Short periods of oscillating fluid pressure directed at a titanium-bone interface in rabbits lead to bone lysis

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Fluctuating high fluid pressures have been reported in pseudojoints after total hip arthroplasty, and may be present throughout the effective joint space. When the pressure extends locally to the bone implant interface, we hypothesized that it might have led to bone resorption. We developed an experimental implant model to study whether oscillating fluid pressure, applied during 2 hours a day, can lead to osteolysis at the bone implant interface. 12 mature rabbits received a titanium implant, which was allowed to osseointegrate. Thereafter, fluid pressure was applied to a specific area of the titanium bone interface at the periosteal side of the cortex in 6 of the rabbits. The pressure, applied during 2 hours a day for 14 days, oscillated between 70 and 150 mm Hg, with a frequency of 0.1 Hz. Bone resorption was not found in any of the control animals, but it occurred under 4 implants exposed to fluid pressure ($p = 0.03$; Fisher's exact test). Localized osteolytic lesions had developed, with evidence of osteocyte death in the surrounding cortical bone. In 1 of the 2 specimens without osteolysis, there was evidence of fluid leakage into the soft tissues. In 4 specimens (3 with and 1 without osteolysis), bone formation was observed at the endosteal side opposite to the pressure zone. This did not occur in the controls. No signs of infection were observed.

Our findings indicate that oscillating fluid pressure, even when present only during short periods, can lead to osteolysis and may be a cause of prosthetic loosening. Endosteal bone apposition may be a result of the interstitial flow that was created, giving false signals of mechanical load to the osteocytes.

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High intracapsular pressures have been reported in pseudojoints after total hip arthroplasty (Schmalzried et al. 1994, Schmalzried and Brown 1995). Pressures of 0–100 mm Hg while standing increased markedly to 700 mm Hg or more during walking, stair climbing or rising from a sitting position (Hendrix et al. 1983). Recently, it has been established that intracapsular pressures are usually elevated in hip joints with loose prosthetic components (Robertsson et al. 1997). In a lytic lesion adjacent to a cemented femoral component, fluctuations of pressure up to 200 mm Hg were induced by passive movement of the pseudojoint (Anthony et al. 1990). Furthermore, fluid communication was shown in cadaveric femora between the pseudojoint and the proximal and distal cement-bone interface along well-fixed femoral components, so that pressure fluctuations were present throughout the effective joint space (Schmalzried et al. 1992, Liebs et al. 1997) This can be an important factor in periprosthetic osteolysis. Such a mechanism could explain osteolytic lesions around stable cemented or uncemented femoral components, especially as wear particles could not always be detected in such lesions (Linder et al. 1983, Maloney et al. 1990b). We evaluated in a rabbit model whether osteolysis can occur when oscillating pressures are applied only during short periods of time.

Animals and methods

Animals

12 skeletally mature New Zealand White rabbits (BMI, Helmond, The Netherlands) with a mean weight of 5 kg were used. The protocol for the animal experiments had been approved by the Animal Research Committee of the University of Amsterdam and all animal handling was performed according to Dutch laws for research animals.

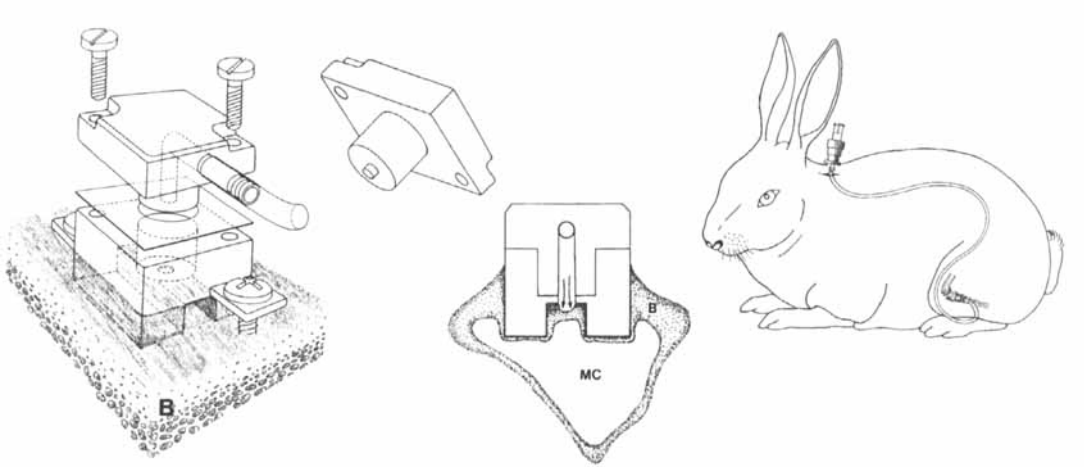


Figure 1. a. Design of the implant to study bone resorption due to fluid pressure in rabbits. B bone.

b. Cross-section of the implant positioned in the proximal rabbit tibia with an impression caused by the fluid pressure. B bone, MC medullary canal.

