluded from the interface evaluation. The HA coating was missing from the metal interface of 2 hips. The median thickness of the remaining HA coating in 14 hips was 137 (6–380)  $\mu\text{m}$ , and the HA-tissue interface included 89% bone and 11% soft tissue contact (Table 2). Zones of atypical bone were found adjacent to the HA coating in 8 hips (Figure 3).

All HA coatings showed degradation with segments partly or completely replaced by soft tissue (Figure 2, Figure 4). This was the general appear-

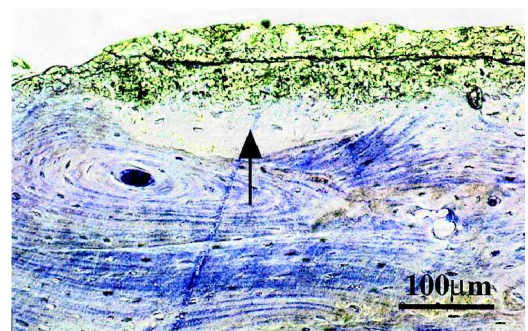


Figure 3. Hip 1 (2.0 years).

Weakly-stained layer of bone (arrow) with empty cellular lacunae between HA coating and normal bone.

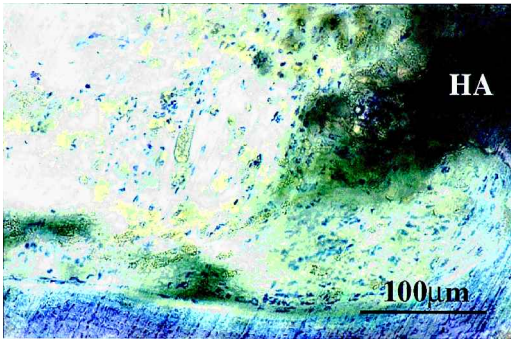
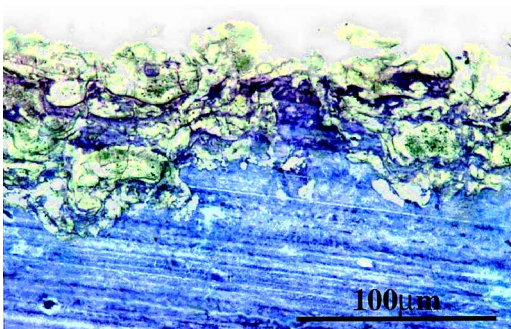


Figure 4. Hip 3 (4.2 years). Degradation of the complete layer of HA, being replaced by a soft tissue area with HA particles, partly internalized in macrophages. The clear blue surface at the bottom represents osteoid-like tissue.

ance, including most areas where polyethylene or metal particles could not be identified. Flakes

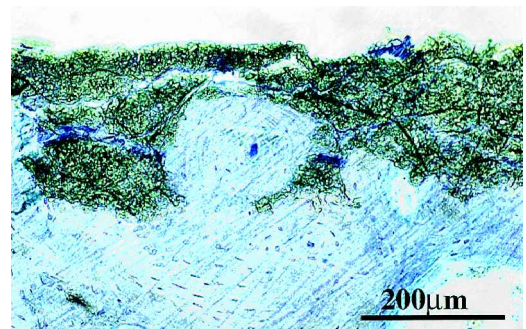
Figure 5. HA replacement by bone.



A. Hip 15 (6.2 years). Transformation of the HA coating by diffuse invasion of osteoid-like tissue.

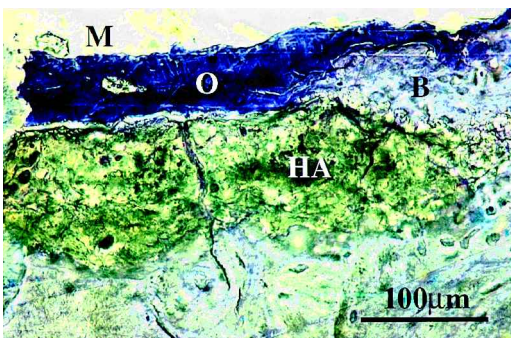
and small particles of HA were invariably found in soft tissue adjacent to the HA coating, and 9 hips showed HA debris in intraosseous soft tissue. Multinucleated giant cells and many macrophages were seen, the latter often containing HA remnants. Osteoclastic bone resorption and bone formation were seen occasionally, but no more than in normal bone remodeling.

