Adverse tissue reactions to wear particles from Co-alloy articulations, increased by alumina-blasting particle contamination from cementless Ti-based total hip implants

A REPORT OF SEVEN REVISIONS WITH EARLY FAILURE

M. Böhler, F. Kanz, B. Schwarz, I. Steffan, A. Walter, H. Plenck Jr, K. Knahr

From the Institute for Histology and Embryology, Vienna, Austria

We revised seven alumina-blasted cementless hip prostheses (Ti-alloy stems, cp Ti threaded sockets) with low- or high-carbon Co-alloy bearings at a mean of 20.1 months after implantation because of pain and loosening. Histological examination of the retrieved periprosthetic tissues from two cases in which the implant was stable and three in which the socket was loose showed macrophages with basophilic granules containing metal and alumina wear particles and lymph-cell infiltrates. In one of the two cases of stem loosening the thickened neocapsule also contained definite lymphatic follicles and gross lymphocyte/plasma-cell infiltrates. Spectrometric determination of the concentration of elements in periprosthetic tissues from six cases was compared with that of joint capsules from five control patients undergoing primary hip surgery. In the revisions the mean concentration of implant-relevant elements was 693.85 µg/g dry tissue. In addition to Cr (15.2%), Co (4.3%), and Ti (10.3%), Al was predominant (68.1%) and all concentrations were significantly higher ($p < 0.001$) than those in the control tissues. The annual rates of linear wear were calculated for six implants. The mean value was 11.1 µm (heads 6.25 µm, inserts 4.82 µm). SEM/EDXA showed

numerous fine scratches and deep furrows containing alumina particles in loosened sockets, and stems showed contamination with adhering or impacted alumina particles of between 2 and 50 µm in size.

J Bone Joint Surg [Br] 2002;84-B:128-36.

Received 11 May 2000; Accepted after revision 24 April 2001

Co-based alloy metal-on-metal bearings with improved surface finishing and a carbon content $< 0.2\%$ were reintroduced in total hip arthroplasty (THA) because of promising higher resistance to wear.^{1,2} However, the chemical nature of and cellular reactions to the metal wear particles are still areas of concern.³⁻⁷ Many studies have analysed the wear particles generated in joint replacement articulations and their effects on periprosthetic tissues. Additional third-body wear has been reported originating, for example, from radiopacifying agents in bone cements and from hydroxyapatite coatings,⁸ but little seems to be known about alumina particles which are generally used for grit blasting the surfaces of most Ti-based prostheses for cementless implantation. In 1992 Ricci et al⁹ found extensive surface inclusions from silicon- and/or aluminium-containing materials when they analysed five retrieved cementless implants with grit-blasted surfaces. Evidence of the same contaminants was found in soft-tissue samples adjacent to these implants, and also in a variety of new, non-implanted devices from different manufacturers. While in one experimental study alumina-blasting particles were considered to be a possible cause of tissue breakdown,¹⁰ in other experimental studies these surface contaminants on blasted titanium implants seemed not to have any negative effects on the rate of bone ongrowth.^{11,12}

In our study, parts of which have been reported previously,¹³ periprosthetic tissues harvested from seven early revisions of cementless THAs with metal-on-metal bearings were investigated by light microscopy and SEM, and the concentrations of elements in the implant material by spectrometry using the ICP-AES method.¹⁴ The rates of linear wear of retrieved ball-and-socket implants were calculated, and these metal gliding surfaces and the alumina-blasted surfaces of loosened implants were evaluated by SEM and energy-dispersive x-ray analysis (EDXA).

M. Böhler, MD

F. Kanz

H. Plenck Jr

Bone and Biomaterials Research, Institute of Histology and Embryology, University of Vienna, A-1090 Vienna, Austria.

K. Knahr

Orthopaedic Hospital Speising, A-1134 Vienna, Austria.

B. Schwarz

Institute of Social Medicine, University of Vienna, A-1080 Vienna, Austria.

I. Steffan

Institute for Analytical Chemistry, University of Vienna, A-1090 Vienna, Austria.

A. Walter

Implant Testing Laboratory for Biomechanics and Experimental Orthopaedics, State Orthopaedic Clinic, D-81650 Munich, Germany.

Correspondence should be sent to Dr M. Böhler.

©2002 British Editorial Society of Bone and Joint Surgery
0301-620X/02/111324 \$2.00

Fig. 1a

Fig. 1b

Photographs of the retrieved stems and sockets of THAs with alumina-blasted surfaces for cementless implantation and Co-based alloy bearings (a, cases 1 and 5, manufactured by Plus Endoprothetik, b) case 6, manufactured by Sulzer-Medica).

