Tissue reactions to cemented hip sockets

Histologic and morphometric autopsy study of 25 acetabula

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To gain an insight into the tissue reactions leading to noninfectious loosening, 25 autopsy specimens of acetabula with well-fixed cemented sockets were analyzed histomorphologically and morphometrically. The mean duration of the implant was 7 (0.2–16) years.

With the exception of some focal direct bone-cement contacts, bone and cement were separated by a soft tissue membrane which increased in thickness with increasing duration of the implant. Necroses in the membrane were also commoner with advancing implant time. The soft tissue membranes developed increasingly dense infiltrates of histiocytes, mainly containing wear particles of the bone cement and—though less abundant—polyethylene. The cancellous bone adjacent to the soft tissue membrane showed an increasing histiocytic infiltration with an increasing duration of the implant. The trabecular bone showed remodeling with formation of a neocortical layer parallel to the border of the cement mantle.

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Submitted 94-02-05. Accepted 94-09-20

Previous studies have demonstrated that in late loosening of cemented hip prostheses soft tissue membranes at the bone-cement interface can usually be found. Most studies have dealt with interface membranes from failed reconstructions, in particular from failed femoral components obtained during revision surgery (Goldring et al. 1983, Goodman et al. 1989, Bos et al. 1990a). However, since these specimens reveal only late stages in the loosening process with tissue changes that could also be caused by mechanical instability, any deduction concerning the primary mechanism of the loosening process would be uncertain. To elucidate the events leading to loosening, detailed analyses of postmortem specimens with well-fixed prostheses seem to be necessary.

Our autopsy study of well-fixed cemented cups which had been in situ between 2 months and 16 years was undertaken to document the sequential reactive morphologic changes in the acetabular region and especially in the bone-cement interface and thereby to improve our knowledge about the loosening mechanism of articular cups.

Material and methods

25 hemi-pelvises with cemented sockets of hip prostheses were analyzed. The specimens were obtained at routine clinical autopsies from 14 women and 8 men (3 had bilateral total hip prostheses), 78 (64–90) years of age, body weights 60 (40–101) kg. Implant duration was 7 (0.2–16) years (Table 1). The prostheses had been inserted between 1973 and 1988 at different hospitals. Most prostheses had been implanted because of severe arthrosis, a few because of femoral neck fracture and coexisting arthrosis. Until the time of death, no patient had symptoms or signs from the hip that indicated loosening of the prosthesis. Specimens from patients with infection of the joint, bone metastases or bone marrow infiltration by malignant lymphoma were excluded from the study.

All of the extracted prostheses had been fixed with bone cement containing zirconium oxide as radiographic contrast medium (Palacos® or Implast®). Conventional cementation techniques without vacuum application were used in all cases. The following types of prostheses had been inserted: Aesculap (7), S+G Implants (Lübecker GHE-Modell) (6), St. Georg (4), Müller (4), Protasul Allo-Pro (3), Lubinus (1).

Material combinations of the prosthetic heads and sockets included: a metallic head with polyethylene socket (16), a ceramic head with polyethylene socket (8), and a ceramic head and ceramic (aluminum oxide) socket (1).

