Response to polyetherimide based composite materials implanted in muscle and in bone

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The *in-vivo* response to a composite material obtained with polyetherimide (PEI) reinforced with carbon/glass fibers was investigated by histological methods by implanting cylinders in muscle and in bone of the New Zealand White rabbit. A common metallic alloy, widely used in orthopaedic surgery, was used as control (Stellite). The aim of the study was to analyze the biological response towards the surface of the material. Composite implants and metallic implants did not induce adverse or inflammatory reactions. The morphological picture produced was similar, in muscle and in bone, for both materials. In muscle, cylinders were confined by an extremely thin fibrous layer and the overall appearance of the muscular tissue was normal. In bone, cylinders were confined by a nearly annular rim of newly formed bone. From these data it is possible to derive that the response to PEI-based composite material is comparable with the response to metallic substrate and, then, the material can be suitable for clinical application.

1. Introduction

The interest of fiber-reinforced polymeric composite materials for the design and manufacturing of flexible femoral stems for total hip replacement prostheses has been stimulated by the concerns about possible alteration in bone remodeling which may occur around the femoral stem. In the case of a metallic prosthesis, bone loss was attributed to stress shielding because of the stiffness of the device.

Carbon fiber-reinforcing thermoset resins, such as epoxies, were the first choice for composite prostheses [1]. The toxic effect of unreacted monomers has driven attention to the thermoplastic polymers as matrix for implant applications [2]. Polymers under investigation as matrix for composite implants include, mainly, polysulphone (PS), polyetheretherketone (PEEK) and polyetherimide (PEI). These engineering polymers are characterized by high mechanical properties, thermal stability, very marginal water absorption and relatively easy processing. In addition, their high level of solvents and thermal resistance allows the production of sterilazable medical devices.

PEEK and PS have demonstrated both positive and negative properties in particular applications. PEEK has excellent mechanical stability but critical processing conditions due to its temperature-sensitive semicrystalline structure. Polysulphone has shown a reduction of mechanical properties following saturation in Ringer's solution.

PEI presents a high service temperature and high organic solvent resistance. There are not so many studies which addressed the issue of PEI biocompatibility [3]. Anyway, PEI sheathed implants showed, in the cat cochlea, to elicit a very minimal tissue response [4].

Previous *in-vitro* and *in-vivo* studies have shown that PEI is an excellent substrate for cell spreading and growth, eliciting no cytotoxic response or haemolysis, coupled with both easy processing and adequate compliance with sterilization procedures [5, 6]. These data suggested that PEI could be an attractive material either alone or as a matrix for a composite structure.

In this study, PEI has been considered as matrix of a composite reinforced with carbon and glass fibers and the analysis has been focused on the muscular and bone response towards the material at its surface. The final goal is to obtain a composite material suitable for application in designing and manufacturing of a hip joint prosthesis.

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2. Materials and methods

2.1. Production of implants

Cylinders of 12 mm length × 2 mm diameter, of carbon/glass fiber-reinforced composite based on PEI were produced by the compression molding processing (Fig. 1). The composite structure was prepared by hot pressing of a predetermined sequence of sheets constituted of carbon and glass fibers together with a fabric pre-impregnated with PEI. Cylinders were then coated with PEI by solution-casting to cover completely any fiber possibly unmasked by the machining procedure. To allow the evaporation of the residual solvent the cylinders were stowed at 180 °C under vacuum for 3 d.

Cylinders of the same dimensions were produced in Stellite 21, a metallic implant substrate respecting the ISO 5832/4 recommendation for implantable device.

2.2. Animal model

New Zealand White rabbits weighing about 2700 g, without preference of sex, were selected as animal model. Twelve implants were performed in the quadriceps muscle of the thigh and 24 implants were performed in the distal meta-epiphyseal canal of the femur. Unoperated controls and ''sham-operated'' controls, where the surgical procedure is performed but no cylinder is actually implanted, were included in the protocol.

Cylinders were sterilized by ethylene oxide and single-packaged in sterile envelopes. Anaesthesia was obtained by administration of intramuscular valium (5 mg kg^{-1}), intramuscular ketalar (50 mg kg^{-1}) and subcutaneous xilocaine. Antibiotic prophylaxis was based on administration of intramuscular rifocin (250 mg) daily.