Figure 2. The pressure system used to induce bone resorption after subcutaneous implantation in a rabbit.

The implant

The implants were designed to perform the experiments in 2 steps. First, a commercially pure titanium surface was placed close to the cortical bone and allowed to "osseointegrate". Secondly, a small opening was created in the titanium surface to allow a local rise in fluid pressure on the bone. The implant was grossly shaped as a cube ($7 \times 7 \times 8$ mm) having two small wings with screw holes for fixation to the bone. One side of this cube had a groove. The bottom of this groove faced the cortical bone surface, whereas the rest of this side of the cube was embedded deeper into the bone (Figure 1). A canal through the cube ended with a 1.0 mm diameter opening in the middle of the bone-facing area. The part of the cube which faced away from the bone towards the skin was exchangeable. When the cube was implanted, this part was just a cover and designed in such a way that it filled and closed the fluid canal at the bottom of the cube. After osseointegration, the cover was exchanged for another piece, so that the fluid canal was opened and a silicon tube was connected to the fluid canal. Water tightness of the system was achieved by a silicon gasket of 0.25 mm thickness between this cover and the cube. The silicon tube with an inner diameter of 1.1mm was proximally connected to an external valve (Figure 2).

Surgical procedures

Anesthesia was induced with 10 mg xylazine and 50 mg ketamine intramuscularly per kg body weight and maintained with halothane/nitrous oxide/oxygen inhalation. During all operations, 5 mg Enrofloxacin was given subcutaneously as a prophylactic antibiotic. The entire right side of the rabbit was shaved, cleaned and prepared with an iodine-alcohol solution. A sterile adhesive iodine drape was used. The proximal medial metaphysis was exposed by a lateral skin incision and mobilization of the skin flap to the medial side. Next, the metaphyseal bone area between the medial collateral ligament and patellar tendon was subperiosteally exposed. A bone bridge was made with the same dimensions as the groove in the implant by using a metal template, fixed onto the bone with two 1.5 mm cortical screws. Through the open slots in the template the cortical bone was removed by a water-cooled low-velocity burr. After removal of the template, the titanium implant was placed over the bone bridge and fixed by the 2 reinserted cortical screws. The first cover that closes the central canal was then placed. By subcutaneous blunt tunneling, the silicon tubing system was put into position with the proximally connected external valve located between the ears of the rabbit. Distally, the silicon tubing was closed by a non-resorbable ligature. The wound was closed in layers using interrupted resorbable mattress sutures. To reduce postoperative pain, 0.03 mg Buprenorphine per kg body weight was given subcutaneously twice a day for 2 days. A 5-week period followed to achieve osseointegration of the implant. After this period, the implant was again surgically exposed and the cover was removed. The fluid canal was cleaned and rinsed with saline and the second cover was put into position after attaching the silicon tube and securing it with a nonresorbable ligature and flushing the system to evacuate air bubbles. By applying a pressure of 200 mm Hg via the external valve, the water tightness of the system was checked.

