BONE RESPONSE TO ZIRCONIA CERAMIC IMPLANTS: AN EXPERIMENTAL STUDY IN RABBITS

Antonio Scarano, DDS
Fabio Di Carlo, DDS
Manlio Quaranta, MD, DDS
Adriano Piattelli, MD, DDS

KEY WORDS

Bone growth
Bone healing
Implants
Zirconia

This study analyzes the bone response to zirconia ceramic implants inserted in New Zealand white mature male rabbits. The implants were inserted into the tibia, and each rabbit received 4 implants. All the animals were euthanatized after 4 weeks. A total of 20 implants were retrieved. Implants and surrounding tissues were immediately fixed in 4% paraformaldehyde and 0.1% glutaraldehyde in 0.15 molar cacodylate buffer at 4°C and pH 7.4 to be processed for histology. The specimens were processed to obtain thin ground sections with the Precise 1 Automated System. The slides were observed in normal transmitted light under a Leitz Laborlux microscope. A great quantity of newly formed bone was observed in close contact with zirconia ceramic surfaces; in some areas, many osteoblasts were present directly on the zirconia. Percentage of bone-implant contact was 68.4% ± 2.4%. Mature bone, with few marrow spaces, was present. Small actively secreting osteoblasts were present in the most coronal and apical portions of the implant. No inflamed or multinucleated cells were present. This study concluded that these implants are highly biocompatible and osteoconductive.

Antonio Scarano, DDS, *is a research fellow and* ***Adriano Piattelli, MD, DDS,*** *is a professor of Oral Pathology and Medicine in the Dental School, University of Chieti, Chieti, Italy. Address correspondence to Dr Piattelli at Via F. Sciucchi 63, Chieti, Italy 66100 (e-mail: apiattelli@unich.it).*

Fabio Di Carlo, DDS, *is a research fellow and* ***Manlio Quaranta, MD, DDS,*** *is a professor of Prosthetic Dentistry in the Dental School, University of Rome, Rome, Italy.*

INTRODUCTION

The family of ceramic materials includes bioinert nonresorbable metal oxides such as alumina (Al_2O_3) or zirconia (ZrO_2), which can be used as dental implants.[1] Zirconia implants are bioinert and have excellent resistance to corrosion and wear, good biocompatibility, and high bending strength and fracture toughness.[2–9] Moreover, zirconia possesses high fracture resistance due to its energy-absorption property during the martensitic transformation of tetragonal particles into monoclinic ones.[4] Zirconia ceramics have twice the bending strength of alumina.[4,10] Zirconia is radiopaque and clearly visible on radiographs, and its ivory color, similar to the color of the natural tooth,[6] renders it extremely useful in aesthetically critical areas of the mouth.[10] Also, zirconia can transmit light, which makes it an ideal candidate for use in aesthetic restorations.[10] Zirconia ceramics have been used as femoral

heads in total hip replacement as an alternative to metal devices, although some researchers have reported poor performance for zirconia heads compared with alumina femoral heads.[11,12]

Microscopical studies in animals have demonstrated that zirconia implants possess good biocompatibility, and direct bone apposition to the implant was observed in zirconia implants inserted in monkeys[5] with a bone-implant contact percentage between 66% and 81%. In a comparative study of unloaded and early loaded zirconia implants, Akagawa et al[4] found high bone-implant contact percentage in both groups, with no fibrous tissues at the interface. The mechanical properties and the elastic modulus of zirconia might also contribute to bone healing.[4] The purpose of the present study was to analyze in vivo cellular reactions and bone healing around zirconia implants inserted in rabbit tibia.

Materials and Methods

Implants made of zirconia ceramic (Norton Desmarquest, Evreux, France) were used in this study. The implants were then passivated (ASTM A380) and cleaned using the following steps: water rinses, 3 ultrasonic cleaning steps, additional water rinses, distilled water agitation, alcohol agitation, and air-blown drying. Five New Zealand white mature male rabbits were used for this study. The implants were inserted into tibia according to a previously described technique.[13] Each rabbit received 4 implants, 2 in the left tibia and 2 in the right tibia. A total of 20 implants were inserted.