2.3. Implants in muscle

The site selected was the vastus lateralis and/or rectus femoris muscle of the thigh. An incision of 2 mm was made distally then a cylinder was smoothly inserted cranially along the direction of the muscle fibers. Retrievals took place at 12 weeks. After cryomicrotomy and haematoxylin and eosin (HE) staining, samples were analyzed by light microscopy.

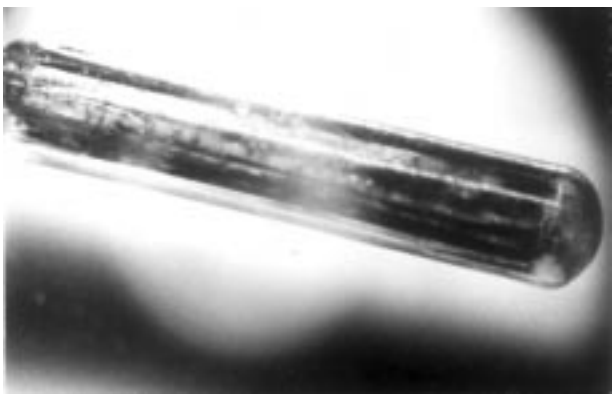

Figure 1 Cylinders of 12 mm length × 2 mm diameter of carbon/glass fibers reinforcing composite-based PEI.

2.4. Implants in bone

The site selected was the distal femoral canal (meta-epiphyseal region). A hole was drilled from the intercondylar groove after access was gained to articular cavity of the knee by a lateral peripatellar approach. Then a cylinder was inserted along the main axis of the femur. This site mimicks (even if at an higher pace) turn-over conditions present in trabecular areas where most implants in humans are placed [7]. Retrievals took place at 4, 12 and 26 wks (Table I). After metacrylate embedding, sections of 100 μm thickness were taken with a rotating diamond-saw microtome; this special saw reduces artefacts due to blade vibrations. Then the samples were analyzed by polarized and light microscopy.

2.5. Retrievals

To retrieve and process the samples, the rabbit was placed in a special sealed chamber where the atmosphere was quickly saturated with CO_2 and left there for 3 min. The cylinder was slipped off from the retrieved muscle which was then placed in formalin. The retrived femur was carefully dissected and then placed in 70% ethyl alcohol. The femur was squared in the distal portion, dehydrated in serial passages in alcohol and embedded in methylmethacrylate.

3. Results and discussion

Composite implants and metallic implants produced a similar response both in muscle and in bone without any significant difference at the morphological level.

3.1. Response in muscle

Muscular architecture was not affected by the implantation procedure and by the presence of the implants. Around the cylinders, and far from them, there is no sign of adverse inflammatory response (Fig. 2). Cylinders were confined by an extremely thin fibrous layer, one or two cells in thickness (Fig. 3); this is a physiological response common to many implanted biocompatible materials in muscle.

3.2. Response in bone

In polarized light microscopy, undecalcified transverse sections show carbon/glass fibers appearing in dark colors in a matrix of translucent PEI. Cylinders were

TABLE I Number of animals who had a single implant; a total of 32 rabbits were operated

	Retrieval at 4 weeks	Retrieval at 12 weeks	Retrieval at 26 weeks
Implants in muscle		8 PEI 4 Stellite	
Implants in bone	4 PEI 2 Stellite	4 PEI 2 Stellite	8 PEI 4 Stellite

A higher number of animals were implanted at 26 weeks to counteract the increased risk of premature death with a longer implant time; at the end of the experiment no premature deaths were recorded.

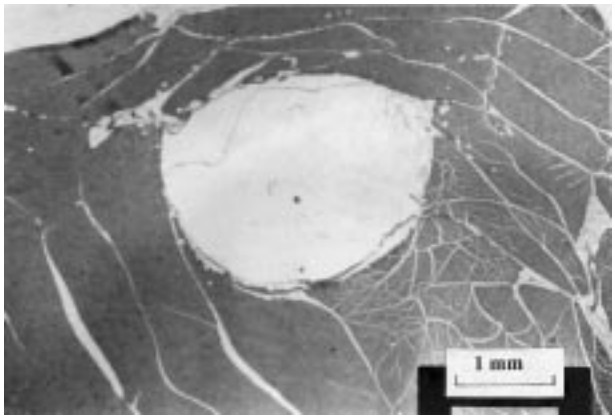

Figure 2 Muscular architecture is not affected by the implant (slipped off in this sample). Around the site of the implant (white area in the center) and far from it, there is no sign of adverse inflammatory response (transverse section; HE staining; 2.5 ×).