Soft tissue degrading HA often bordered on additional segments of osteoid-like tissue or immature bone (Figure 2). All HA coatings showed partial HA replacement by mature bone, completely replacing segments of the coating in 10 cases (Figure 2). 8 hips demonstrated diffuse invasion of the HA coating by osteoid-like tissue, and 2 hips showed single osteons penetrating the coating (Figure 5). In 6 hips, we found a layer of bone with a median thickness of 163 (43–297) µm

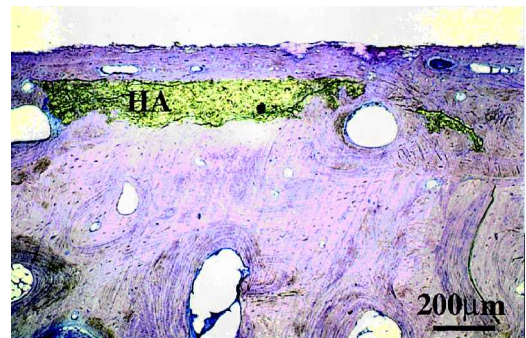


B. Hip 19 (6.8 years). Osteon penetrating the HA coating.

Figure 6. Bone between metal and HA coating.

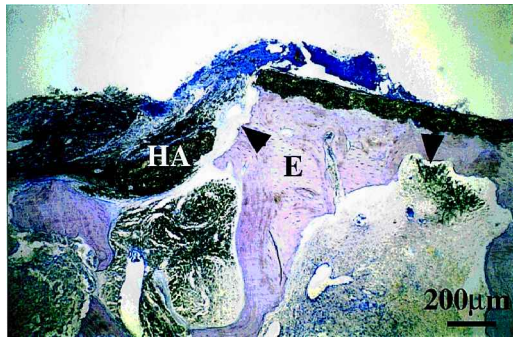


A. Hip 17 (6.3 years). Osteoid-like tissue (O) between HA coating and previous metal (M). Bone (B) on right.

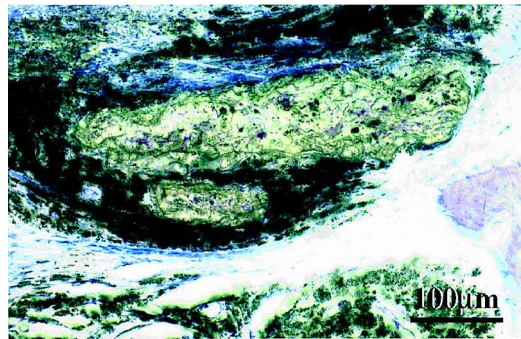


B. Hip 15 (6.2 years). Mature bone almost completely enveloping a segment of HA coating, also filling up between HA and metal.

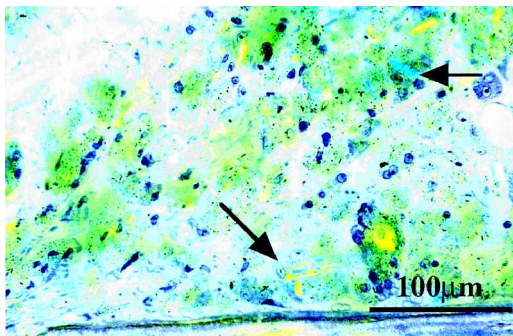
Figure 7. Hip 11 (5.9 years). Bone resorptive areas and release of HA particles adjacent to the joint.