Table 1. Histologic and morphometric autopsy observations in 25 acetabula

A	B	C	D	E	F	G	H	I	K	L	M	N	O
1	87	2	55	0.2	2	0.13	0.05	0.47	0	0	1	0	4
2	90	2	56	0.8	1	0.17	0.00	0.37	2	0	2	6	8
3	70	1	95	1.0	2	0.41	0.12	0.66	3	0	2	8	8
4	80	2	42	2.0	1	0.08	0.04	0.28	1	0	1	4	5
5	77	2	72	2.5	1	0.10	0.00	0.48	6	4	7	2	8
6	79	1	68	3.5	1	0.13	0.00	0.30	6	2	6	0	8
7	75	2	59	4.0	2	0.26	0.16	0.40	10	3	8	8	6
8	87	2	45	4.0	2	0.36	0.31	0.32	10	1	7	4	7
9	77	1	61	4.5	2	0.41	0.11	0.47	3	0	5	2	8
10	88	2	50	5.0	1	0.26	0.08	0.54	7	5	4	1	4
11	75	2	40	5.0	1	0.64	0.03	0.50	8	8	8	8	8
12	67	1	54	5.0	1	0.31	0.02	0.37	2	2	1	6	8
13	80	2	81	6.0	1	0.17	0.06	0.70	6	6	7	6	5
14	83	2	101	10.0	1	0.39	0.18	0.43	8	6	8	6	6
15	83	2	101	10.0	1	0.37	0.11	0.54	5	2	5	8	8
16	80	1	62	10.0	1	0.68	0.12	0.36	10	4	8	9	8
17	80	1	62	10.0	1	0.36	0.35	0.53	6	2	8	8	8
18	77	2	58	10.0	2	0.69	0.13	0.33	8	2	10	10	10
19	88	2	49	10.0	3	0.18	0.17	0.43	10	0	6	4	8
20	72	2	42	11.0	2	1.45	0.66	0.38	8	7	8	10	6
21	80	1	82	11.0	2	1.47	0.27	0.31	8	1	9	7	6
22	69	1	45	12.0	1	1.06	0.61	0.17	6	9	10	9	3
23	64	1	70	12.5	1	1.55	0.32	0.40	9	6	10	9	6
24	79	2	40	15.0	1	1.37	0.00	0.24	6	10	10	8	6
25	80	2	81	16.0	1	1.44	0.50	0.50	9	7	6	8	7

A Case number
B Age of the patient (years)
C Sex
  1 male
  2 female
D Weight (kg)
E Implant duration (years)
F Combinations of material of the gliding surfaces
  1 metal-polyethylene
  2 ceramic-polyethylene
  3 ceramic-ceramic
G Thickness of the soft tissue membrane (mm)
H Depth of the histiocytic bone marrow infiltration (mm)
I Thickness of the neocorticalis (mm)
K Granular bone cement wear (grade)
L Polyethylene wear (grade)
M Histiocytes in the soft tissue membrane (grade)
N Necroses
O Fibrosis

5 acetabula of patients with intact hip joints served as controls for the morphometric bone measurements. The exclusion criteria were the same as in cases with prostheses. The specimens were obtained from 3 women and 2 men with a mean age of 78 years.

At the time of autopsy, pelvic bone, pseudocapsule, and proximal femur were fixed in formalin en bloc to enable a topographically exact radiographic analysis. Each specimen was then examined with fine-detail radiography in 2 planes.

After fixation for 1 week, acetabular and femoral components were separated by careful removal of the pseudocapsule and adjacent soft tissue. All cups were manually tested by traction for relative motion between the cement mantle and the acetabular bone, without any evidence of loosening.

Subsequently the acetabula were immersed in acetone for 3 days to facilitate the extraction of the cup by partial dissolution of the bone cement. However, even after this treatment, considerable manual force was needed to extract the cups. During removal of the cups, they loosened along the cup-cement interface or with adherent parts of the softened bone cement mantle. Inspection of the remaining specimens without cups and bone cement revealed that the soft tissue membranes had been preserved. In addition, the distribution of the soft tissue membranes and the number and depth of drill holes were documented.

Subsequently, the acetabular bones were cut with exact topographical orientation into 4 mm thick craniocaudal and ventrodorsal sections. A water-cooled saw having an emery band with a diamond coating was used (EXACT, Ost-Steinbek, Germany). For the histologic analysis, representative portions measuring 1 cm × 1 cm from 5 topographic regions (central, cranial, caudal, ventral, and dorsal) were embedded in polymethylmethacrylate (PMMA). All other sections were decalcified in EDTA, embedded in paraffin, cut into 5 μm sections and stained with hematoxylin and eosin (HE), Prussian blue and Masson-

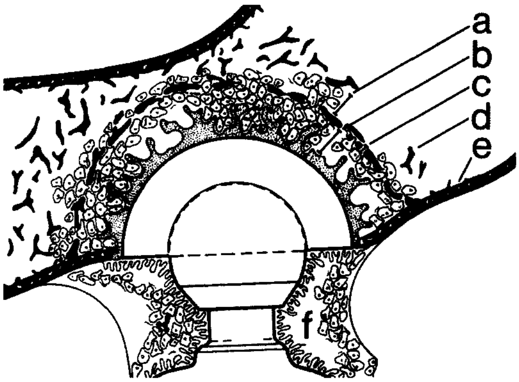

Figure 1. Schematic presentation of the histologic alterations. Central: Prosthesis with bone cement mantle. a Depth of the histiocytic bone marrow infiltration, b Thickness of the soft tissue membrane, c Thickness of the neocortex, d Cancellous bone, e Cortex, f Pseudocapsule.