Materials and Methods

Between 1994 and 1997 seven patients (six women and one man) with a mean age of 57.7 years (46 to 72) had cementless THA using press-fit Ti-Al-Nb stems with a rectangular cross-section and threaded cp Ti sockets, both with alumina-blasted surfaces. The socket inserts and ball heads were made from Co-based alloys (revisions 1 to 5, low-carbon alloy (<0.1%; Plus Endoprothetik, Vienna, Austria; revisions 6 to 7, Metasul high-carbon alloy (0.2%), Sulzer-Medica, Winterthur, Switzerland) (Fig. 1). Table I gives details of the patients and diagnoses at the initial operations. In no patient was there a history of inflammatory arthritis of the hip before the first operation. At a mean of nine months (1 to 27) after implantation the patients presented with pain in the groin and/or thigh at rest and on walking, and radiological signs of loosening of either the socket ($n = 3$), stem ($n = 1$) or both components ($n = 1$). Revision surgery was carried out at a mean of 20.1 months (4 to 44) after implantation.

In all patients plain radiographs were taken at follow-up of the prostheses in two phases. Radiographically-controlled aspiration for bacterial culture was performed before revision.

At revision neocapsule and periprosthetic connective-tissue membranes from the loosened socket- or stem-bone interfaces were retrieved from all seven patients, fixed immediately in neutral-buffered formalin (except for case 4, see below), embedded in methylmethacrylate and exam-

ined by transmitted and polarised light microscopy,¹⁵ and by SEM and EDXA.

We measured the elements (Co, Cr, Ni, Mo, Ti, Nb and Al) in the retrieved tissue and joint capsule using inductively-coupled plasma-atomic emission spectrometry (ICP-AES) (ARL 3580 ICP-AES; Applied Research Laboratories, Lausanne, Switzerland). Spectral interferences caused by the sample matrix were avoided by line selection and background corrections, and a pneumatic nebuliser was used for introduction of the samples.¹⁴ Those of case 4 could only be analysed by light microscopy and SEM/EDXA, but representative tissue samples from the other six cases were analysed, and the results compared with those of the joint capsule retrieved from five control patients undergoing primary hip surgery (Table I). We performed a statistical comparison of the pooled results from these six cases and the five control cases for each element, using the Mann-Whitney U test.

For the tribological evaluation of linear wear, sphericity deviations were measured according to ISO 6318 (roundness measuring device: Talyround 30-PC, Rank Taylor Hobson, Wiesbaden, Germany) on exchanged metal heads and corresponding inserts from all revisions, except case 2. For the latter it was considered that four months between implantation and revision was too short a period for meaningful results to be obtained (Table I).

The bearing surfaces of all exchanged gliding implants and the blasted surfaces of three explanted components, one loosened stem (case 1: labelled Plus 11403), and two

Table I. Details of the revision and control groups

Case	Age at operation (yrs)	Diagnosis at operation	Duration of symptoms before revision (mths)	Pain at	Duration between implantation and revision (mth)	Exchanged components at revision	Contralateral side (THA)
Revisions							
1	60	Osteoarthritis	6	Thigh	13	Stem, insert, head	
2	47	Head necrosis	4	Thigh	4	Socket, insert, head	
3	46	Osteoarthritis	18	Groin, thigh	18	Insert, head	
4	53	Hip dysplasia	4	Groin, thigh	16	Insert, head	
5	54	Osteoarthritis	17	Groin, thigh	44	Socket, insert, head	
6	72	Osteoarthritis	21	Groin, thigh	28	Socket, stem, insert, head	
7	72	Osteoarthritis	8	Thigh	18	Socket, insert, head	
Controls							
1	68	Osteoarthritis					THA cementless (alumina-on-alumina articulation)
2	79	Osteoarthritis					None
3	57	Osteoarthritis					THA cementless, explanted for infection (metal-on-metal articulation)
4	78	Osteoarthritis					THA cementless (alumina-on-peararticulation)
5	69	Osteoarthritis					None

loosened sockets (case 5: labelled Plus 13210; case 7: labelled Sulzer E 3533), were analysed by SEM and EDXA. Adherent organic residues were cleaned from the specimens in repeated ultrasonic baths (acetone, methanol, distilled water, and again acetone). The usual gold sputtering for the SEM analysis was omitted to avoid superpositioning of alumina and oxygen peaks in EDXA.

