Biological Impact of Polyacetal Particles on Loosening of Isoelastic Stems

Klemen Stražar,*,† Andrej Cör,‡ and Vane Antolič†

Department of Orthopaedic Surgery, University Medical Centre Ljubljana, Zaloška 9, 1000 Ljubljana, Slovenia, and Institute for Histology and Embryology, Medical Faculty Ljubljana, Vrazov trg 2, 1000 Ljubljana, Slovenia

Received March 13, 2006; Revised Manuscript Received June 27, 2006

The aim of our study was to identify biological factors responsible for premature loosening of polyacetal hip stems. The results of histological analyses of the tissue around 11 total hip prostheses with loosened polyacetal femoral stems were compared to those obtained in a group of 11 total hip prostheses with loosened metal (CoCr) femoral components. A higher number of polymer wear particles surrounded by giant cells, more bone chips, and a more extensive necrosis were found around loosened polyacetal stems. Histomorphological characteristics of polyacetal wear particles containing $BaSO_4$ granules in the tissue around loosened polyacetal stems were described. Radiological evaluation of the wear of polyethylene cups suggested that elastic modulus of the stem had no influence on the wear of polyethylene cups. This study indicates that polyacetal wear particles have a great biological potential accelerating the process of loosening.

Introduction

Total hip arthroplasty is a routine orthopaedic surgical procedure with excellent early results and less encouraging long-term results. Its basic complication, aseptic loosening, can be related to various biomechanical and biological factors associated with the implant material, prosthetic design, and initial fixation method. Artificial stems currently in use are made of metal materials with an elastic modulus more than ten times higher than that of the bone.[1−6] The undesired effect of the mechanical mismatch of the stiff stem with the elastic bone is stress protection.[4] Trabecular bone around such a stiff stem atrophies, which enhances mechanical destabilization of the stem. In the early 1970's, Morscher and Mathys introduced a femoral stem coated by polyacetal resins with an elastic modulus ($E = 5-13$ GPa) similar to that of the bone.[5,7] Thus having provided the condition of isoelasticity, such a stem was supposed to transfer stresses to the bone in a more physiological way, thereby preventing trabecular bone stress protection. Another important advantage of the use of the polyacetal femoral stem was fixation without using cement, which was supposed to prevent deposition of poly(methyl methacrylate) wear particles in the periprosthetic tissue. This deposition had been implicated as a major biological culprit for osteolysis of the bone around cemented stems.[8,9]

Against all expectations, long-term results after implantation of polyacetal femoral components were discouraging.[10−16] The majority of the inserted polyacetal stems were revised in less than ten years, which falls short compared to other designs of artificial stems.[17] Histological studies conducted to find possible biological causes for premature loosening of polyacetal stems were scarce.[15,18] By using a simple microscopic observation, no significant differences in histological criteria between the periprosthetic tissue of loosened polyacetal femoral components and that of loosened metal stems have been found.[18] Although polyacetal wear particles have been identified in the periprosthetic tissue, the debris from the polyacetal coating has not been proven to be a potent biological factor responsible for premature aseptic loosening of polyacetal stems.[15,18,19]

The biological impact of specific material on prosthetic loosening depends on the velocity of its wear and the amount of inflammatory cell reaction triggered by wear particles. The aim of our study was to evaluate the biological role of polyacetal wear particles in the process of premature aseptic loosening of polyacetal femoral stems.

Materials and Methods

Patients and Tissue Samples. Periprosthetic tissue samples were collected during 11 revision hip arthroplasties for aseptic loosening of second-generation polyacetal femoral stems (Betlach, Switzerland), done in 5 male and 6 female patients. Loosening was proven by comparing X-rays taken immediately after insertion and prior to revision arthroplasty (Figure 1). Patients with laboratory signs and local or general clinical signs or symptoms of infection were excluded from the study. At the time of revision arthroplasty, at least 1 cm^3 of periprosthetic tissue was taken from five different sites: from the proximal, medial, and distal parts of the interface membrane around the loosened stem, from the pseudocapsule and, in cases of acetabular loosening, from the interface membrane in the acetabular bed. In eight patients, polyethylene acetabular components also became loose and were therefore removed. Microbiological evaluation of periprosthetic tissue was conducted to prove the aseptic nature of loosening. The total number of tissue samples was 52 (11×3 samples from the femoral canals + 11 samples from pseudocapsules + 8 samples from the acetabular beds). All tissue samples were fixed in 10% formalin immediately after removal and embedded in paraffin. Slides (5 μm thickness) were stained with haematoxylin and eosin for microscopic examination. One additional section from each tissue sample was stained with Oil-O−Red for differentiation between polyethylene and polyacetal particles.[20]