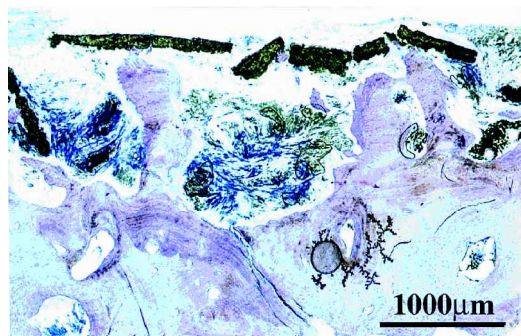
A. Intact HA coating with acellular soft tissue in the HA-metal interface at the top on the right. The underlying bone is in continuity and direct contact with the coating. Large bone resorptive areas with ragged edges (E - arrow heads) are penetrating deep into the bone. On the left, the HA coating ends abruptly in a cavity at the calcar adjacent to the joint, containing dark-stained soft tissue and large free flakes of HA coating.



B. Higher magnification shows that the HA flakes are accompanied by many small metal particles, largely internalized in macrophages.



C. Polyethylene particles seen with the aid of polarizing filters. Larger particles are internalized in multinucleated giant cells (arrows), whereas smaller particles seem to be internalized in macrophages. Intracellularly submicron metal particles are also present.



D. Loss of HA coating support by bone resorption undermines the coat. Acellular soft tissue in the HA-metal interface suggests disruption of the HA-metal interface. The HA coating is broken into free pieces in the open space adjacent to the stem communicating with the articulation.

between the smooth surface and the HA coatings, which had a median length of 427 (130–3450)  $\mu\text{m}$  and a median thickness of 118 (28–237)  $\mu\text{m}$ . We observed osteoid-like tissue and soft tissue between the surface and the HA coating in some places, but most of the HA was enveloped by mature bone in direct contact with the HA (Figure 6).

We analyzed all biopsies as regards bone resorption and particles. 14 hips demonstrated bone resorptive areas, all containing large amounts of polyethylene and metal particles, except for one hip with a ceramic head which had only polyethylene particles (Figure 7, Table 2). 9 hips showed extensive undermining of the HA coating and liberation

of large flakes of HA (Figure 7). We found free HA particles in another 9 hips, including 6 where bone resorption could not be observed (Table 2). Despite a marked concentration in bone resorptive areas, polyethylene and metal particles were not seen in neighboring intraosseous soft tissue. 6 hips showed no bone resorption or metal particles, however, 1 contained polyethylene particles. We found an association between bone resorptive areas and the presence of metal ( $p < 0.001$ , Fisher's exact test) and polyethylene ( $p < 0.001$ , Fisher's exact test) particles, but not between bone resorption and HA particles.

## Discussion

The smooth and uniformly-shaped biopsy surfaces corresponding to the stem were interpreted as disruption of the interface between metal and HA/tissue, favoring previous suggestions that the HA-metal interface is the weak point of the coating (Lemons 1988, Morscher 1991, Ducheyne and Cuckler 1992). We suspect that soft tissue surfaces were more affected by the biopsy harvesting procedure than hard tissue and HA, hence may be underestimating soft tissue in the metal interface.

Only one half of the interface between metal and HA/tissue comprised HA. Studies of retrieved human hip prostheses have shown no resorption of HA up to 9 months after surgery (Furlong and Osborn 1991, Hardy et al. 1991). Other studies up to 6 years after surgery have shown wide variations in coating loss (Bauer et al. 1991, Collier et al. 1993, Hardy et al. 1994, Lintner et al. 1994, Overgaard et al. 1997, Tonino et al. 1999), including complete resorption of a 60 µm thick HA coating after 4 years (Buma and Gardeniers 1995). We believe that most coating defects and HA particles in our hips must have been produced after insertion. The thickness of the remaining HA coating was nearly the same as that reported by the manufacturer, illustrating the extent to which complete segments of coating were broken down, whereas the remainder stayed relatively unaffected. The explanation may be that once HA degradation has started, it will continue until the coating is completely resorbed.