Figure 2. Case 23. Section through the acetabular region after 12 years in situ. Broad continuous soft tissue membrane between cement mantle and bone up to 4 mm in thickness (white arrowheads). Bottom: Bone cement herniation into the pelvis with fibrous capsule (bar 1cm).

Goldner's trichrome stain. Per acetabulum, 40 sections were evaluated histologically.

Microscopic evaluation

All sections were examined with light microscopy for the presence of a soft tissue membrane between bone and cement. Its thickness and the depth of the histiocytic bone marrow infiltration were measured with an integrating eye-piece graticule (Zeiss, Oberkochem, Germany) (Figure 1). Measurements were performed every 0.75 mm along the soft-tissue membrane.

The histologic characteristics of the soft tissue membrane, including the amount of wear particles, were graded semiquantitatively from 1 to 10 as defined in previous publications (Bos et al. 1990a, 1991).

The following wear particles were noted: bone cement wear in the form of larger extracellular and fine granular particles, polyethylene and ceramic wear. In addition, density and amount of cellular infiltrates as well as histologic changes in the soft tissue membrane were recorded, including histiocytes, necroses, fibrosis and hemosiderin.

In the acetabular bone, the thickness of the neocortex and the percentage of the soft tissue membrane that was covered by bone were determined with an image analysis computer (VIDEOPLAN, Kontron, Eching, Germany).

The measurements of the different topographical regions: central, cranial, caudal, ventral and dorsal, each of them covering one fifth of the acetabular surface, were evaluated separately.

Statistics

The average width of the soft tissue membrane, the histiocytic marrow infiltrates and the neocortex for each acetabulum were tested for correlation with implant duration, age and weight of the patients and the quantity of histiocytes in the soft tissue membrane, using Spearman's rank correlation coefficient. In the same way, we sought for a possible correlation with the amount of fine granular bone cement wear and polyethylene wear. Friedman's two-way analysis of variance by ranks was used to detect differences between the various topographic regions of the acetabulum. A possible dependence of the parameters mentioned above on the gender of the patients or the material combinations of the gliding surfaces was checked by the four-score table method (test of dependence of 2 dichotomous categories).

Results

In the majority of cases (19) a covering of the acetabular cavity by a grey-reddish or yellowish soft tissue membrane was found after removal of the cement mantle (Figure 2). In most cases, varying numbers of drill holes had been cut into the cancellous bone during insertion of the prosthesis. In 12 of the 25 cases, this had led to perforations of the cortical bone, in 8 cases associated with cement intrusions into the pelvis.

In sections through the center of the acetabulum in the cranio-caudal direction, the cancellous bone was sparse or absent, so that the border of the acetabular

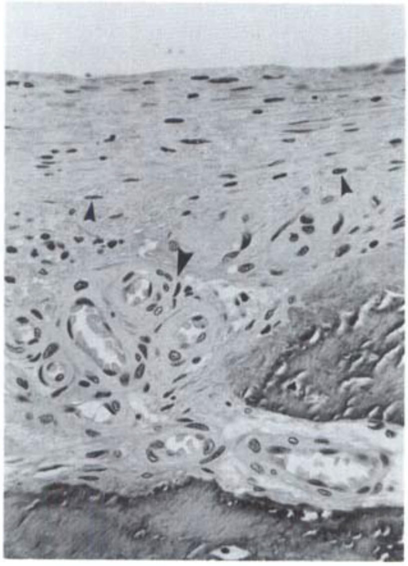

Figure 3. Thin interface membrane after 2 years in situ without wear particles, composed of cellular connective tissue (small arrowheads) and well vascularized granulation tissue (big arrowhead). Goldner's trichrome, ×360.