The results obtained in the group of patients with aseptically loosened polyacetal stems were compared to those obtained in 11 patients−4

* To whom correspondence should be addressed. Tel: +386 1 522 4174. Fax: +386 1 522 2474. E-mail: klemenstrazar@yahoo.com.
† University Medical Centre Ljubljana.
‡ Medical Faculty Ljubljana.

10.1021/bm060239t CCC: $33.50
Published on Web 07/26/2006

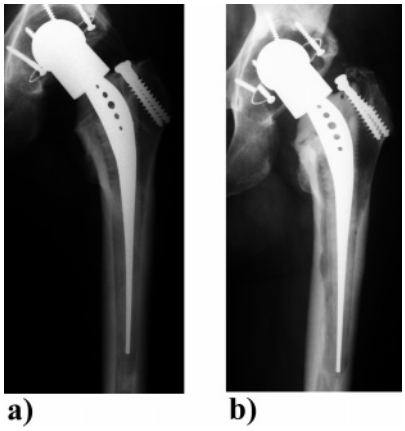

Figure 1. Radiographs of total hip prosthesis with polyacetal stem: (a) immediately after insertion, (b) prior the revision with signs of aseptic loosening (osteolytic lines around the stem, sinking of the stem in the femur, lateralization of the distal tip of the stem, broken screws).

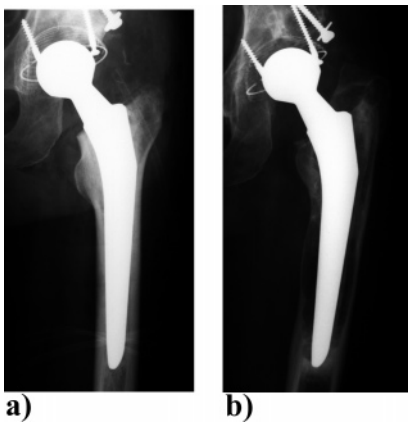

Figure 2. Radiographs of total hip prosthesis with CoCr stem: (a) immediately after insertion, (b) prior the revision with signs of aseptic loosening (osteolytic foci around the stem, sinking of the stem in the femur).

males and 7 females—with aseptically loosened metal stems, all made of CoCr alloy (Figure 2). There were 7 polyethylene acetabular components revised in this group, and the total number of tissue samples collected was 51 (11 × 3 samples from the femoral canals + 11 samples of pseudocapsules + 7 samples from the acetabular beds).

Radiological Evaluation of Polyethylene Wear. The amount of polyethylene wear particles was determined by calculating end volumetric wear of polyethylene cups from X-rays taken following the insertion and prior to the revision of the hip prosthesis. The equation used takes into account the direction of the wear of polyethylene cups (Figure 3).[21]

Histological Analyses. Histological slides were analyzed by light and polarized microscopy (Opton, Germany).

In each haematoxylin-eosin (HE)-stained slide, 10 microscopic fields at 100× and 400× magnification were examined, and histological criteria of foreign body granuloma were estimated by Mirra's semiquantitative method.[22]

The number of giant cells with polymeric particles was determined semiautomatically using the IBAS 1000 image-based analysis system (Kontron, Germany). The first microscopic field in each HE stained slide was chosen randomly, and giant cells with polymeric particles were counted. The next 19 fields were determined intermittently. Numeric areal density was calculated and expressed by the number of giant cells per square millimeter.

Statistics. Statistical analyses were done by the statistical software package *SPSS 13.0* for Windows. The nonparametric Mann−Whitney test was used to find differences in the semiquantitative estimation of