All HA coatings showed cellular-mediated degradation by multinucleated giant cells and macrophages in adjacent soft tissue, indicating that this is a consistent and continuous process (Bauer et al. 1991, Hardy et al. 1994, Lintner et al. 1994, Tonino et al. 1999). Some of the resulting HA particles were large, but further disintegration seemed to produce small particles that were finally digested by macrophages. HA degradation was a general finding, that also occurred in the absence of metal and polyethylene particles. However, degradation of HA was greater in areas with marked concentrations of metal and polyethylene particles. Zones of osteoid-like tissue were seen between soft tissue and HA or bone. This may indicate that the HA coating is degraded by soft tissue and then

replaced by bone, in addition to being replaced directly by bone.

The findings of soft tissue, osteoid-like matrix, and bone between the metal and an HA layer of about the original thickness are best explained by delamination. Bone may initially grow into the coating, which accords with reports of enhanced gap healing and bone apposition with HA-coated implants subjected to micromotion (Søballe et al. 1991, 1993). Repetitive compressional and distraction movements of the proximal part of the stem during loading, may eventually cause fatigue failure of the HA-metal interface with HA remaining attached to the calcar bone. Finally, tissue ingrowth can take place between the HA coating and the metal.

Excessive polyethylene wear and juxtaarticular osteolysis have been reported with some HA-coated hip prostheses (Bloebaum et al. 1994, 1997, Morscher et al. 1998, Røkkum et al. 1999). We found an association between bone resorptive areas and polyethylene or metal particles, but not between bone resorption and HA particles. Our demonstration of polyethylene and metal particles internalized in multinucleated giant cells and macrophages suggests a reaction to these particles as one cause of bone resorption (Agins et al. 1988, Schmalzried et al. 1992, Kadoya et al. 1998).

After delamination, bone resorption undermined the HA coating, with a loss of support on either side. The HA coating could then be easily broken into free pieces in the bone resorptive areas adjacent to the stem. These cavities communicated with the artificial hip joint, as shown by the large amounts of particles from the articulating surfaces. Hence, HA particles could be swept into the articulation by the flow of joint fluid caused by variations in pressure during joint movement. This mechanism may explain why reoperations routinely showed disappearance of the HA coating from the uncovered surfaces of the stems. We found proximal lines adjacent to these HA coated stems in 75 of 94 hips at the 5-year follow-up (Røkkum and Reigstad 1999). These lines could have been caused by disruption of the HA-metal interface and resorptive undermining of the HA coat. If so, a large amount of HA particles might be available for migration into the joint.

The thick HA coating on our stem may have poorer mechanical properties than thin coatings. Fatigue fracture has commonly been found in coatings thicker than 100 µm, and the weak point seems to be the HA-metal interface (De Groot et al. 1987, Geesink et al. 1987, Wang et al. 1993). On the other hand, long-term clinical success has been reported with the Furlong stem, which has a 200 µm thick HA coating, used with a ceramic head and a cemented polyethylene cup (McNally et al. 2000). Our findings do not favor the use of thick HA coatings because of the risk of delamination and the fact that thick coatings provide large reservoirs of HA, which may break down to become harmful particles. The addition of an HA coating to porous implants may improve fixation, especially the tensile and shear strength. Animal studies have shown that push-out testing causes delamination of HA-coated grit-blasted implants, but not of HA-coated and porous-coated implants (Overgaard et al. 1997, 1998). However, the long-term clinical effect of these coatings remains to be proved.

HA particles embedded in the polyethylene sliding surface have been shown in a few of these components (Lausmaa et al. 1998) and in some other HA-coated hip prostheses (Bloebaum et al. 1994, 1997, Morscher et al. 1998). The hard-edged HA scratches the prosthetic head, causing the production of metal and polyethylene particles. As the particle levels rise, bone resorption and HA particle release increase, thereby inducing a process that accelerates polyethylene wear due to this prosthesis (Røkkum and Reigstad 1998).

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