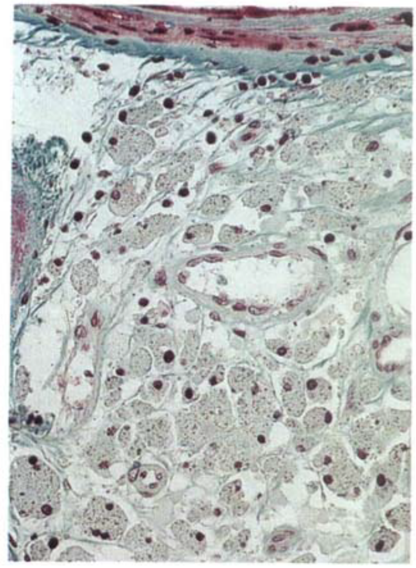

Figure 4. Dense histiocytic infiltration with abundant small granular zirconium oxide particles (indicating bone cement) within the cytoplasm. Goldner's trichrome, ×360.

fossa against the pelvic cavity in some cases consisted of a cortical bone lamella of not more than 1 mm in thickness. In the center, the average thickness was 5 mm compared to 12 mm in the control acetabula without prostheses.

Radiographically in only one case (12 years in situ) in a lateral projection a continuous radiolucent line was seen. An additional 4 specimens which had been in situ for more than 10 years demonstrated discontinuous radiolucent zones extending over more than 50 percent of the bone-cement border.

Microscopic changes at the bone-cement interface

The changes in the soft tissue membrane at the bone-cement interface as well as in the cancellous bone were dependent on the duration of the implant. Even the case with the shortest implant duration (2.5 months) showed a separation of cement and bone by well vascularized granulation tissue with siderophages and fibrin exudates. In 2 cases with an implant duration of 1 year, marked fibrosis was seen in the soft tissue membrane, consisting of equal amounts of granulation tissue and fibrous tissue (Figure 3).

After a longer implant duration, the histologic appearance of the soft tissue membrane was found to be substantially influenced by the type and quantity of released wear particles from the prostheses and the cement mantles.

The wear particles were identified according to the morphologic criteria which had been verified in previous investigations by laser microprobe mass analysis (Bos et al. 1990a,b).

Apart from large bone cement inclusions, which often demonstrated a polycyclic configuration with complete PMMA pearls, we found fine granular bone cement wear that had mostly been phagocytosed by histiocytes. The PMMA of the bone cement is either dissolved by the conventional tissue embedding and staining techniques or remains invisible in undecalcified sections, so that only the zirconium oxide particles, i.e., the radiographic contrast medium, could be recognized microscopically. Light microscopy revealed zirconium oxide particles as round grains of about 0.5 μm in diameter (Figure 4).

Bone cement wear was the most abundant foreign material in the soft tissue membrane. Large amounts of cement wear particles with concomitant infiltration of histiocytes rich in cytoplasm were already seen in a case with an implant duration of 2.5 years.

Small amounts of polyethylene fragments—i.e., the wear particles from polyethylene cups—were found after 2.5 years in situ. They are easily identified by a bright luminescence in polarized light (Figure 5). The size varied widely between lengths of 0.5–200 μm The larger particles (> 30 μm) were enclosed in histiocytic giant cells which dominated the histologic picture of cases with high-grade polyethylene wear.

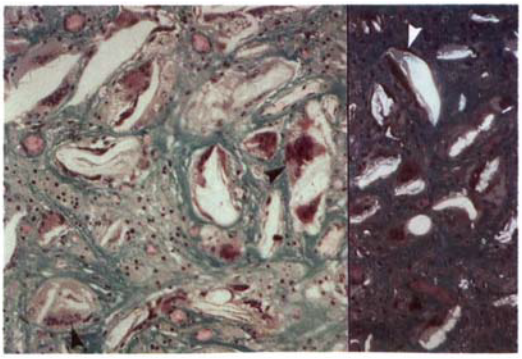

Figure 5. Soft tissue membrane with extensive polyethylene wear. Histiocytic infiltration with numerous foreign body giant cells (black arrowheads) containing polyethylene fibers. Right: Polyethylene fibers in polarized light (white arrowhead). Goldner's trichrome, ×360.

The histologic appearance of the tissue membrane after a longer implant duration was dominated by wear particles containing histiocytes which formed infiltrates of varying thickness. The remaining parts of the membrane consisted of connective tissue and granulation tissue.

Small amounts of ceramic wear particles in the soft tissue membrane were detected in the single case of a prosthesis with a ceramic-on-ceramic combination (10 years in situ). Metallic wear particles were not detected in any case.