Test phase

In the first group of 6 rabbits, a pressure oscillating

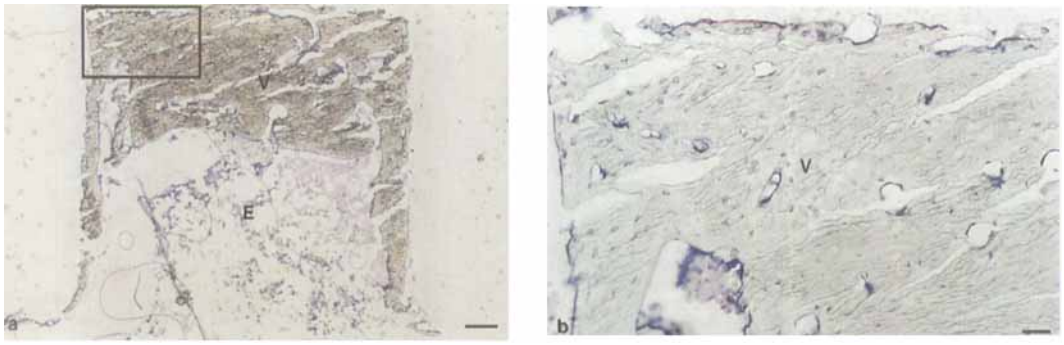


Figure 3. Photomicrograph of a control specimen showing normally structured vital bone (V) in the central bone bridge with lacunae containing osteocytes and blood vessels containing erythrocytes (Cryostat section, Giemsa, a bar = 200 μm, b bar = 40 μm).

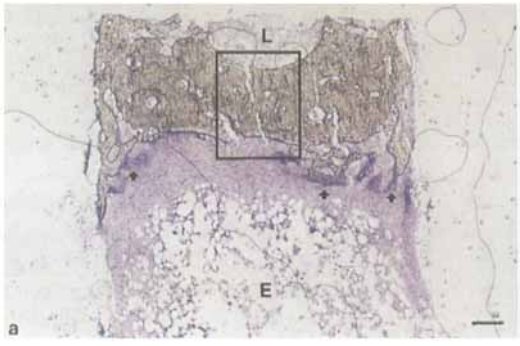
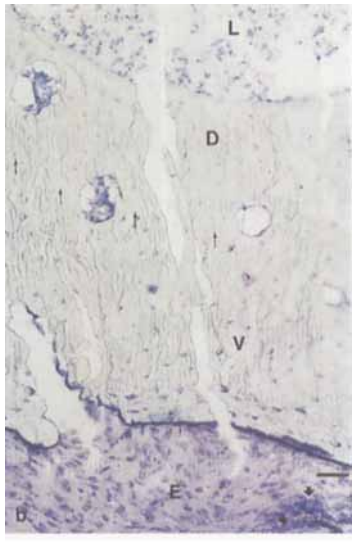


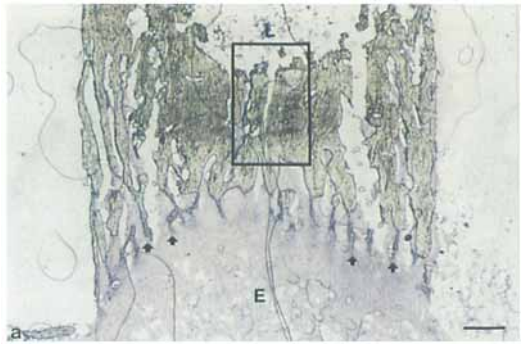
Figure 4. Photomicrograph of one of the test specimens showing a central lytic area (L) situated at the level of the pressure site. Lacunae close to the lytic area are empty (D). The lesion contains some fibrous tissue with a few macrophages. The endosteal side (E) shows osteoblast activity and bone formation (arrows). V, vital bone. (Cryostat section, Giemsa, a bar = 200 μm, b bar = 40 μm)



between approximately 70 and 150 mm Hg was simultaneously applied via the external valves for 2 hours a day for 14 days. For this purpose, a closed system was constructed consisting of a 100 mL plastic infusion sack containing 0.9% saline connected by means of sterile catheters and T-valves to the 6 external valves of the rabbits. All connections were assembled in a strictly aseptic way. The infusion sack was placed under an electronically controlled hydraulic press, which exerted an oscillating compressive force on the sack with a frequency of 0.1 Hz. Pressure in this system was recorded with a pressure transducer connected to a bridge amplifier. Measurement of the individual flow in each animal was technically not feasible and therefore, the weight of the infusion sack was measured before and after each 2 h pressure session instead, to determine the total amount of fluid loss. While the rabbits were connected to this system, they were sedated with 0.3 mL Hypnorm® subcutaneously. The second group of 6 rabbits served as controls. The control animals underwent all the procedures described above except that, after they were connected to the closed pressure system, the oscillating pressure was not applied.

