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ORIGINAL ARTICLE

Specific material effects of wear-particle-induced inflammation and osteolysis at the bone—implant interface: A rat model

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Summary *Introduction:* Wear particles produced from prosthetic joints may play critical roles in periprosthetic inflammatory reactions and osteolysis. The objective of this study was to quantify and compare the response to wear debris from different biomaterials at the bone—implant interface in a rat knee model.
Methods: Sixty rats were divided into titanium alloy (Ti—6Al—4V), cobalt chromium (Co—Cr), ceramic (Al_2O_3), ultrahigh molecular weight polyethylene (UHMWPE), and control (phosphate buffered saline) groups with 12 animals per group. A nonweight-bearing titanium rod was implanted into the right distal femur of each rat followed by intra-articular injections of the biomaterial particles to the surgical knees for up to 16 weeks. Micro-computed tomography scanning was performed monthly and at the time of sacrifice to determine bone densities around the bone—implant interface. Histological evaluations were executed to quantify local inflammatory reactions and osteoclastogenesis.
Results: Co—Cr particles resulted in the most severe reductions in bone density. UHMWPE and ceramic particles resulted in a rapid reduction in bone density followed by a recovery. Inflammatory pseudo-membranes were ubiquitously present close to the femoral condyle and pin insertion site. Ceramic particles significantly promoted periprosthetic tissue formation compared with the other groups ($p < 0.05$). Cathepsin K positive cells were dominantly present at the peri-implant site following challenges of metallic alloy and ceramic particles.
Conclusion: Different biomaterials in particulate form exert different forms of adverse effects in terms of the amount of osteolysis and inflammatory reactions on bone tissue at

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the bone—implant interface. It provides information for engineering more appropriate materials for arthroplasty components.

Introduction

Periprosthetic osteolysis following prosthetic joint arthroplasty has been a subject of increasing concern in the orthopaedic research community as well as a dominant limiting factor in the longevity of the prosthetic device. Depending on the distribution and severity, osteolysis can lead to aseptic loosening, periprosthetic fracture, and daunting reconstructive problems at revision surgery [1—3]. It is widely recognised that polyethylene wear debris is one of the main causes of long-term prosthesis loosening. The longevity of prosthetic joint replacements is often jeopardised by particulate wear debris associated aseptic loosening and osteolysis [4—6].

Small wear particulate debris generated at the periprosthetic site have been identified as a main causative factor leading to periprosthetic osteolysis because they often stimulate a range of inflammatory cellular responses (including foreign-body reactions), which may ultimately result in osteoclastogenesis and bone resorption [6]. The amount of particulate debris, the composition of debris, and the location of debris generation all must be considered when trying to resolve design issues and minimise particulate wear debris. Because osteolysis is predominantly a biologic response to particulate wear and corrosion products, alternative bearing surfaces and cross-linked ultrahigh molecular weight polyethylene (UHMWPE) have been developed in an attempt to reduce the incidence of wear-induced periprosthetic osteolysis. These alterative bearing surfaces currently include ceramic-on-UHMWPE, ceramic-on-ceramic, metal-on-metal, and metal-on-UHMWPE. However, it has been shown in many studies that even these alternative bearing surfaces as well as UHMWPE lead to periprosthetic osteolysis and inflammation [7,8]. In addition, the biologic response to debris generated from bearing surfaces has been highly debated in recent years [7].

Howie et al [9] examined the resorption of bone and the formation of a membrane at the interface between an acrylic cement implant and bone. A nonweight-bearing plug of methylmethacrylate was inserted through the knee joint into the distal part of the femur of the rat representing similarities to human joint prostheses. The resorption of bone that occurred around the plug after the injection of high-density polyethylene wear particles to the rat knee took place in the absence of mechanical causes for loosening. This rat model technique was more recently applied to the mouse and has successfully been used to study osteolysis, inflammatory responses, and cellular reactions to wear particles [10,11]. The model has repeatedly been shown to be a reliable representation to help further elucidate the problems with prosthetic joint prostheses [12—16]. To our knowledge, there is no published report using a rat model in which a nonweight-bearing sterile titanium rod (eliminating the variable of mechanical loosening) placed in the distal part of a viable femur to investigate the effects of different particulate wear debris biomaterials on inflammatory reactions and the osteolytic process at the bone—implant interface, and no study to date has compared the effects of each of the particulate debris with the extent of osteolysis on the bone. This model theoretically allows evaluation of the biocompatibility of orthopaedic particulate biomaterials, and evaluation of the wear particles that cause resorption of bone and formation of connective tissue leading to loosening of prostheses simultaneously. We hypothesise that wear debris from different composition of the biomaterials act differently to promote local tissue response. The objective of this study was to test the hypothesis to quantify and compare the response with wear debris from different particulate biomaterials (UHMWPE, cobalt chromium, titanium alloy, and ceramic particles) at the bone—implant interface in a rat knee joint with a distal femur implant model.

Materials and methods

Experimental protocol and grouping

The animal protocol has been approved by the Institutional Animal Care and Use Committee. A total of 60 female Lewis rats with the body weight range of 200—225 g (Envigo, 800-793-7287) were used for this study. The animals were housed in cages of three for a total of 20 cages according to the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International). They were kept in the Wichita State University animal facility 1 week prior to surgical implantation and randomly assigned to five groups ($n = 12$ for each group): UHWMPE particles, cobalt—chromium alloy (Co—Cr) particles, titanium alloy (Ti—6Al—4V) particles, ceramic (Al_2O_3) particles, and phosphate buffered saline (PBS). All groups had a titanium rod insert into the left distal femur with injections of the particles with carrier solution (PBS) as defined by each group respectively. Group 5 (control) had a titanium rod insert into the left distal femur with injection of PBS solution alone without any particles. This study was conducted over a 16-week period allowing the first 4 weeks for implant stability and healing to take place and the following 16 weeks for particle injections, assessment, and animal sacrifice.

Biomaterial particles

Four orthopaedic biomaterials in particulate form were evaluated for reactions in the rat distal femur model alone