Results

Radiological examination showed signs of loosening in four sockets (cases 2, 5, 6 and 7) and two stems (cases 1 and 6).

At revision, neocapsules of varying thickness from a few millimetres up to 4 cm (case 1) were found. All pre-operative bacterial cultures were negative and clear joint fluid was visible in all cases. Macroscopically, the pseudosynovial layer at the inner side of the neocapsule appeared to be red to greyish in colour. In no case was there an impingement between the stem and the socket. The exchanged gliding couples were replaced by either metal or alumina ceramic on polyethylene bearings.

Histological examination of the retrieved neocapsules and periprosthetic tissues from cases 3 and 4 in which both implants were stable and from cases 2, 5, 6 and 7 with loosened sockets, showed fibrin-coated pseudosynovial layers with numerous macrophages containing basophilic granules, barely visible metal wear and birefringent alumina particles, accompanied by diffuse or perivascular lymph-cell infiltrates. In case 1 which had loosening of the stem, we found a grossly thickened neocapsule with an oedema-

tous pseudosynovial layer and severe lymphocyte and plasma-cell infiltrates in the fatty tissue underlying a fibrovascular interlayer (Fig. 2a). Around larger vessels definite lymphatic follicles with high endothelial venules had formed (Fig. 2b). In the germinal centres and within lymph-cell infiltrates, macrophages were found containing basophilic granules with metal and birefringent alumina wear particles (Fig. 2c). Similar foreign-body reactions with osteoclastic resorption of adjacent, partly necrotic bone were found in the femoral periprosthetic connective tissue membrane retrieved from around the loosened stem.

The mean total concentration of elements in the revision tissues was 693.85 µg/g dry tissue (59.2 to 2906). The highest values were found in the tissues adjacent to sockets (1484.9 µg/g) followed by the connective-tissue membrane around the one loosened stem (951.9 µg/g), and the neocapsules (647.6 µg/g). The respective total amounts of the four major elements in the six revisions and of the pooled values in the control group are shown in Figure 3a. Statistical comparison showed that the concentrations for most elements were significantly higher in the revisions than in the control group ($p < 0.001$, Table II). As shown in Figure 3b, the concentration of the element Al was predominant in all specimens (mean 68.1%), followed by Cr (mean 15.2%), Co (mean 4.3%), and Mo (0.7%) and Ni (0.2%) for the gliding surfaces. Ti and Nb, originating from the threaded sockets and stems, had mean concentrations of 10.3% and 1.3%, respectively.

In case 4 the periprosthetic tissue taken could only be evaluated by light microscopy and SEM/EDXA which

Fig. 2

Photomicrographs showing a) the neocapsule of case 1 consisting of an oedematous pseudosynovial layer (PsSy), a fibrovascular interlayer, and gross lymph-cell infiltration with lymph follicles (LyFoll) in the adjacent fatty tissue, b) enlarged detail ($\times 150$) from the left rectangle in a) with a germinal centre (GermCtr) and high endothelial venules (HEV) of a lymph follicle and c) enlarged detail ($\times 120$) from the right rectangle in a) with macrophages and basophilic granules (arrows) and perivascular lymphocyte infiltration (Giemsa stain).

showed larger and smaller alumina particles and titanium wear from the socket (Fig. 4).

The rates of linear and annual wear were calculated from tribological analysis of the corresponding gliding couples from six revisions (Table III). The mean total linear wear was $17.3 \mu\text{m}$ (6.57 to 23.16) and the mean total annual rate of wear was $11.1 \mu\text{m}$ (2.81 to 15.44).

SEM/EDXA of socket inserts and heads showed only fine scratches and round bumps of carbides in non-contact areas. In main load-bearing areas furrows up to $20 \mu\text{m}$ wide were found (Fig. 5a), EDXA of which revealed alumina particles (Fig. 5b) besides numerous deeper and finer scratches (Fig. 5c).

SEM/EDXA of blasted surfaces of three exchanged components (stem from case 1, sockets from cases 5 and 7)

Table II. Mean (sd) concentrations ($\mu\text{g/g}$ /dry tissue) of elements in periprosthetic tissues from six revisions and capsules from five control hips

Elements	Revisions	Controls	p values
Al	472.02 (582.12)	10.61 (10.68)	<0.001
Co	29.72 (37.37)	0.03 (0.06)	<0.001
Cr	105.48 (156.43)	0.16 (0.09)	<0.001
Ni	1.14 (0.8)	0.3 (0.31)	0.043
Mo	4.88 (8.1)	0.05 (0.05)	<0.001
Ti	71.22 (108.88)	6.31 (10.08)	<0.001
Nb	9.39 (13.15)	2.0 (1.14)	<0.001

identified large numbers of alumina particles in the roughened surfaces (Fig. 6). The size of the larger, apparently impacted particles was up to $50 \mu\text{m}$ (Fig. 7), but also many particles 2 to $5 \mu\text{m}$ in size were found.