A synovial-like lining of the surface bordering on the cement mantle was rarely present. Histiocytes with large amounts of phagocytosed wear particles often revealed degenerative changes like chromatin agglomeration, disintegration of cell borders, cell dissociation and single cell necroses. Large confluent and sharply delineated necrotic areas of histiocytic infiltrates as well as of fibrous tissue were also seen. Smaller foci of tissue necroses were already detectable after 4 years' implant duration in all cases. After a long-term implantation, necroses sometimes constituted more than 50 percent of the membrane sections.

Morphometric and semiquantitative evaluation of the soft tissue membrane

The thickness of the soft tissue membrane varied considerably between specimens and between the different regions of the acetabulum. The average thickness ranged from 0.08 mm to 1.55 mm (Table 1). At some points, the membrane reached up to 5.5 mm in thickness. There was a significant increase in the thickness with increasing implant duration ($P < 0.001$).

No correlation was found between the thickness of the membrane and the weight or gender of the patients or the material combination of the articulating surfaces. No significant differences in membrane thickness were found between the various topographic areas in the acetabulum. The thickness of the membrane correlated positively with the estimated amount of histiocytes which, in turn, showed a positive correlation with the quantity of wear particles ($P < 0.001$).

The estimated amount of fine granular bone cement wear was graded in one fourth of the cases as little, if any (grades 0–3), in one third as moderate (grades 4–6) and in nearly half of the cases as severe (grades 7–10). In contrast, we found little, if any, polyethylene wear in half of the cases, moderate wear in one fourth and severe polyethylene wear in one fifth of the acetabula. The amount of bone cement wear ($P < 0.01$) and polyethylene wear ($P < 0.001$) as well as the amount of histiocytes ($P < 0.001$) within the soft tissue membrane increased with increasing implant duration (Table 1).

Comparing prostheses with a metal-on-polyethylene combination with a ceramic-polyethylene combination, more polyethylene wear was found in metal-on-polyethylene designs ($P < 0.01$).

Regarding the other alterations of the soft tissue membrane that were analyzed—i.e., necroses, fibrosis and hemosiderin—a positive correlation with implant duration was found only for the amount of necroses ($P < 0.001$).

Alterations in the cancellous bone

After an implant duration of more than 4 years, the cancellous bone adjacent to the soft tissue membrane revealed in all cases a predominantly histiocytic infiltration of the same composition as in the soft tissue membrane. The depth of this infiltration increased significantly with increasing time in situ ($P < 0.001$). The maximal depth of the infiltration was 0.6 mm on the average after 11 years in situ. At some points, it extended up to 4.8 mm.

In 15 acetabula, focal metaplastic formation into cartilage was seen at the bone-cement junction. The cartilage was often in direct contact with the bone cement.

Analysis of the architecture of the acetabular cancellous bone revealed a fundamental remodeling process after prosthesis insertion. In nearly all acetabula, the reparative changes following the insertion trauma had been completed. After a few months, a reorientation of the trabeculae with formation of a bone lamella (neocortex) parallel to the cement mantle border had occurred. An increased formation of trabeculae parallel to the cement mantle and connected with the cortical layer by radially oriented trabeculae was seen in the other parts of the cancellous bone. The neocortex consisted of small trabeculae with numerous gaps that rarely reached the density and thickness of the outer cortex. The maximal average thickness of 0.7 mm was seen in a case 6 years after implantation. A positive correlation of the thickness of the neocortex with the body weight of the patients occurred ($P < 0.01$). The surface of the neocortex covered from 64 percent to 96 percent of the surface of the adjacent soft tissue membrane.

Discussion

Until now, only a few detailed morphologic studies of the tissue reactions around stable acetabular sockets have been reported. Delling et al. (1987), Fornasier et al. (1991) and Schmalzried et al. (1992) analyzed 12–14 specimens with somewhat divergent results. In accordance with the present study in which direct bone-cement contact was observed only focally, Delling et al. (1987) found—even in cases with a short implant duration—a complete intervening soft-tissue layer between bone and cement. On the other hand, Schmalzried et al. (1992) described an intimate contact between cement and bone in the center of the acetabula in most cases. In accordance with our observations, the 3 studies revealed an often-extended histiocytic infiltration in the interface membrane with wear particles and necroses comparable to the more pronounced alterations in failed arthroplasties.