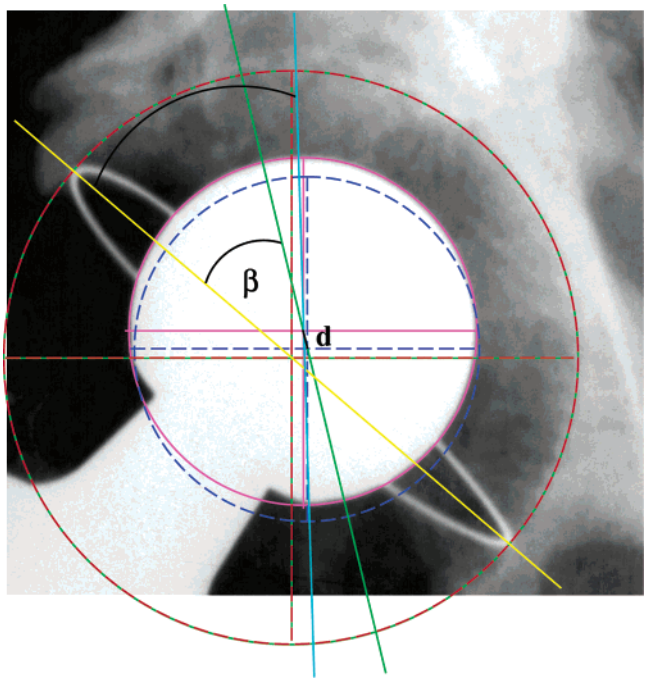

Figure 3. Radiological evaluation of polyethylene wear. Centers of the prosthetic head and polyethylene cup are determined on two radiographs: one taken immediately after insertion and the other just prior to the revision of the hip prosthesis. Radiographs are superpositioned in such a way that the centers of the polyethylene cups coincide. The extent of linear wear of polyethylene cup (d) is measured as the length of the shift of the center of the prosthetic head (straight black line). It is expressed in millimeters after magnification is taken into consideration; the reference is the radius (R) of the prosthetic head, 14 mm in all our cases. The direction of the linear wear is defined as an angle (β) between the extension of the straight line representing the shift of the center of the prosthetic head (green line) and the line through both poles of the polyethylene cup (yellow line). End volumetric wear of polyethylene cup (V) is calculated on basis of equation $V = \pi R^2 d/2(1 + \sin \beta)$.

histological criteria between tissue samples in the group of loosened polyacetal stems and those obtained in the group of loosened metal stems. Differences in patient age, volumetric wear of polyethylene cups, and numeric areal density of polymeric giant cells between the two groups were tested by the t-test for nonpaired data groups. The correlation test for independent paired data was used to check for a correlation between numeric areal density of giant cells with polymeric particles, volumetric wear of polyethylene cups, and clinical data, including age, sex, and body mass index.

Results

Patients showing loosening of polyacetal stems were significantly younger than those with loosened metal stems (average 57.7 years and 69.3 years, respectively) ($p < 0.05$). No significant differences were found between the two groups concerning other clinical data, sex ($p = 0.31$) and body mass index (average 26.3 kg/m^2 and 25.0 kg/cm^2, respectively) ($p = 0.24$).

The time between insertion and revision due to aseptic loosening was significantly shorter in the group of patients with polyacetal isoelastic stems compared to that in the group of patients with metal stems (average 10.3 years and 13.5 years, respectively) ($p < 0.05$).

Radiological Evaluation of Polyethylene Wear. The mean end volumetric wear values of polyethylene cups in the group of loosened polyacetal stems and in the group of loosened metal stems were 1417.39 mm^3 and 1644.35 mm^3, respectively. The difference between the groups was not statistically significant

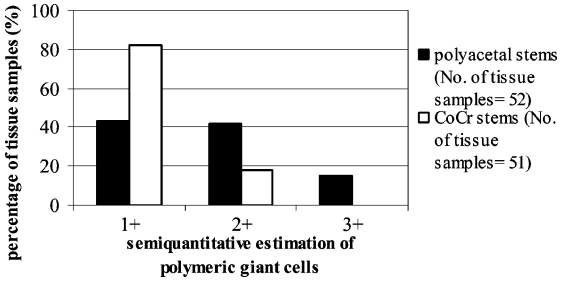

Figure 4. Semiquantitative estimation of polymeric giant cells in periprosthetic tissue. Histogram showing the percentages of tissue samples with one giant cell (1+), two to four giant cells (2+), and five or more giant cells (3+) with polymeric wear particles per microscopic field at 400× magnification. More giant cells with polymeric wear particles were found in the tissue around loosened polyacetal stems than in the tissue around loosened CoCr stems ($p < 0.05$).