The rabbits were anesthetized with intramuscular injections of fluanisone (0.7 mg/kg body weight) and diazepam (1.5 mg/kg body weight), and local anesthesia was given using 1 mL of 2% lidocaine/adrenalin solution. A skin incision with a periosteal flap was used to expose the tibia. The preparation of the bone site was done with burs under generous saline irrigation. The zirconia implant insertion was performed by hand. The periosteum and fascia were sutured with catgut and the skin with silk. There were no postoperative complications or deaths; all animals were euthanatized with an overdose of intravenous pentobarbital after 4 weeks.

A total of 20 implants were retrieved. The implants and surrounding tissues were washed in saline solution and immediately fixed in 4% paraformaldehyde and 0.1% glutaraldehyde in 0.15 molar cacodylate buffer at 4°C and pH 7.4 to be processed for histology. The specimens were processed to obtain thin ground sections with the Precise 1 Automated System (Assing, Rome, Italy).[14] The specimens were dehydrated in an ascending series of alcohol rinses and embedded in a glycolmethacrylate resin (Technovit 7200 VLC, Kulzer, Wehrheim, Germany). After polymerization, the specimens were sectioned along their longitudinal axis with a high-precision diamond disc at about 150 μm and ground down to about 30 μm with a specially designed grinding machine.