Preparation of the specimens

All rabbits were killed at the end of the second week with an overdose of barbiturates, and after removal of all soft tissue layers, the implants were carefully cleaned from any bone overgrowth and gently lifted from the bone. Next, the entire proximal metaphysis was removed with an oscillating saw. All specimens were embedded in 8% gelatin white (Sigma, St. Louis, MO, USA) and slowly frozen in liquid nitrogen. Undecalcified cryostat sections (8 μm thick) were prepared at a right angle to the test surface using adhesive tape to keep the integrity of the sections intact (Van Noorden and Vogels 1986). A tungsten carbide-tipped knife was used to allow cutting of hard material such as undecalcified bone. Morphological studies



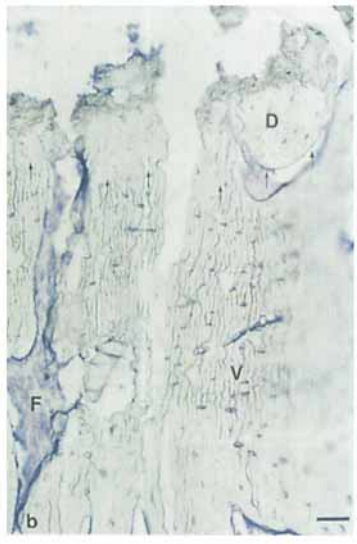


Figure 5. Photomicrograph of the bone bridge of one of the test specimens showing an irregularly bordered lytic area (L) containg a small amount of tissue. Bone formation at the endosteal side is visible. D, bone devoid of osteocytes; V, vital bone. (Cryostat section, Giemsa, a bar = 200 μm, b bar = 40 μm)

were carried out after staining briefly with solutions of toluidine blue or Giemsa. After staining, the sections were rinsed briefly with distilled water and the pieces of tape to which the sections were adhered were cut out and mounted in a double layer of glycerol jelly (Van Noorden and Vogels 1986). Photomicrographs were made immediately.

Statistics

Presence of bone lysis directly in contact with the site of the central opening of the implant was noted as a positive test result. Significance of the occurrence of bone lysis in the pressure group, as compared with the control group, was established by Fisher's exact test.

Results

In the 6 control specimens, resorption zones were not detected either in the vicinity or at a distance from the central hole of the chamber. Bone showed a normal structure and did not differ from the surrounding cortical bone (Figure 3). Lacunae containing osteocytes and blood vessels containing erythrocytes did not show any abnormalities.

In 4 specimens of the test group, bone resorption was found at the site of the central opening of the chamber ($p = 0.03$). Lytic zones with a mean depth of 0.27 mm (0.13–0.37) mm were present in these 4 specimens. They were surrounded by cortical bone (Figure 4). Fibrous tissue was observed in various amounts in the lytic areas (Figure 5). Macrophages, sometimes containing intracellular bone particles, were found, but not in large quantities (Figure 6). Osteoclasts were seldomly present. There was evidence of leakage of fluid into the soft tissues in one of the 2 specimens without lysis. When pressure was reapplied via the silicon tubing, fluid leaked from under this implant. In the 4 specimens showing bone lysis, osteocyte lacunae close to the pressure area were generally empty. At a depth of approximately 100 μm in the remaining bone, osteocytes were present and the cortical bone showed the characteristics of healthy tissue, as observed in the control specimens (Figures 4 and 5). Remarkably, evidence of bone formation was noted at the endosteal side of the cortical bone opposite the pressure site in 3 specimens showing bone lysis and in the specimen without lysis, in which fluid leakage did not take place (Figures 4 and 5). This was never found in the controls ($p = 0.03$). In none of the specimens were signs of infection present such as round cell infiltrates or polymorphonuclear cells. The mean weight loss of the infusion sack per 2 hour session was 4.3, SD 0.4 gram, which corre-

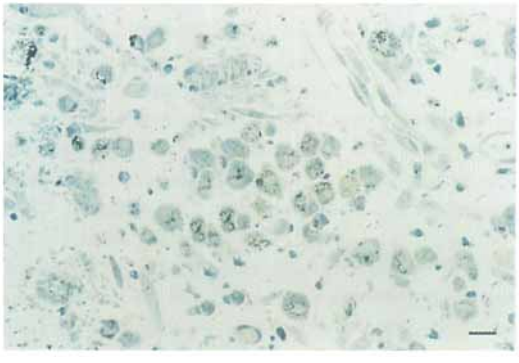


Figure 6. High power photomicrograph of a group of macrophages containing intracellular bone particles. (Cryostat section, von Kossa, bar = 20 μm)

sponded to a loss of fluid of approximately 4 mL in all 6 test animals.