Schmalzried et al. (1992) found no dependence of the structure of the membrane on the implant duration. In agreement with our results, Fornasier et al. (1991) reported a positive correlation between the amount of histiocytes in the membrane and the amount of polyethylene wear particles with implant duration. However, unlike in our results, they found no correlation between the thickness of the soft tissue membrane with the implant duration. This difference could be due to the smaller number of specimens analyzed in those studies which, moreover, had a shorter average implant duration. Whereas Fornasier et al. (1991) observed larger bone cement particles incorporated into the soft tissue membrane, Schmalzried and co-workers (1992) described only the polyethylene wear and suggested that this was an essential factor for the formation of the soft tissue membrane and for late aseptic loosening of the prostheses. Fine granular intracellular bone cement wear, which was the dominant foreign material in the present study, was not reported by the other two groups. An explanation may be that the barium sulfate-containing bone cement is not detectable intracellularly by the tissue embedding and staining techniques which they used.

Bone cement wear in well-fixed prostheses has also been observed in studies of pseudocapsules and regional lymph nodes (Bos et al. 1990b, Bos and Löhrs 1991) as well as in soft tissue membranes or osteolytic areas from femurs with stable hip joint prostheses (Jasty et al. 1986, Delling et al. 1987, Malcolm 1988, Anthony et al. 1990, Maloney et al. 1990). It is probably caused by micromovements between cement mantle and bone which occur when an artificial joint is used (Ma et al. 1983, Maloney et al. 1990, Burke et al. 1991, Kwong et al. 1992). The existence of such micromovements has been proved experimentally (Maloney et al. 1990, Burke et al. 1991, Kwong et al. 1992). Our data indicate that all small particulate foreign materials causing an accumulation of histiocytes initiate successive thickening of the interface membrane which may lead to late loosening.

The remodeling of the acetabular bone represents a tissue reaction to altered mechanical stresses after prosthesis insertion. The neocortex, a bone lamella which develops parallel to the cement mantle, seemingly is needed as an equivalent for the original subchondral bone plate to enable an even load transfer from the prosthesis to the supporting bone structures. With respect to the pathogenesis of chondroid metaplasia, it has been suggested that chronic irritation due to micromotion and local stresses in the soft tissue membrane are of importance.

There is a discussion as to the conclusions that can be drawn from this study concerning the etiology of socket loosening. Details of the mechanism and the sequence of events taking place in the loosening process remain obscure. However, biological and mechanical factors are thought to be important (Harris 1994).

Cement fractures and abrasion of the bone cement mantle due to shear forces during load transfer at the bone cement interface are important mechanical factors. Poor cementation technique or malpositioning of the prosthesis leading to insufficient initial stability of the implant are considered to be predisposing factors for premature loosening, since they intensify mechanical stresses in the implant and bone (Courpied and Postel 1986, Aldinger 1987).

This study shows that, after a few years in situ, wear particles, especially from the bone cement, can be found in all cases and that the amount of wear particles increases with increasing implant duration.

The width of the soft tissue membrane and the extent of necroses show a positive correlation with the length of time in situ. It seems obvious that a broad and necrotic soft tissue membrane cannot permanently keep the cup in position, so that complete loosening of the cup may finally develop. The mechanism of bone resorption, which is an essential prerequisite for the formation of the soft tissue membrane and for late loosening, has not yet been exactly determined. Most authors consider that the histiocytes in the membrane are essential effector cells releasing tissue hormones and cytokines and thus directly causing bone resorption (Linder et al. 1983, Murray and Rushton 1990, Santavirta et al. 1990, Kossovsky et al. 1991, Athanasou et al. 1992) or activating osteoclasts (Goldring et al. 1983, 1986, Goodman et al. 1989, Murray et al. 1989, Dorr et al. 1990). As these substances are released during the necrotic disintegration of cells (Freeman et al. 1982), accelerated bone resorption can be expected in the end-stage of the loosening process when degenerative changes in cells due to the high concentration of wear particles and to mechanically-induced necroses in the broad soft tissue membranes predominate. In addition, the increasing histiocytic reaction in the cancellous bone leads to direct contact between histiocytes and the surface of the bone trabeculae which may further facilitate bone resorption. These mechanisms may result in a vicious circle, since the increasing bone resorption leads to progressive mechanical instability which, in turn, accelerates the bone cement wear and the recruitment of histiocytes, until loosening of the socket is complete.

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