A total of 3 slides were obtained for each zirconia implant. The slides were stained with acid fuchsin and toluidine blue, then observed in normal transmitted light under a Leitz Laborlux microscope (Leitz, Wetzlar, Germany) at magnifications of ×50. The percentage of bone contact was calculated using a Laborlux-S light microscope (Leitz, Wetzlar, Germany) connected to a high-resolution video camera (3CCD, JVC KY-F55B, JVC Professional Products, Milan, Italy) and interfaced to a monitor and an Intel Pentium III 1200 MMX (Intel Ireland Ltd, Kildare, Ireland). This optical system was associated with a digitizing pad (Matrix Vision GmbH, Oppenweiler, Germany) and a histometry software package with image-capturing capabilities (Image-Pro Plus 4.5, Media Cybernetics, Inc, Immagini & Computer Snc, Milan, Italy).

Results

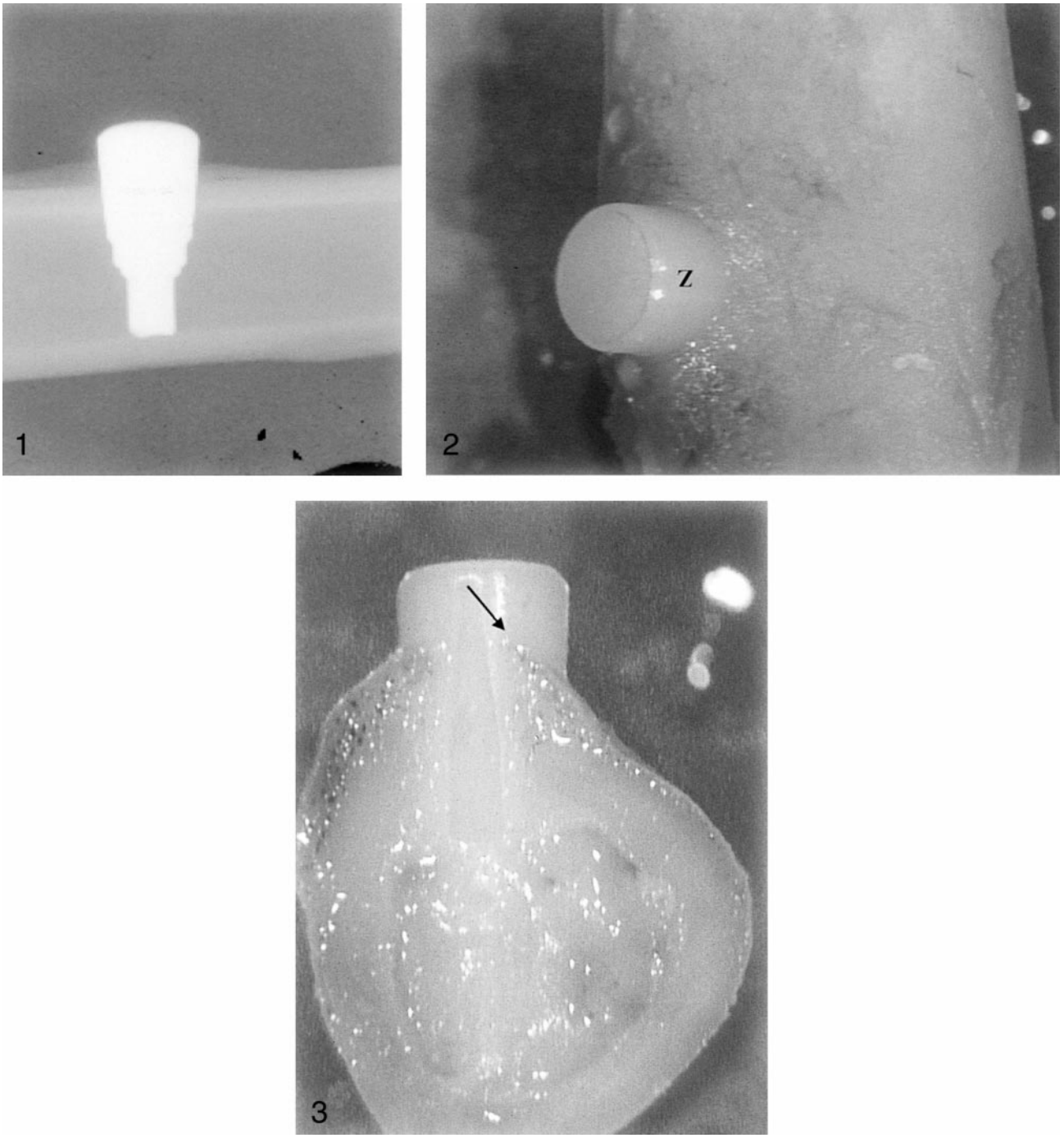
From a radiographic (Figure 1) and clinical (Figures 2 and 3) point of view, all implants appeared to be osseointegrated. No clinical signs of inflammation or mobility were present. It was possible to observe the presence of newly formed bone trabeculae in direct contact with the implant surface (Figure 4), but in a few areas unmineralized matrix was present. Newly formed bone surrounded the implant surfaces, and many osteoblasts secreting osteoid matrix were observed. In other areas of the implant perimeter, it was possible to observe the formation of osteoid matrix directly on the implant surface (Figure 5). Resorption areas and inflammatory or multinucleated giant cells were not present.