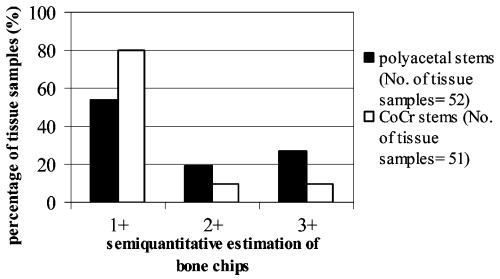

Figure 5. Semiquantitative estimation of bone chips in periprosthetic tissue. Histogram showing the percentages of tissue samples with five or less bone chips (1+), six to ten bone chips (2+), and ten or more (3+) bone chips per microscopic field at 100× magnification. A greater number of bone chips were found in the tissue around prostheses with loosened polyacetal stems than in the tissue around prostheses with loosened CoCr stems ($p < 0.05$).

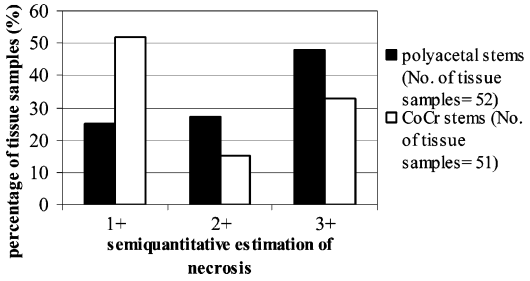

Figure 6. Semiquantitative estimation of necrosis in periprosthetic tissue. Histogram showing the percentages of tissue samples with necrosis of less than 2 mm^2 (1+), of 3−9 mm^2 (2+), and of more than 10 mm^2 (3+) per slide. A more extensive necrosis was found in the tissue around prostheses with loosened polyacetal stems than in the tissue around prostheses with loosened CoCr stems ($p < 0.05$).

($p = 0.13$). The mean direction of wear value of polyethylene cups in the group of prostheses with loosened polyacetal stems did not differ significantly from that observed in the group of prostheses with loosened metal stems (6° and 11°, respectively, both laterally) ($p = 0.12$).

Histological Analyses. A higher number of foreign body giant cells with polymeric wear particles ($p < 0.05$) (Figure 4), more bone chips ($p < 0.05$) (Figure 5), and more extensive necrosis ($p < 0.05$) (Figure 6) were seen in the tissue around loosened polyacetal stems than in the tissue around loosened metal stems. There were no differences between the two groups concerning the number of macrophages ($p = 0.14$), chronic inflammatory cells ($p = 0.09$), metal wear particles ($p = 0.55$), and extension of necrobiosis ($p = 0.63$), calcinosis ($p = 0.21$), or fibrosis ($p = 0.26$).

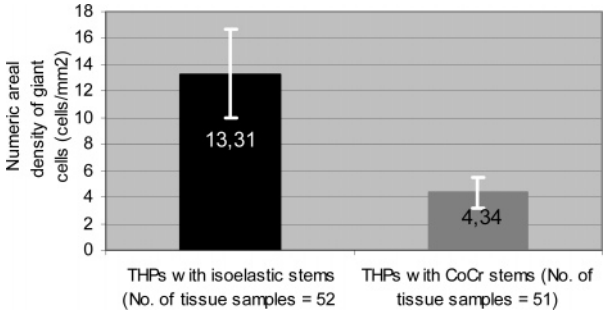

Figure 7. Numeric areal density of giant cells with polymeric wear particles in the periprosthetic tissue. The numeric areal density of giant cells with polymeric wear particles in the tissue around prostheses with loosened polyacetal stems (13.31 ± 3.34 mm^2) exceeded that in the tissue around prostheses with loosened CoCr stems (4.34 ± 1.13 mm^2) ($p < 0.05$). THPs = total hip prostheses.

The mean numeric areal density of polymeric giant cells was significantly higher ($p < 0.05$) in the granuloma around loosened polyacetal stems than in the granuloma around loosened metal stems (Figure 7), but no correlation was found comparing it with the volumetric wear of polyethylene cups in any of the groups of patients ($p = 0.24$ and 0.31, respectively). There was no correlation between the numeric areal density of polymeric giant cells and clinical data, age ($p = 0.36$), sex ($p = 0.53$), and body mass index ($p = 0.09$).

A thorough examination of histological slides of the tissue around prostheses with loosened polyacetal stems revealed two different types of polymer wear particles showing different morphological characteristics.

Type I polymer particles corresponded to polyethylene wear particles described in the literature[23−27] and were also found in the histological slides in the group of loosened metal stems (Figure 8). Most of them were spindle-like in shape, 30 μm large in average (maximum 100 μm), with typical shiny appearance under the polarized light microscope.

