IN VIVO QCT AND PET SCANNING OF THE MURINE FEMUR CONTAINING PMMA PARTICLES

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STATEMENT OF PURPOSE

Polymethylmetacrylate (PMMA) particles contribute to osteolysis through upregulation of inflammatory processes, osteoclast activations and inhibition of osteoblastic proliferation and differentiation. However, the direct link between PMMA particles and osteolysis remains uncertain.

Quantitative computed tomography (QCT) has been used for the clinical measurement of bone mineral density (BMD), to accurately assess bone mass. Functional imaging techniques such as ^{18}F-fluoride positron emission tomography scanner (PETscan) allow a direct quantitative assessment of skeletal metabolism at specific sites.

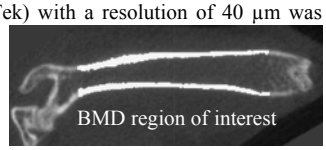
The aim of this study was to analyze the changes in the BMD, in adult wild type mice that have been previously injected with PMMA particles into the femoral intramedullary canal. Bone turnover has been measured by ^{18}F-fluoride PETscan.

METHODS

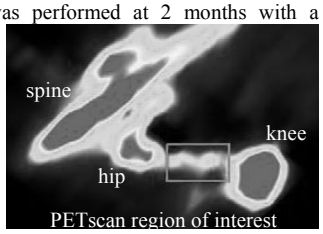
Four groups of adult (6 months old) male C57BL/6 wild type mice were studied. The experimental group (5 animals) was injected with PMMA into the femoral intramedullary canal. One negative control group (4 animals) was not injected. A second negative control group (5 animals) was injected with phosphate-buffered saline (PBS) which was the carrier solution for the PMMA preparation injected in the experimental group. A positive control group (5 animals) was injected with PMMA particles contaminated with endotoxin.

Under anesthesia, and through a transpatellar tendon approach, a 29-gauge needle on a 0.3 cc syringe previously filled with the substance to be injected was inserted 5 mm into the right femoral intramedullary canal. The injection volume was of 10 µl. 8.8×10^6 PMMA particles were delivered per femur. For the positive control group, lipopolysaccharide (LPS) was added back to the endotoxin-free PMMA particles prior to injection. The level of adherent endotoxin on the particles was 5.68 Units/ml in the PMMA+LPS preparation.

MicroQCT (MicroCAT II, ImTek) with a resolution of 40 µm was used preoperatively and at day 1, 8, 15, 25 and 32. BMD was assessed using the Microview software (GE Healthcare) within a specific region of interest (ROI) which was represented by ten mm of the cortical bone of the right femoral shaft.



The bone turnover analysis was performed at 2 months with a microPETscanner (R4, Concorde Microsystems). Using the Amide software, the ROI was defined as a cylinder of 6 mm long and 4 mm diameter involving the right femoral shaft. The hip and the knee were excluded from the analysis to avoid artifacts from growth plate activity.

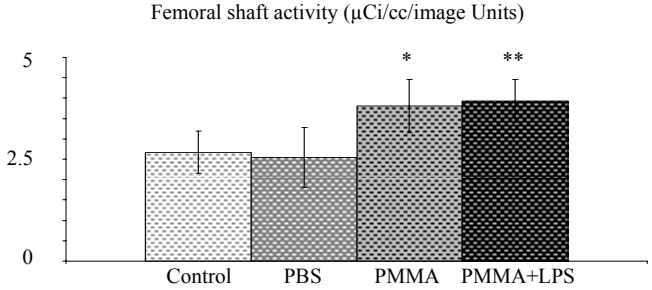


Results were expressed as mean ± standard deviation and statistical differences between groups were calculated using non parametric tests of Kruskal-Wallis and of Mann-Whitney with 0.05 as the critical p-value.

RESULTS

Crude values of BMD ranged from a maximum of 725 mg/cc (± 82) at day 15 to a minimum of 588 mg/cc (± 83) at day 25 for the control group, from 766 mg/cc (± 113) preoperatively to 597 mg/cc (± 101) at day 25 for the PBS group, from 688 mg/cc (± 122) at day 1 to 537 mg/cc (± 88) at day 25 for the PMMA group, and from 729 mg/cc (± 58) preoperatively to 507 mg/cc (± 129) at day 32 for the PMMA+LPS group. No statistical difference was found between groups and over time.

At 2 months, uptake of ^{18}F-fluoride by the femoral shaft was higher in the PMMA group than in the control group ($p = 0.05$) or the PBS group ($p = 0.0472$). Furthermore, uptake was higher in the PMMA+LPS group than in the control group ($p = 0.0143$) or the PBS group ($p = 0.009$). There was no difference between the control group and the PBS group ($p = 0.6242$) or between the PMMA group and the PMMA+LPS group ($p = 0.9168$).



DISCUSSION

The present study was designed to demonstrate a link between PMMA particles and osteolysis using an *in vivo* murine model and advanced imaging techniques. Using a 40µm resolution microCTscanner, we did not observe osteolysis in presence of PMMA particles, even when they were contaminated with endotoxin. The scanner resolution may be a limitation of this study. However, the cement used for orthopedic implant fixation in humans includes other additives including opacifiers. These substances may have their own biological influence on osteolysis.

^{18}F-fluoride PETscan allows measurement of the osteoblastic activity which is related to bone remodeling. PMMA particles increased the osteoblastic activity after injection in the intramedullary canal. This effect is coupled to bone resorption and activation of osteoclastogenesis by PMMA particles, as demonstrated by Revell's group.

Although a direct link between PMMA particles and osteolysis was not found using BMD, the increase in bone turnover using ^{18}F-fluoride PET scan, indicates that the PMMA particles affects bone metabolism. This study using computed tomography and functional PET scan imaging for *in vivo* animal biomaterials research represents a novel approach for future studies on biocompatibility, osteointegration and osteolysis.

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