Percentage of bone-implant contact was 68.4% ± 2.4%. No gaps or fibrous tissue were present at the interface. No foreign-body reaction was found at the bone-implant interface. No epithelial downgrowth was observed at the interface. Wide marrow spaces were present, with some of them abutting on the implant surface (Figure 6). The newly formed bone showed many viable osteocytes.

Discussion

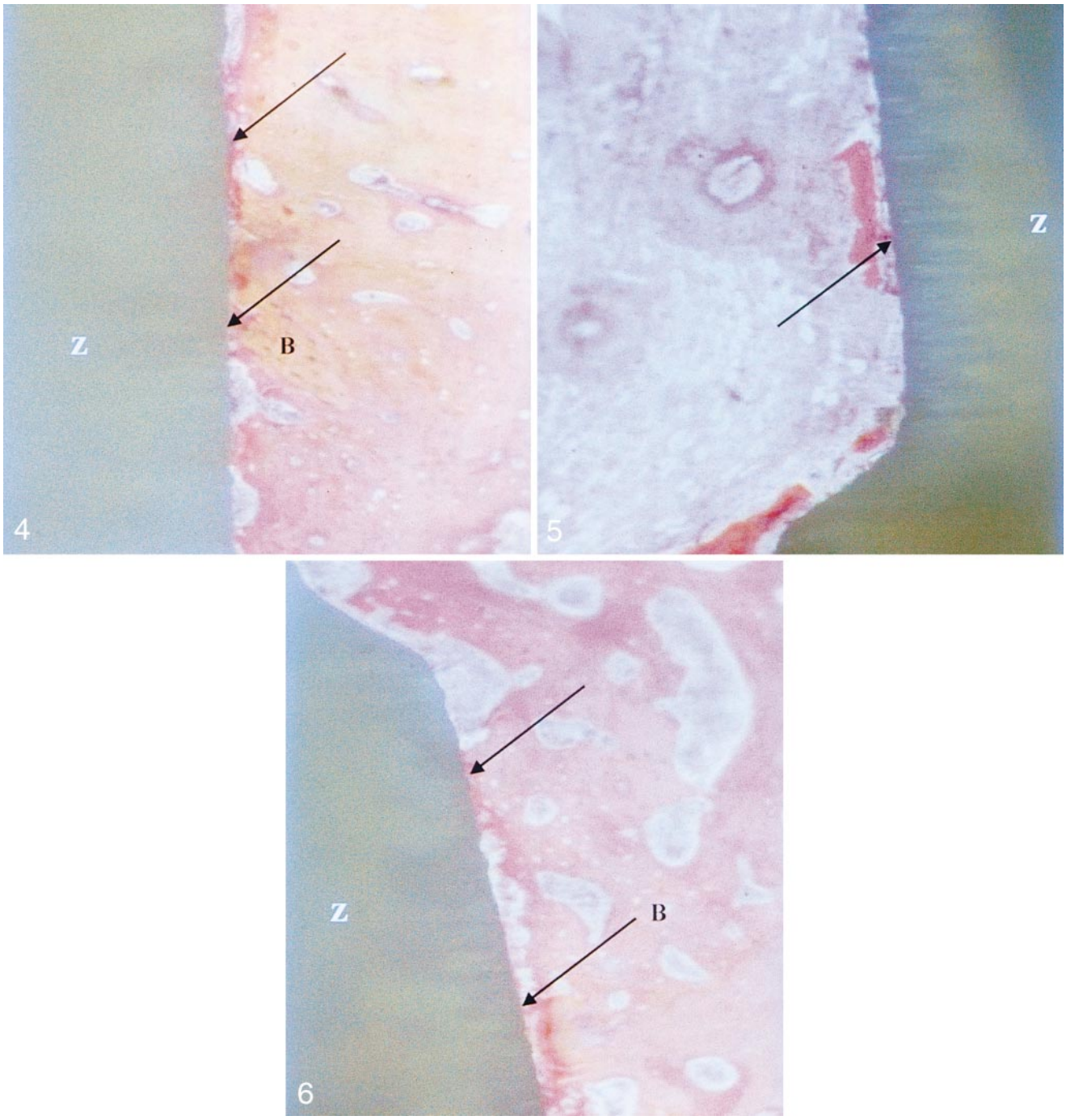
Ceramic implants have been demonstrated to be chemically stable, mechanically hard, and highly resistant to degradation. This combination of mechanical properties and excellent biocompatibility makes zirconia ceramic one of the best biomaterials for prosthetic joints, including hip joints.[7] Zirconia may have better affinity to bone tissue than other biocompatible ceramics.[4] The values of elastic modulus of zirconia are half that of single-crystal sapphire, which may contribute to biomechanical integration of the bone-implant interface.[6]

The addition of a fraction of zirconia to alumina resulted in a composite material of increased toughness.[15] In an experimental study in minipigs, Schultze-Mosgau et al[8] found that alveolar bone apposed exactly the steps and lacunae on the surface of the implants, and these authors concluded that the interface around zirconia implants was similar to



FIGURES 1–3. FIGURE 1. Radiography of a retrieved zirconia implant inserted in rabbit tibia. FIGURE 2. Zirconia implant (Z) inserted in rabbit tibia after removal of the surrounding soft tissues. FIGURE 3. Cut surface of the implant and bone: the bone (arrow) is closely adapted to the implant.

that seen around titanium implants. The biocompatibility of zirconia ceramics was investigated in vivo by implanting them in bone and soft tissues; in zirconia implants inserted into subcutaneous tissue, only a small inflammatory cell infiltrate was found, and the implant was completely encapsulated by a thin fibrous connective tissue.[6] Hulbert et al[16] implanted discs and tubes of CaO + Al_2O_3, CaO + TiO_2, and CaO + ZrO_2, as porous materials with a pore size from 45 to 150 μm and as nonporous materials, into rabbit muscles. Histological analysis of all the materials tested did not reveal signs of toxic, immunological, or carcinogenic effects.[16] Zirconia has no oncogenic effects in vitro.[7]



FIGURES 4–6. FIGURE 4. Newly formed bone (B) is in close contact with the implant surface (Z). No gaps or fibrous tissues are present at the interface (Toluidine blue and acid fuchsin, original magnification ×100). FIGURE 5. Osteiod matrix is deposited directly on the implant surface (arrow). Z = Zirconia implant (Toluidine blue and acid fuchsin, original magnification ×100). FIGURE 6. Newly formed bone (B) and wide marrow spaces are present at the bone-implant interface. Z = Zirconia implant (Toluidine blue and acid fuchsin, original magnification ×100).