Type II polymer particles were not found in the tissue around prostheses with loosened metal stems (Figure 9). Most of them were surrounded by foreign body giant cells, yet they were occasionally seen lying freely in the areas of necrosis or necrobiosis. The particles had a polygonal shape and were much larger than type I polymer wear particles. Their average size was 100 μm, maximum 500 μm. They contained 1-μm-large sooty gleaming particles. Under the polarized light, they did not shine but showed a dusty appearance (Figure 9b). Type II polymer particles were ascribed to polyacetal containing granules of $BaSO_4$.

Oil-O-Red Method. Both types of polymer wear particles were stained by the Oil-O-Red method (Figures 8c and 9c). Extracellular polyacetal wear particles surrounded by foreign body giant cells were larger (average estimated size of 100 μm compared to average size of extracellular polyethylene particles of 30 μm), polygonal in shape and contained granules of $BaSO_4$. Smaller particles of both polyethylene and polyacetal may be present in Oil-O-Red positive macrophages, but they could not be distinguished.

Discussion

The first short-term clinical and radiological results after implantation of polyacetal femoral stems were encouraging.[28,29] Anterior−posterior radiographs taken up to two years after implantation showed formation of new trabecular bone (neocortex) around the whole surface of the polyacetal stems. Yet, the initial enthusiasm was followed by great disappointment after

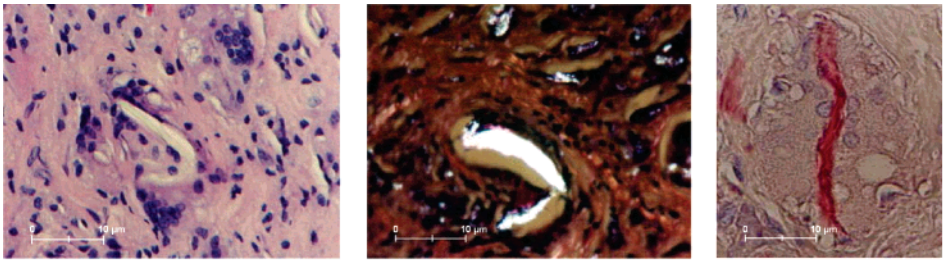

Figure 8. Photomicrographs showing polymer type I (polyethylene) wear particles: (a) haematoxylin-eosin (HE) staining, 400× magnification; (b) polarized microscope, 400× magnification; (c) Oil-O-Red stainining, 400× magnification.

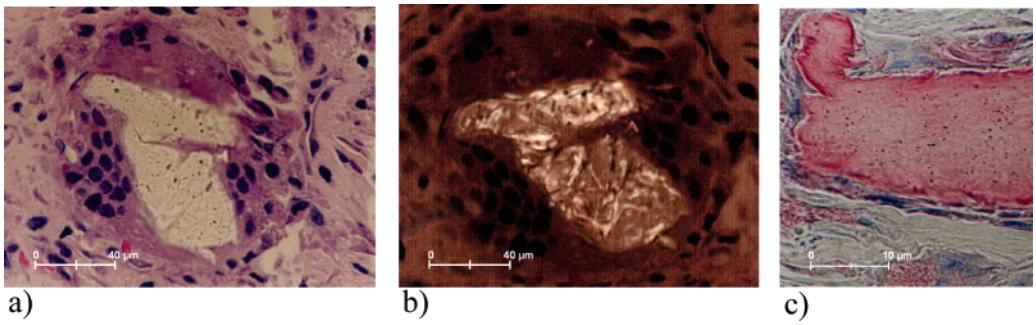

Figure 9. Photomicrographs showing polygonal polymer type II (polyacetal) wear particle containing granules of $BaSO_4$: (a) haematoxylin-eosin (HE) staining, 100× magnification; (b) dusty appearance under polarized microscope, 100× magnification; (c) Oil-O-Red staining, 400× magnification.

long-term results had been published.[9−16] Radiological follow-up revealed clear signs of loosening around the majority of polyacetal stems in a relatively short time after insertion. Radiolucent lines around the whole polyacetal stem and unexpected extensive osteolytic foci in the zone of the calcar and greater trochanter were observed. Radiological signs were accompanied by clinical signs and symptoms of loosening, and the majority of inserted polyacetal stems had to be revised in less than ten years.[17] Because of such a short life, polyacetal stems have been abandoned in total hip replacement surgery.