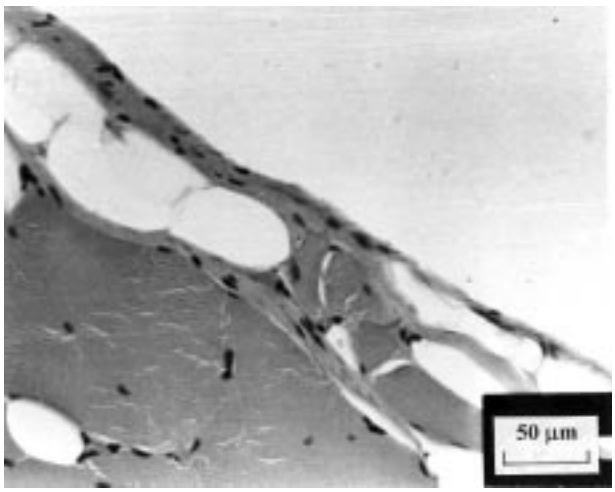

Figure 3 Physiological muscular arrangement and absence of adverse inflammatory response in the region facing the implant (white area, after the implant has been removed). Cylinders were confined by an extremely thin fibrous layer, one or two cells in thickness (transverse section; HE staining; 40 ×).

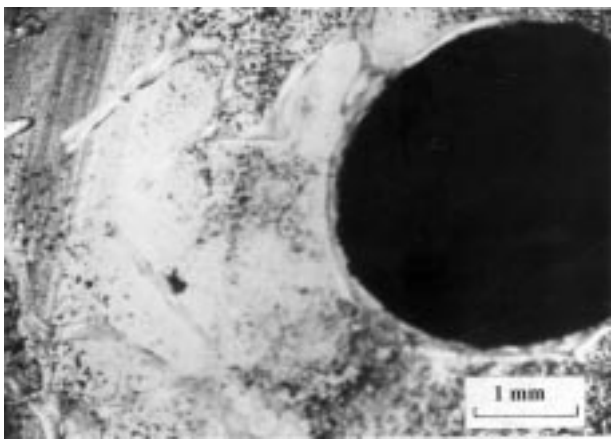

Figure 4 Polarized light microscopy of undecalcified transverse section of trabecular bone, with the control metallic implant (Stellite). An annular rim of newly formed bone surrounds and confines the implant (magnification 2.5 ×).

confined by a nearly annular rim of newly formed bone which surrounds and confines the implant (Figs 4 and 5). Trabecular bone in the area was remodeling with a physiological pattern. A remodeled coarse trabecular can be seen, at times, facing the surface of the implant (Fig. 6). Anyway, the most descriptive picture is that of an encircling growth of trabecular bone around the implant, without any direct contact with it (Fig. 7). This is a physiological response common to any implanted biocompatible material in bone, apart from bioceramics

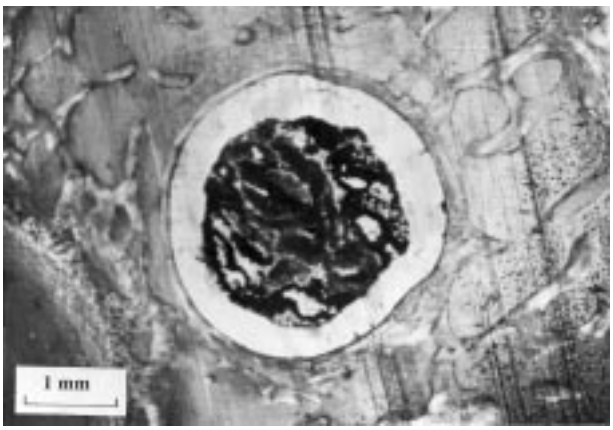

Figure 5 Polarized light microscopy of undecalcified transverse section of trabecular bone, with the composite implant. Fibers appear in dark colors in a matrix of translucent PEI (magnification 2.5 ×).