Fig. 3a

Fig. 3b

Graph showing a) the major concentrations ($\mu\text{g/g}$ dry tissue) of elements in the periprosthetic tissues from six revisions compared with pooled values in joint capsules from the five controls and b) a comparison of individual and mean element concentrations (%) in the periprosthetic tissues from the six revisions with respect to their origin.

Table III. Calculated linear wear (μm) and annual rate of wear ($\mu\text{m/yr}$) of the gliding couples from the revisions

Case	Duration between implantation and revision (mths)	Linear wear			Annual wear		
		Ball head	Insert	Total	Ball head	Insert	Total
1	13	6.6	8.6	15.2	6.09	7.94	14.03
2	4	NE*	NE	NE	NE	NE	NE
3	18	11.4	8.3	19.7	7.60	5.53	13.13
4	16	6.5	4.1	10.6	4.88	3.08	7.95
5	44	3.3	14.4	17.7	0.90	3.93	4.83
6	28	0.74	5.83	6.57	0.31	2.49	2.81
7	18	17.7	5.46	23.16	11.8	3.64	15.44
Mean	20.1	9.1	8.17	17.3	6.25	4.82	11.1

*not estimated

Discussion

Our study has focused on the specific reactions to wear particles from cobalt-based alloy articulations, and on the evidence of third-body wear produced by alumina particles from the grit-blasting of cementless Ti-based hip endoprostheses.

When plasma and whole blood concentrations of the respective metal constituents were monitored, considerably elevated levels of Co were found for both the low-carbon ($<0.1\%$) and high-carbon (0.2%) Co alloys which increased in relation to movement of the joint.^{16,17} While this could have toxicological consequences, particularly in patients with metabolic diseases,¹⁸ so far no increased

Fig. 4

Photomicrograph of a ground section of periprosthetic tissue from case 4 showing black deposits and smaller and larger crystalline particles (Paragon stain). (1) EDXA of the area in the rectangle shows peaks for oxygen (O), aluminium (Al), and titanium (Ti), besides a carbon peak (C). (2) Spot EDXA of the large crystalline particle (arrow) shows peaks for O and Al.

Fig. 5

Figure 5a – SEM of the load-bearing area of the surface of the head from case 1 showing a deep furrow and finer scratches. Figure 5b – Spot EDXA of the particle (arrow) in the deep furrow in a) showing mainly aluminium (Al), besides peaks for O, Cr, Co and Ti. Figure 5c – SEM showing numerous, partly regular deeper and finer scratches.

Fig. 6

Figure 6a – Low-power SEM micrograph of the alumina-blasted surface of the stem from case 1. Figure 6b – The corresponding EDXA of aluminium signals, showing large impacted alumina particles (arrows) and smaller contaminations and background signals.

Fig. 7

Figure 7a – Enlarged SEM detail from the rectangle in Figure 6a showing an impacted alumina particle about 50 μm in size. Figure 7b – The corresponding EDXA.

carcinogenic risk has been reported¹⁹ for such a systemic cobalt overload. Our findings, however, point to another local or even systemic effect of this metal-on-metal wear production. There was always a clinical reaction of lymph cells to the foreign-body response to metal wear particles, but in addition severe synovitis with formation of lymphatic nodules was observed in case 1. The stem implant had been stable and painless for seven months, then loosened at 13 months after insertion. Bone resorption was observed adjacent to the above adverse tissue reactions. Similar morphological observations and activation of B- and T-lymphocytes have recently been described by Willert et al⁷ in 14 cases of retrieved THAs with the new, high-carbon Co-alloy bearings. These tissue reactions seem to differ in intensity from those observed with so-called classical metal-on-metal bearings,⁷ and could well be a cell-mediated immune response or expression of a delayed type of hypersensitivity. It has been shown *in vitro*²⁰ that the new low-carbon (< 0.1%) alloys seem to have a higher rate of wear thus producing larger amounts of smaller wear particles. This would give an increased surface area for reactions with the biological environment. The third-body wear by alumina particles which we observed is another type of biologically active wear, i.e., alumina particles covered with abraded Co-based alloy or Ti-based materials, which will warrant further investigation.