Identifying mechanical and biological reasons for premature aseptic loosening of polyacetal stems presented a challenge to many researchers. Studies using finite element analysis have demonstrated that because of its lower elastic modulus polyacetal material affords better transfer of compressive stresses to the surrounding bone under loading conditions. It avoids stress protection but at the same time it paradoxically produces greater interface stresses due to the inevitable bending moment.[4,30−32] Excessive interface micromotion that prevents the anticipated bony ingrowth was recognized as a major mechanical cause of the higher failure rate of polyacetal stems. Biological factors responsible for polyacetal stem loosening have not yet been fully understood. Boss and co-workers reported on large polymer granulomas in the interface membrane arising in the space between the loosened polyacetal stem and the bone.[18] Although polyacetal wear particles were identified in the periprosthetic tissue, debris from the polyacetal coating was only assumed to be a major biological factor enhancing premature aseptic loosening of polyacetal stems.[19]

Using the Mirra's semiquantitative method,[22] we found more large polymeric wear particles surrounded by foreign body giant cells in the tissue around loosened polyacetal stems than in the tissue around loosened cemented metal stems. Biological activity of polymer wear particles in the periprosthetic tissue was quantified by the determination of numeric areal density of polymeric foreign body giant cells. This was found to be greater in patients with prostheses with loosening of polyacetal stems than in patients showing loosening of cemented stems. Using a new radiological model,[21] which takes into account the direction of wear of the cups, we found no difference in the end volumetric wear of polyethylene cups between the two groups of prostheses with loosened stems of different elastic modulus materials. This important finding led us to assume that in prostheses with loosened polyacetal stems there must be another source of polymer wear particles besides polyethylene particles from the cups. A detailed microscopic observation of histological slides revealed two distinctive types of large polymer particles in the tissue around prostheses with loosened polyacetal stems. Type I polymer particles, which were also found in the tissue around prostheses with loosened metal stems, had the same morphological characteristics as larger polyethylene particles described in the literature.[23−27] Type II polymer particles were only found in the tissue around loosened polyacetal stems. Minovič and co-workers isolated polyacetal particles from the tissue around polyacetal stems, and the presence of 1 μm $BaSO_4$ particles in polyacetal matrix was proven by the backscattered SEM analysis.[19] $BaSO_4$ is added to polyacetal in the process of polymerization to achieve radiopaque appearance of the inserted stem. The average size of isolated polyacetal particles they described corresponded to the size of type II polymer particles in our study, and the dusty appearance of type II polymers under the microscope was found to be due to the presence of $BaSO_4$ granules. The presence of $BaSO_4$ particles in type II polymer particles was additionally proven using nuclear microprobe and in-air PIXE method.[33] The measured Ba concentration in particles matched well the Ba concentration of the polyacetal coating of the unused polyacetal stem. In vivo studies have shown that particles of contrast medium $BaSO_4$ play an important biological role in the process of prosthetic loosening by activation of osteoclasts.[34−36] Polyacetal and polyethylene wear particles together with $BaSO_4$ granules and metal wear particles that are present in the tissue surrounding the loosened hip prostheses trigger the aseptic inflammation in the periprosthetic tissue. The process leads to osteolysis of the femur and

finally results in loosening of the hip prosthesis. Extensive necrosis observed in the periprosthetic tissue seemed to be due to intense biological activity of all the above-mentioned wear particles. It is clear that the interface stress itself is responsible for abrasive wear of the surface of polyacetal stems. Polyacetal wear particles and $BaSO_4$ granules are released into the space between the bone and the insufficiently osseointegrated stem. According to Caravia and co-workers, $BaSO_4$ particles floating in the sinovial fluid are harder than plastic or metal materials and are therefore to be blamed for the third body abrasion of polyethylene cups and the stem.[37] Contact and the third body abrasion are hence responsible for delamination of the polyacetal stem and for such an extensive number of polyacetal particles and bone chips of large size.

There have been controversial reports on the efficiency of the Oil-O-Red method for identification of polyethylene particles in histological slides.[20,27,38] Willert and Buchhorn criticized the authors of the method, maintaining that possible staining of the particles was most probably due to uptake of the lipophilic dying substance by fat cells released after the cell death.[27] Our study has proven that the Oil-O-Red technique is an efficient method for identification of submicron-sized polymer particles in macrophages and larger particles surrounded by giant cells. Furthermore, the technique can be used for the differentiation between large polyacetal and polyethylene particles, based on their shape and the presence or absence of $BaSO_4$ granules.