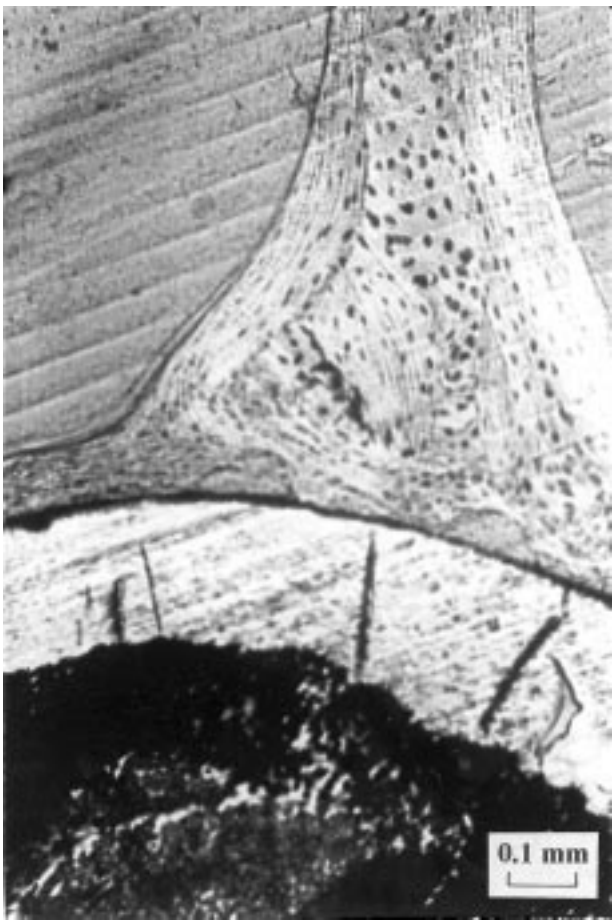

Figure 6 Polarized light microscopy of undecalcified transverse section of trabecular bone, with the composite implant. Fibers appear in dark colors in a matrix of translucent PEI. A physiologically remodeled coarse trabecular faces the surface of the implant (magnification 20 ×).

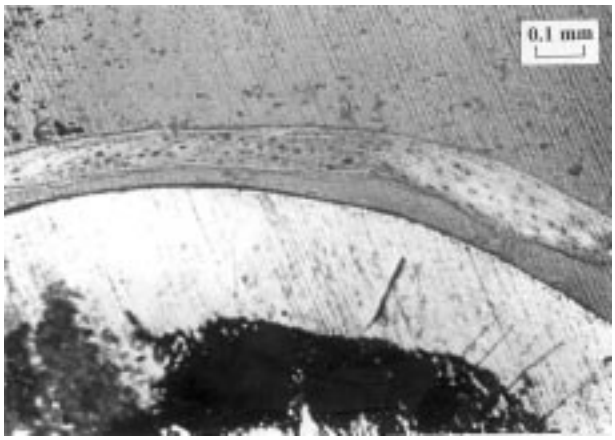

Figure 7 Polarized light microscopy of undecalcified transverse section of trabecular bone, with the composite implant. Fibers appear in dark colors in a matrix of translucent PEI. An annular rim of newly formed bone surrounds and confines the implant (magnification 20 ×).

(hydroxyapatite and bioactive glass) where a tight apposition with bone is present.

4. Conclusions

Composite implants based on carbon/glass fiber reinforcing PEI and metallic implants made of Stellite do not induce adverse or inflammatory reactions in the animal model. The morphological picture produced was similar for both materials in muscle and bone. From these data it is possible to derive that the response to PEI-based composite is comparable with the response to the metallic substrate and then the material may be suitable for clinical applications.

References

1. L. M. WENZ, K. MERRIT, S. A. BROWN, A. MOET and A. D. STEFFE, *J. Biomed. Mater. Res.* **24** (1990) 207.
2. G. PELUSO, L. AMBROSIO, M. CINQUEGRANI, L. NICOLAIS, S. SAIELLO and G. TAJANA, *Biomaterials* **12** (1991) 231.
3. R. R. RICHARDSON JR, J. A. MILLER and W. M. REICHERT, *ibid.* **14** (1993) 627.
4. H. S. HAGGERTY and H. S. LUSTED, *Acta Otolaryngol.* **107** (1989) 13.
5. G. PELUSO, O. PETILLO, L. AMBROSIO and L. NICOLAIS, *J. Mater. Sci. Mater. Med.* **5** (1994) 738.
6. O. PETILLO, G. PELUSO, L. AMBROSIO, L. NICOLAIS, W. J. KAO and J. M. ANDERSON, *J. Biomed. Mater. Res.* **28** (1994) 635.
7. P. TRANQUILLI LEALI, A. MEROLLI, O. PALMACCI, C. GABBI, A. CACCHIOLI and G. GONIZZI, *J. Mater. Sci. Mater. Med.* **5** (1994) 345.

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