Introduction

Positron emission tomography (PET) using F-18 fluorodeoxyglucose (FDG) is a promising new imaging modality for bone infections. Recent clinical studies have suggested that FDG-PET is highly sensitive in imaging of chronic osteomyelitis (1). PET is an inherently quantitative imaging method, which therefore permits potentially also treatment monitoring. The method is based on intensive use of glucose by mononuclear cells and granulocytes during infection. $^3$F-FDG uptake and metabolism is elevated only in activated inflammatory cells. Under normal physiological conditions, white cells are inactive and bone marrow is barely visible in PET-FDG. Normal bone healing, however, involves an inflammatory phase and the whole process of new bone formation and remodeling represents a highly activated state of cell metabolism and glucose consumption. Therefore, the process of normal bone repair may be difficult distinguished from bone infections. The current study was designed to compare the PET-FDG characteristics of normal bone healing and bone infection.

Material and methods

The ethical committee of the University of Turku and the Provincial State Office of Western Finland approved the animal protocol. The experimental localized osteomyelitis model was adopted and modified from that of Mader’s rabbit model (2) and Fitzgerald’s canine model (3). Surgery was performed on adult male New Zealand white rabbits (n=12) (Harlan, Netherlands) (weight range 2470g-5600g). Under standard sterile surgical conditions, a cortical bone window of 6 mm x 2.3 mm size was drilled in the medial cortex of the proximal tibial metaphysis. Bone marrow was removed with saline lavage. The defect was filled with bone cement, which acted as foreign body. Solution containing Staphylococcus aureus (strain 5252A/80, kindly provided by Dr. Jon T Mader) $1 \times 10^9$ /ml was prepared. Deep soft tissue layers were closed over the defect and 0.1 ml of the bacterial suspension was injected into the defect next to bone cement. Finally skin wound was closed in layers. The procedure was performed unilaterally in the right tibia, while the contralateral right tibia served as the control. After surgery, the animals were closely monitored. Functional activity of the animals was not limited. Foreign body related infection was allowed to develop for two weeks, when the bone cement was surgically removed. Osteomyelitis was confirmed with positive bacterial cultures during the 2nd surgery and again 6 weeks later at the time of sacrifice.

The pre-surgery PET-imaging was carried out in four animals to standardize FDG-PET-imaging techniques and to confirm that there were no differences between the two tibiae before surgery. The comparative study involved eight control animals and four experimental animals. The two ROIs tended to serve as a better indicator of osteomyelitis than the single ROI divided by the relative injected dose expressed per animal body weight. The ratios of SUV-values between the operated and non-operated sides were measured. SUV-ratio greater than 2 (between osteomyelitic region vs. control area) is generally considered to be diagnostic for clinical osteomyelitis. The statistical significance of the differences was calculated using paired t-test and one-way ANOVA with Tukey t-test.

Results

There were no significant differences between the two sides (ROI in right and left tibia) in FDG-PET-imaging at the preoperative stage. Compared with the intact bone value, the healing controls defects (n=8) showed a significantly increased uptake of FDG (p=0.019) at 3 weeks (Fig. 1). The FDG-PET tended to normalize within 6 weeks, when the uptake of the healing defects did not differ significantly from the intact bone value (Fig. 1). SUV-values of the healing defects varied between 0.51-1.21 (average 0.75) at 3 weeks and between 0.30-0.96 (average 0.46) at 6 weeks. Mean SUV-ratio was 2.35 at 3 weeks and 1.32 at 6 weeks.

In untreated osteomyelitis (n=4), the FDG activity of the infected region was significantly (p<0.001) increased both at 3 and 6 weeks compared with intact bone value (Fig. 1). The uptake of the osteomyelitis region was also significantly higher than that of non-infected control defects both at 3 weeks (p=0.006) and at 6 weeks (p<0.001). The osteomyelitis regions did not show a marked decrease of activity over time, dissimilar to healing defects (Fig. 2). The actual SUV values of the osteomyelitis region varied between 0.83-2.74 (average 1.83) at 3 weeks and between 0.76-2.20 (average 1.21) at 6 weeks. These SUV values were statistically significant both at 3 weeks (p=0.004) and at 6 weeks (p=0.020). In osteomyelitic animals, SUV ratios varied between 2.7-5.2 (average 3.7) at 3 weeks and between 3.2-5.5 (average 4.3) at 6 weeks.

Discussion

The current study showed that uncomplicated healing of a bone defect is associated with a significant increase of FDG-PET activation. However, this activity is only transient and tends to normalize over time within 6 weeks. Standardized osteomyelitis of the current model was shown to result in an intense FDG-PET activation, which is higher than that of a healing defect and tends to remain high. In general, the difference between the two sides (paired comparison of SUV-values of two ROIs) tended to serve as a better indicator of osteomyelitis than the actual SUV-values. Although the actual SUV-values were confirmed to be significantly increased in osteomyelitis, the SUV-ratios showed less variation.


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