A typical radiological pattern of loosening of isoelastic polyacetal stems has been described by many authors.[4,18,30−32] The presence of radiolucent lines around the greater part of the surface of polyacetal stems is the proof of low-degree osseointegration. Extensive osteolytic foci, especially those of the calcar and the greater trochanter, seem to be the consequence of intense biological activity of all wear particles and of polymer particles in particular.

Until now, it has been believed that sophisticated analytical techniques have to be used for the differentiation of polymeric materials, such as gas chromatography, mass spectrometry, measurement of melt and recrystallization temperature, or determination of refractive indices by the Becke method.[24,39] These methods, however, are of limited availability and difficult to apply for detection of the particulate material deeply embedded in the cellular tissue.

The results of our study have proven that quantification of histological criteria in the interface membrane is a useful tool for comparing two or more different designs of loosened prosthetic components and provides important information about the biological causes of loosening. The presence of polyacetal particles in the tissue around loosened polyacetal stems was confirmed, and coarse estimation of their biological activity was unravelled for the first time. It was demonstrated that histological analyses are accurate enough to differentiate between polyacetal and polyethylene wear particles in periprosthetic tissue. Although the exact role of biomechanical and biological causes of aseptic loosening of polyacetal stems remains yet to be clearly elucidated, it may already be concluded that polyacetal wear particles have a major biological impact on premature aseptic loosening of isoelastic hip stems coated by polyacetal.

Acknowledgment. We thank Patricia Campbell, Ph.D., Joint Replacement Institute at Orthopaedic Hospital Los Angeles, U.S.A., for preediting the manuscript and for giving valuable comments.

