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# Fluorine-18-FDG PET in Paget's Disease of Bone

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Paget's disease of bone is common in the elderly and is associated with increased osteoblastic and osteoclastic activity at affected sites in the skeleton. It is not known whether this high metabolic activity is associated with increased glycolysis and, hence, uptake of [$^{18}$F]FDG. The appearances of Paget's disease with [$^{18}$F]FDG PET have not been described and it is not known whether Paget's may cause false-positive studies in those undergoing oncological staging or whether [$^{18}$F]FDG PET can reliably differentiate benign pagetic change from osteosarcoma that may complicate Paget's disease. We reviewed [$^{18}$F]FDG PET scans in patients with uncomplicated Paget's disease and documented its appearances. **Methods:** Eighteen patients with established Paget's disease and typical radiological features had $^{99m}$Tc-MDP bone scans and [$^{18}$F]FDG PET scans performed. Serum alkaline phosphatase (ALP) was also measured. **Results:** All patients showed high uptake of MDP in affected bones. Of the 18 patients only six showed any uptake of [$^{18}$F]FDG. This occurred in some but not all bones shown to be involved on MDP bone scans. Three patients demonstrated low-grade uptake and three showed marked accumulation of [$^{18}$F]FDG. The [$^{18}$F]FDG-positive group had higher serum ALP levels than the [$^{18}$F]FDG-negative patients ($p < 0.05$). **Conclusion:** Paget's disease of bone is not associated with abnormal [$^{18}$F]FDG uptake in the majority of patients and, therefore, there is potential for discriminating between benign Paget's disease and associated Paget's sarcoma. However, low-grade uptake may be seen in patients with more active disease as measured by ALP. Rarely, marked uptake of [$^{18}$F]FDG may be seen and Paget's disease should be included as a possible cause of false-positive scans in elderly patients who are being assessed for metastatic disease.

**Key Words:** Paget's disease; fluorine-18-FDG; PET; technetium-99m-MDP bone scintigraphy

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Paget's disease of bone, first described by Sir James Paget in 1877 (*1*), is a disease of uncertain etiology. It is characterized by an imbalance of osteoclastic and osteoblastic activity with a rise in serum alkaline phosphatase (ALP) and abnormal remodelling of bone leading to typical radiograph appearances. Paget's disease may be present in up to 5% of the population, but there are wide regional variations and the majority of cases are asymptomatic (*2*).

Paget's causes increased osteoblastic activity in bone as demonstrated by bone scintigraphy, but it is not known whether glycolysis is similarly enhanced as appearances on [$^{18}$F]FDG PET scans have not been recorded. If the osteoblastic and osteoclastic activity of this disease is associated with increased glycolysis and as there is a relatively high incidence in some areas, it could potentially cause false-positive [$^{18}$F]FDG PET studies in those with incidental Paget's disease undergoing oncological staging.

Complications of Paget's due to abnormal remodeling may result in pressure effects on neighboring tissues or pathological fracture, but the most serious complication of sarcomatous change is relatively rare, occurring in less than 1% of affected patients (*3*). However, it is notoriously difficult to differentiate benign pagetic change from complicating osteosarcoma with current imaging techniques. Fluorine-18-FDG PET can differentiate benign from malignant tissue in many tumors, in that increased glycolysis of malignant tissue being reflected in enhanced accumulation of this tracer. Fluorine-18-FDG PET could be a useful tool in distinguishing the benign changes of Paget's disease from associated osteosarcomas.

In a preliminary investigation, we studied 18 patients with uncomplicated Paget's disease of bone using [$^{18}$F]FDG PET to see if false-positive oncological PET scans resulted and examined the potential of [$^{18}$F]FDG PET to differentiate benign changes from Paget's sarcoma.