Discussion

Our findings indicate that an oscillating fluid pressure can induce osteolysis, probably as a result of osteocyte death. This effect could be achieved either by interference with the vascular supply or by the direct traumatic effects of an exaggerated interstitial flow. As the intraosseous pressure in the rabbit tibia varies between 20 and 60 mm Hg, an externally applied oscillating fluid pressure between 70 and 150 mm Hg would be enough to reduce intraosseous blood flow (Kiær 1994). Periods of ischemia up to 2 hours are probably not long enough to cause irreversible damage to osteocytes (James and Steijn-Myagkaya 1986, Kälebo et al. 1986). Possibly, a pressure-induced interstitial fluid flow has caused intraosseous edema and vascular compression in the direct pressure area resulting in an extension of the ischemic period (Kiær 1994). On the other hand, the pressure-induced interstitial flow could also have disturbed the composition of the interstitial fluid which, in turn, would have affected osteoblast and osteoclast function (Carano et al. 1993, Ramp et al. 1994). We were not able to determine the fluid flow in each individual animal and probably a large portion of the total fluid loss that was measured was due to leakage which was observed in only 1 animal.

Histological appearances ruled out infection as a possible cause of the osteolysis. Furthermore, although the outside of the silicon tubing system may have been colonized by bacteria, the bone-titanium interface after osseointegration is a perfect seal against infection, as reported with the Brånemark dental implant experiments in rabbits (Ivanoff et al. 1996).

Macrophages were not observed in high numbers. Because only small amounts of bone were resorbed and there were comparatively low amounts of bone debris, there was not much material for macrophages to clear away. In this respect the microscopic appearance of the lesions differed from that is usually seen in osteolytic lesions around total hip arthroplasties, where large numbers of macrophages, histiocytes and foreign body giant cells are present (Maloney et al. 1990a). However, it has also been reported that in smaller lesions (less than 2 cm), only occasional macrophages were present and particulate debris was rare or not identified (Maloney et al. 1990b). Possibly, the lesions found in our study resemble cystic lesions around total hip arthroplasties in an early stage of development.

Endosteal bone formation opposite the pressure area was an unexpected phenomenon. The direct pressure-induced effects on blood flow and interstitial homeostasis must have been limited to a small area within the bone underneath the site where pressure was exerted. Further away from that site, the blood supply and vitality of the bone seemed undisturbed. Endosteal bone formation is probably not the result of normal remodeling processes caused by the induced cyclic compressive load on the periosteal side of the cortical bone because the fluid pressure could not have imposed enough load to deform the bone. There may be another explanation: Osteocytes are believed to detect bone load through the interstitial fluid flow caused by bone deformation, and then to mediate signals to lining cells on the bone surface to increase bone formation (Duncan and Turner 1995). In our experiment, pressure gradients must have produced an intermittent interstitial flow towards the endosteum. This flow may have caused the surviving osteocytes to induce endosteal bone apposition as if the bone had been deformed by mechanical load. Bone formation has been reported in localized lesions around femoral components and has also been observed in bone surrounding osteoarthritic cysts (Landells 1953, Linder et al. 1983). Possibly the mechanism of initial formation of cystic lesions and osteoarthritic cysts is basically the same.

Our findings show that fluctuating high fluid pressures in pseudojoints can lead to osteolysis even when only present during short periods of time provided that the pressure reaches bone regions via the effective joint space.

Another interesting effect of fluctuating fluid pressure, when present throughout the effective joint space, could be the relation to thigh pain. Well-localized thigh pain corresponding exactly to the sites of cystic lesions has been reported in patients after cemented total hip arthroplasty (Huddleston 1988). Nerve fibers have been observed in Haversian canals and bone marrow trabeculae (Arnoldi 1994) and it may be possible that fluctuating pressure inside the medullary canal can produce pain by stimulating nociceptors. Thigh pain is reported to appear mainly when the patient rises from a sitting position, during stair climbing or walking on uneven ground (Petrou et al. 1994). These activities, in particular, cause the highest pseudojoint pressures (Hendrix et al. 1983).

It would be of interest to evaluate whether the reported fluctuations in high pseudojoint pressures are present throughout the effective joint space—for instance, by recording simultaneous pressures in pseudojoints and osteolytic lesions.