References and Notes

(1) Turner, T. M.; Sumner, D. R.; Urban, R. M.; Rivero, D. D.; Galante, J. O. *J. Bone Jt. Surg., Am. Vol.* **1986**, *68-A*, 1396−1409.
(2) Maloney, W. J.; Jasty, M.; Burke, D. W.; O'Connor, D. O.; Zalenski, E. B.; Bradgon, C.; Harris, W. H. *Clin. Orthop*. **1989**, *249*, 129−140.
(3) Rosenberg, A. *Orthopaedics* **1989**, *12*, 1223−1233.
(4) Huiskes, R. *Clin. Orthop.* **1990**, *261*, 27−38.
(5) Maistrelli, G. L.; Fornasier, V.; Binnington, A.; McKenzie, K.; Sessa, V.; Harrington, I. *J. Bone Jt. Surg., Br. Vol.* **1991**, *73-B*, 43−46.
(6) Kiratli, B. J.; Heiner, J. P.; McBeath, A. A.; Wilson, M. A. *J. Orthop. Res.* **1992**, *10*, 836−844.
(7) Morscher, E.; Mathys, R. *Acta Orthop. Belg.* **1974**, *40*, 639−647.
(8) Charkosky, C. B.; Bullough, P. G.; Wilson, P. D. *J. Bone Jt. Surg., Am. Vol.* **1973**, *55-A*, 49−58.
(9) Jones, L. C.; Hungerford, D. S. *Clin. Orthop.* **1987**, *225*, 192−206.
(10) Izquierdo, R. J.; Northmore-Ball, M. D. *J. Bone Jt. Surg., Br. Vol.* **1994**, *76-B*, 34−39.
(11) Matricali, G. A.; Thibaut, H.; Hendrickx, M.; Thibaut, R. *Acta Orthop. Belg.* **1993**, *59 Suppl. 1*, 374−376.
(12) Trager, D.; Rode, P.; Krause, W. *Chirurg* **1985**, *56*, 718−722.
(13) Rosso, R. *Arch. Orthop. Trauma Surg.* **1988**, *107*, 86−88.
(14) Au, M. K. *J. Formosan Med. Assoc.* **1994**, *93*, 497−502.
(15) Niinimaki, T. J.; Puranen, J. P.; Jalovaara, P. K. *Int. Orthop.* **1995**, *19*, 298−303.
(16) Trebše, R.; Milošev, I.; Kovač, S.; Mikek, M.; Pišot, V. *Acta Orthop.* **2005**, *76*, 169−176.
(17) Herberts, P.; Malchau, H. *Acta Orthop. Scand.* **2000**, *71*, 111−121.
(18) Boss, J. H.; Shajrawi, I.; Soudry, M.; Mendes, D. G. *Int. Orthop.* **1990**, *14*, 399−403.
(19) Minovič, A.; Milošev, I.; Pišot, V.; Cör, A.; Antolič, V. *J. Bone Jt. Surg., Br. Vol.* **2001**, *83-B*, 1182−1190.
(20) Schmalzried, T. P.; Jasty, M.; Rosenberg, A.; Harris, W. H. *J. Appl. Biomater.* **1993**, *4*, 119−125.
(21) Košak, R.; Antolič, V.; Pavlovčič, V.; Kralj-Iglič, V.; Milošev, I.; Vidmar, G.; Iglič, A. *Skeletal Radiol.* **2003**, *32*, 679−686.
(22) Mirra, J. M.; Amstutz, H. C.; Matos, M.; Gold, R. *Clin. Orthop.* **1976**, *117*, 221−240.
(23) Mirra, J. M.; Marder, R. A.; Amstutz, H. C. *Clin. Orthop.* **1982**, *170*, 175−183.
(24) Buchhorn, G. H.; Willert, H. G. In *Biocompatibility of Orthopaedic Implants*; Wiliams, D. F., Ed.; CRC Press: Boca Raton, FL, 1982; Vol. 1, pp 249−267.
(25) Shanbhag, A. S.; Jacobs, J. J.; Glant, T.; Gilbert, J. L.; Black, J.; Galante, J. O. *J. Bone Jt. Surg., Br. Vol.* **1994**, *76-B*, 60−67.
(26) Doorn, P. F.; Campbell, P. A.; Amstutz, H. C. *Clin. Orthop.* **1996**, *329*, 206−216.
(27) Willert, H. G.; Buchhorn, G. H. In *European Instructional course lectures*; Jakob, R., Fulford, P., Horan, F., Eds.; The British Editorial Society of Bone and Joint Surgery: London, 1999; Vol. 4, pp 58−82.
(28) Andrew, T. A.; Flanagan, J. P.; Gerundini, M.; Bombelli, R. *Clin. Orthop.* **1986**, *206*, 127−138.
(29) Dick, W.; Morscher, E. *Med. Orthop. Technol.* **1986**, *106*, 6−10.
(30) Huiskes, R.; Weinans, H.; Van Rietbergen, B. *Clin. Orthop.* **1992**, *274*, 124−134.
(31) Huiskes, R. *Acta Orthop. Scand.* **1993**, *64*, 699−716.
(32) Weinans, H.; Huiskes, R.; Grootenboer, J. H. *J. Orthop. Res.* **1992**, *10*, 845−853.
(33) Stražar, K.; Kavčič, M.; Simčič, J.; Pelicon, P.; Šmit, Ž.; Kump, P.; Jaćimović, R.; Antolič, V.; Cör, A. *Nucl. Instr. Methods Phys. Res., Sect. B* **2006**, *249*, 719−722.
(34) Santavirta, S.; Nordström, D.; Metsärinne, K.; Konttinen, Y. T. *Clin. Orthop.* **1993**, *297*, 100−110.
(35) Sabokbar, A.; Fujikawa, Y.; Murray, D. W.; Athanasou, N. A. *J. Bone Jt. Surg., Br. Vol.* **1997**, *79-B*, 129−134.
(36) Weir, E. C.; Horowitz, M. C.; Baron, R.; Centrella, M.; Kacinski, B. M.; Insogna, K. L. *J. Bone Miner. Res.* **1993**, *8*, 1507−1518.
(37) Caravia, L.; Dowson, D.; Fisher, J.; Jobbins, B. *Proc. Inst. Mech. Eng.* **1990**, *204*, 65−70.
(38) Willert, H. G.; Buchhorn, G. H.; Semlitsch, M. In *Tribology of natural and artificial joints*; Dumbleton, J. J., Ed.; Elsevier Science Publishers: Amsterdam, 1981; pp 381−419.
(39) Lüderwald, I.; Henkel, M. In *Ultrahigh molecular weight polyethylene as biomaterial in orthopedic surgery*; Willert, H. G., Buchhorn, G., Eyerer, P., Eds.; Hogrefe & Huber Publishers: Bern, 1990; pp 114−118.

BM060239T