Determination of elements in the periprosthetic tissues of the revisions showed the presence of those associated with metal-on-metal bearings and Ti and Nb from sockets and stems, and predominantly high amounts of aluminium. The levels were all significantly higher than those seen in control tissues retrieved at primary THA. The levels of Co are always lower than those of Cr⁴ but the effect of the implantation time on these and all other concentrations of elements was best observed in case 5 (Fig. 3a). The highest

case concentrations were found in tissues around the sockets, and the two loosened sockets (case 2 and 5) also produced higher concentrations of Ti than the loosened stem (case 1, Fig. 3a), which could be explained by the lower resistance to abrasion of cp Ti sockets. When trying to explain the high amounts of aluminium found in all six revisions evaluated so far, the aluminium content of the Ti-alloy stem must be taken into consideration, but cannot be the only origin of aluminium. The presence of crystalline alumina particles in the otherwise badly preserved tissues of case 4 was the first indication of alumina particles originating from blasting, which were then detected not only on all surfaces of the retrieved endoprostheses, but also within the periprosthetic tissues. This finding agrees with reports in the literature,⁹ and these surface contaminations seem to be known and accepted as inevitable by all manufacturers, since the usual ultrasonic cleaning procedures apparently do not remove impacted alumina particles, as demonstrated in our study. The different sizes of the alumina particles detected on the surfaces of the implant may be due to different grain fractions used for grit-blasting procedures, or to a high blasting energy so that colliding large grains were split into smaller particles which were then impacted and contaminated the surface. The grit-blasting procedures applied at present seem to need improvement, and they should be better standardised in order to avoid these unnecessary contaminations.

The alumina particles can apparently invade the periprosthetic tissues and produce abrasive metal wear of the endoprosthetic surfaces, at least around loosened implants. In addition, the so-called 'extended joint space' seems not only to be open for the transport of wear particles from articulations towards the bone-implant interfaces, but also reversely for the transport of these alumina-blasting particles into the articulation. In our study, particles of alumina

could be detected in the deeper scratches and furrows of the gliding surfaces. Similar deeper scratches were reported in a series of 114 retrievals of the new, high-carbon Co-alloy,² but no explanation for their origin was given. The resulting rates of linear wear and annual wear of the gliding couples evaluated in our study were within the range of or slightly above the values reported for high-carbon Co-alloy bearings.² Rates of linear wear, however, were only calculated from sphericity deviations which do not take into account the material loss at deeper and finer scratches in the gliding surfaces.

In conclusion, wear particles from both low- and high-carbon Co-alloy bearings cause specific macrophagic reactions, accompanied by a lymph-cell response. This is consistent with other findings from high-carbon Co-alloy bearings,⁷ and points to a local or systemic immune reaction. Within macrophages and in the periprosthetic tissues alumina particles were also detected, and their presence proven by elemental analyses. These apparently originated from contaminations of the grit-blasted surfaces of the Ti-based endoprostheses. They not only caused metal wear at implant-tissue interfaces, but also third-body wear of the metal-on-metal bearings. Previous findings⁹ and further evidence from additional revisions collected by the present authors, indicate that most grit-blasted endoprostheses presently in use for cementless implantation show these alumina contaminations. Therefore, these very hard third-body wear particles should not only cause concern for metal-on-metal bearings, but also for metal-on-polyethylene and alumina ceramic-on-polyethylene bearings. The only surface which is safer in this respect seems to be the ceramic-on-ceramic bearing. Its excellent long-term resistance to wear has been shown in other studies.^{21,22}

This study initiated and is part of a project evaluating and standardising a protocol for implant retrieval analyses, in collaboration with H. G. Willert, Goettingen, Germany, and supported in part by Sulzer-Medica, Winterthur, Switzerland. The authors thank G. Reinisch, BMF, Vienna, Austria, for contributing the EDXA of the revision 4 sample.

One or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.