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References

Anthony P P, Gie G A, Howie C R, Ling R S. Localised endosteal bone lysis in relation to the femoral components of cemented total hip arthroplasties. J Bone Joint Surg (Br) 1990; 72 (6): 971-9.

Arnoldi C C. Vascular aspects of degenerative joint disorders. A synthesis. Acta Orthop Scand (Suppl 261) 1994; 65: 72-4.

Carano A, Schlesinger P H, Athanasou N A, Teitelbaum S L, Blair H C. Acid and base effects on avian osteoclast activity. Am J Physiol 1993; 264: 694-701.

Duncan R L, Turner C H. Mechanotransduction and the functional response of bone to mechanical strain. Calcif Tissue Int 1995; 57: 344-58.

Hendrix R W, Wixson R L, Rana N A, Rogers L F. Arthrography after total hip arthroplasty: a modified technique used in the diagnosis of pain. Radiology 1983; 148 (3): 647-52.

Huddleston H D. Femoral lysis after cemented hip arthroplasty. J Arthroplasty 1988; 3 (4): 285-97.

Ivanoff C J, Sennerby L, Lekholm U. Influence of soft tissue contamination on the integration of titanium implants. An experimental study in rabbits. Clin Oral Impl Res 1996; 7 (2): 128-32.

James J, Steijn-Myagkaya G L. Death of osteocytes. Electron microscopy after in vitro ischaemia. J Bone Joint Surg (Br) 1986; 68: 620-3.

Kälebo P, Johansson C, Albrektsson T. Temporary bone ischaemia in the hind limb of the rabbit. A vital microscopic study. Arch Orthop Trauma Surg 1986; 105: 321-5.

Kiær T. Bone perfusion and oxygenation. Animal experiments and clinical observations. Acta Orthop Scand (Suppl 257) 1994; 65: 28-32.

Landells J W. The bone cysts of osteoarthritis. J Bone Joint Surg (Br) 1953; 35 (2): 643-9.

Liebs T R, Noble P C, Alexander J W, Monroe W T. Interface pressures during cyclic loading of cemented femoral stems. Transactions of the 43rd Annual Meeting of the Orthopaedic Research Society 1997; 288.

Linder L, Lindberg L, Carlsson A. Aseptic loosening of hip prostheses. A histologic and enzyme histochemical study. Clin Orthop 1983; 175: 93-104.

Maloney W J, Jasty M, Harris W H, Galante J O, Callaghan J J. Endosteal erosion in association with stable uncemented femoral components. J Bone Joint Surg (Am) 1990a; 72 (7): 1025-34.

Maloney W J, Jasty M, Rosenberg A, Harris W H. Bone lysis in well-fixed cemented femoral components. J Bone Joint Surg (Br) 1990b; 72 (6): 966-70.

Petrou G, Gavras M, Diamantopoulos A, Kapetsis T, Kremmydas N, Kouzoupis A. Uncemented total hip replacements and thigh pain. Arch Orthop Trauma Surg 1994; 113: 322-6.

Ramp W K, Lenz L G, Kaysinger K K. Medium pH modulates matrix, mineral and energy metabolism in cultured chick bones and osteoblast-like cells. Bone Miner 1994; 24 (1): 59-73.

Robertsson O, Wingstrand H, Kesteris U, Jonsson K, Önnerfalt R. Intracapsular pressure and loosening of hip prostheses. Preoperative measurements in 18 hips. Acta Orthop Scand 1997; 68 (3): 231-4.

Schmalzried T P, Brown I C. Mechanisms of prosthetic hip joint failure. In: Total Hip Revision Surgery (Eds. Galante J O, Rosenberg A G, Callaghan J J). Raven Press Limited, New York 1995; 91-107.

Schmalzried T P, Jasty M, Harris W H. Periprosthetic bone loss in total hip arthroplasty. Polyethylene wear debris and the concept of the effective joint space. J Bone Joint Surg (Am) 1992; 74 (6): 849-63.

Schmalzried T P, Guttmann D, Grecula M, Amstutz H C. The relationship between the design, position and articular wear of acetabular components inserted without cement and the development of pelvic osteolysis. J Bone Joint Surg (Am) 1994; 76 (5): 677-88.

Van Noorden C J, Vogels I M. Enzyme histochemical reactions in unfixed and undecalcified cryostat sections of mouse knee joints with special reference to arthritic lesions. Histochemistry 1986; 86 (2): 127-33.