In our study, the presence of mature compact lamellar bone and osteocytes near the implant surface indicated good biocompatibility, and certainly the presence of the implant did not disturb the processes of bone formation at the interface. Dubruille et al[1] found that the mean percentage of implant-bone contact was better for ceramic implants than for titanium implants. Our results confirm the data already reported that the bone-implant interface around zirconia implants is similar to that observed around titanium implants. The surface of the zirco-

nia implants appeared to be highly biocompatible, and no gaps, fibrous tissue, multinucleated cells, or inflammatory cell infiltrate were found at the bone-implant interface.

ACKNOWLEDGMENTS

This work was partially supported by the National Research Council (CNR), Finalized Project ''Materials Tailored for Advanced Technologies,'' PF MSTA II, Rome, Italy; and by the Ministry of Education, University, and Research (MIUR), Rome, Italy.

REFERENCES

1. Dubruille JH, Viguier E, Le Naour G, Dubruille MT, Auriol M, Le Charpentier Y. Evaluation of combinations of titanium, zirconia, and alumina implants with 2 bone fillers in the dog. *Int J Oral Maxillofac Implants.* 1999; 14:1–7.

2. Rosengren A, Pavlovic E, Oscarsson S, Krajewski A, Ravaglioli A, Piancastelli A. Plasma protein adsorption pattern on characterized ceramic biomaterials. *Biomaterials.* 2002;23: 1237–1247.

3. Jackson MC. Restoration of posterior implants using a new ceramic material. *J Dent Technol.* 1999;16:19–22.

4. Akagawa Y, Ichikawa Y, Nikai H, Tsuru H. Interface histology of unloaded and early loaded partially stabilized zirconia endosseous implant in initial bone healing. *J Prosthet Dent.* 1993;69:599–604.

5. Akagawa Y, Hosokawa R, Sato Y, Kameyama K. Comparison between freestanding and tooth-connected partially stabilized zirconia implants after two years function in monkeys: a clinical and histological study. *J Prosthet Dent.* 1998;80:551–558.

6. Ichigawa Y, Akagawa Y, Nikai H, Tsuru H. Tissue compatibility and stability of a new zirconia ceramic in vivo. *J Prosthet Dent.* 1992;68:322–326.

7. Covacci V, Bruzzese N, Maccauro G, et al. In vitro evaluation of the mutagenic and carcinogenic power of high purity zirconia ceramic. *Biomaterials.* 1999;20:371–376.

8. Schultze-Mosgau S, Schliephake H, Radespiel-Troger M, Neukam FW. Osseointegration of endodontic endosseous cones: zirconium oxide vs titanium. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2000;89:91–98.

9. Josset Y, Oum'Hamed Z, Zarrinpour A, Lorenzato M, Adnet J, Laurent-Maquin D. In vitro reactions of human osteoblasts in culture with zirconia and alumina ceramics. *J Biomed Mater Res.* 1999;47:481–493.

10. Ahmad I. Yttrium-partially stabilized zirconium dioxide posts: an approach to restoring coronally compromised nonvital teeth. *Int J Periodont Restor Dent.* 1998;18:455–465.

11. De Aza AH, Chevalier J, Fantozzi G, Schehl M, Torrecillas R. Crack growth resistance of alumina, zirconia and zirconia toughened alumina ceramics for joint prostheses. *Biomaterials.* 2002;23:937–945.

12. Allain J, Le Mouel S, Goutallier D, Voisin MC. Poor eight-year survival of cemented zirconia-polyethylene total hip replacement. *J Bone Joint Surg Br.* 1999;81:835–842.

13. Piattelli A, Scarano A, Piattelli M. Detection of alkaline and acid phosphatases around titanium implants: a light microscopical and histochemical study in rabbits. *Biomaterials.* 1995;16: 1333–1338.

14. Piattelli A, Scarano A, Quaranta M. High-precision, cost-effective system for producing thin sections of oral tissues containing dental implants. *Biomaterials.* 1997;18:577–579.

15. Affatato S, Testoni M, Cacciari GI, Toni A. Mixed oxides prosthetic ceramic ball heads. Part 1: effect of the ZrO_2 fraction on the wear of ceramic on polyethylene joints. *Biomaterials.* 1999;20:971–975.

16. Hulbert SF, Morrison SJ, Klawitter JJ. Tissue reaction to three ceramics of porous and non-porous structures. *J Biomed Mater Res.* 1972:6: 347–374.