References

- Schmidt M, Weber H, Schön R.** Cobalt chromium molybdenum metal combination for modular hip prostheses. *Clin Orthop* 1996;329:35-47.
- Rieker CB, Köttig P, Schön R, Windler M, Wyss UP.** Clinical tribological performance of 144 metal-on-metal hip articulations. In: Rieker CB, Windler M, Wyss UP, eds. *Metasul: a metal-on-metal bearing*. Bern, etc: H. Huber, 1999:83-91.
- Black J.** Metal on metal bearings: a practical alternative to metal on polyethylene total joints? *Clin Orthop* 1996;329 Suppl:244-55.
- Merritt K, Brown SA.** Distribution of cobalt chromium wear and corrosion products and biological reactions. *Clin Orthop* 1996;329 Suppl:233-43.
- Willert HG, Buchhorn H, Göbel D, et al.** Wear behaviour and histopathology of classic cemented metal on metal hip endoprostheses. *Clin Orthop* 1996;329Suppl:160-86.
- Hallab N, Jacobs JJ, Black J.** Hypersensitivity to metallic biomaterials: a review of leukocyte migration inhibition assays. *Biomaterials* 2000;21:1301-14.
- Willert HG, Buchhorn GH, Fayyazi A, Lohmann CH.** Histopathologische Veränderungen bei Metall/Metalle- Gelenken geben Hinweise auf eine zellvermittelte Überempfindlichkeit: vorläufige Untersuchungsergebnisse von 14 Fällen. *Osteologie* 2000;9:2-16.
- Rokkum M, Brand M, Bye K, et al.** Polyethylene wear, osteolysis and acetabular loosening with an HA-coated hip prosthesis: a follow-up of 94 consecutive arthroplasties. *J Bone Joint Surg [Br]* 1999;81-B:582-9.
- Ricci JL, Kummer FJ, Alexander H, Casar RS.** Technical note: embedded particulate contaminants in textured metal implant surfaces. *J Appl Biomater* 1992;3:225-30.
- Darvell BW, Samman N, Luk WK, Clark RK, Tideman H.** Contamination of titanium castings by aluminium oxide blasting. *J Dent* 1995;23:319-22.
- Goldberg VM, Stevenson S, Feighan J, Davy D.** Biology of grit-blasted titanium alloy implants. *Clin Orthop* 1995;319:122-9.
- Piattelli A, Manzon L, Scarano A, Paolantonio M, Piattelli M.** Histological and histomorphometrical analysis of the bone response to machined and sandblasted titanium implants: an experimental study in rabbits. *Int J Oral Maxillofac Implants* 1998;13:805-10.
- Boehler M, Knahr K, Gottsauner-Wolf F, et al.** *Histology and tribology of metal/metal bearings in cementless THA*. Paper presented at EORS meeting Brussels, 1999.
- Pomazal K, Prohaska C, Steffan I, Reich G, Huber JFK.** Determination of Cu, Fe, Mn and Zn in blood fractions by SEC-HPLC-ICP-AES coupling. *Analyst* 1999;124:657-63.
- Plenk H Jr.** The microscopic evaluation of hard tissue implants. In: Williams DF, ed. *Techniques of biocompatibility testing*. Vol. I. Boca Raton, Florida: CRC Press Inc, 1986:35-81.
- Brodner W, Bitzan P, Meisinger V, et al.** Elevated serum cobalt with metal-on-metal articulating surfaces. *J Bone Joint Surg [Br]* 1997;79-B:316-21.
- Lhotka C, Steffan I, Zhuber K, Szekeres T, Zweymüller K.** Whole-blood cobalt and chromium levels in patients managed with total hip replacements involving different metal-on-metal combinations. In: Willmann G, Zweymüller K, eds. *Bioceramics in hip joint replacement*. Stuttgart: Thieme, 2000:107-11.
- Brodner W, Grohs JG, Bitzan P, et al.** Serumcobalt und Serumchromspiegel bei zwei chronisch niereninsuffizienten Patientinnen mit Hüfttotalendoprothese und Metall-Metall-Gleitpaarung. *Z Orthop Ihre Grenzgeb* 2000;138:425-9.
- Visuri T, Pukkala E, Paavolainen P, Pulkkinen P, Riska EB.** Cancer risk after metal on metal and polyethylene on metal total hip arthroplasty. *Clin Orthop* 1996;329 Suppl:280-9.
- Fisher J, Ingham E, Stone MH, et al.** Wear and debris generation in artificial hip joints. In: Sedel L, Willmann G, eds. *Reliability and long-term results of ceramics in orthopaedics*. Stuttgart: Thieme, 1999:78-81.
- Böhler M, Mochida Y, Bauer TW, Plenk H Jr, Salzer M.** Wear debris from two different alumina-on-alumina total hip arthroplasties. *J Bone Joint Surg [Br]* 2000;82-B:901-9.
- Sedel L, Willmann G.** *Reliability and long-term results of ceramics in orthopaedics*. Stuttgart, etc: Thieme, 1999:1-117.