## MATERIALS AND METHODS

Eighteen patients (11 men, 7 women; mean age 71 yr) with established Paget's disease and typical radiological features had $^{99m}$Tc-MDP whole-body bone and [$^{18}$F]FDG scans performed. Thirteen patients previously had received treatment with disodium pamidronate at a mean of 19 mo (range 1–48 mo) before scanning. Seventeen patients had no history of cancer. One patient had carcinoma of the prostate diagnosed 4 yr after diagnosis of Paget's disease. Bone scan findings had not changed over a 9-yr period,

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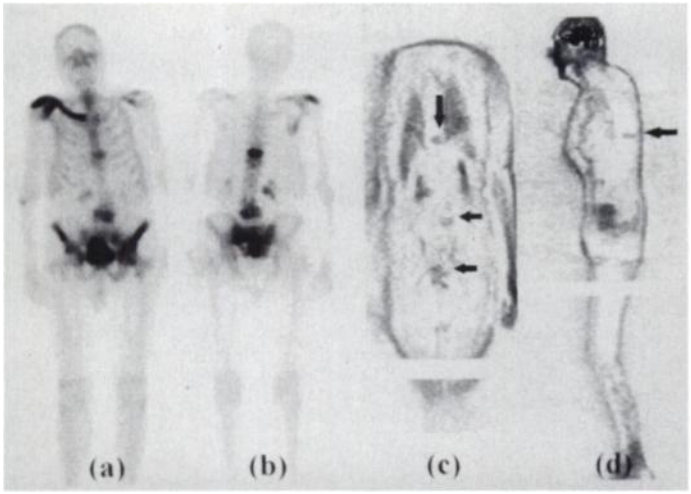


**FIGURE 1.** (A) Anterior and (B) posterior $^{99m}$Tc-MDP bone scans show increased uptake in several bones affected by Paget's disease in a patient previously treated with disodium pamidronate. (C) Coronal and (D) sagittal [$^{18}$F]FDG PET slices showing only mildly increased uptake of tracer in lower thoracic and lumbar vertebrae and sacrum (arrows). Other bones shown to be affected on $^{99m}$Tc-MDP bone scan showed no abnormality with [$^{18}$F]FDG PET.

and there was no clinical or radiological evidence of metastatic bone disease.

Bone scans were obtained with a high-resolution collimator 3–4 hr following the injection of 550 MBq $^{99m}$Tc-MDP. Whole-body PET scans were obtained on a Siemens/CTI ECAT 951R PET scanner, 60 min after the injection of 370 MBq [$^{18}$F]FDG. Patients fasted 6 hr. Transmission studies were not performed. Emission studies were acquired for 5 min per bed position (9.8 cm) until the whole-body had been included. Technetium-99m-MDP scans and [$^{18}$F]FDG PET scans were interpreted separately. All patients had serum ALP levels measured at the time of bone and PET scans.

## RESULTS

All patients showed increased uptake of $^{99m}$Tc-MDP in affected bones. In the study group, 66 bones were abnormal on the bone scans compared to 16 on [$^{18}$F]FDG PET images. Only six of the 18 patients showed abnormal bone uptake of [$^{18}$F]FDG. Five of these six patients showed fewer bones to be affected with [$^{18}$F]FDG PET than with $^{99m}$Tc-MDP; one patient showed uptake of [$^{18}$F]FDG and $^{99m}$Tc-MDP into monostotic disease. Three patients showed low-grade uptake (less than liver) (Fig. 1), and three patients showed accumulation of [$^{18}$F]FDG that was marked (Fig. 2) and appeared to have a cortical distribution (Fig. 3).

Serum ALP levels (normal $<$ 126 U/liter) ranged from 55–982 U/liter (mean 275 U/liter). The six [$^{18}$F]FDG-positive patients had serum ALP levels greater than 280 U/liter (mean 520 U/liter). Only one of the remaining 12 [$^{18}$F]FDG-negative patients had a serum ALP level above this (545 U/liter; mean for group, 153 U/liter). A statistically significant difference was found in ALP levels between these two groups ($p < 0.05$, Mann Whitney U test) (Fig. 4). Five of six [$^{18}$F]FDG-positive and eight of 12 [$^{18}$F]FDG-negative patients had had previous disodium pamidronate therapy at means of 15 mo and 20 mo, respectively, before scanning.

## DISCUSSION

Although Paget's disease shows evidence of increased osteoblastic and osteoclastic activity, it had not been previously determined whether these are coupled with increased use of glucose and enhanced glycolysis. This preliminary study shows

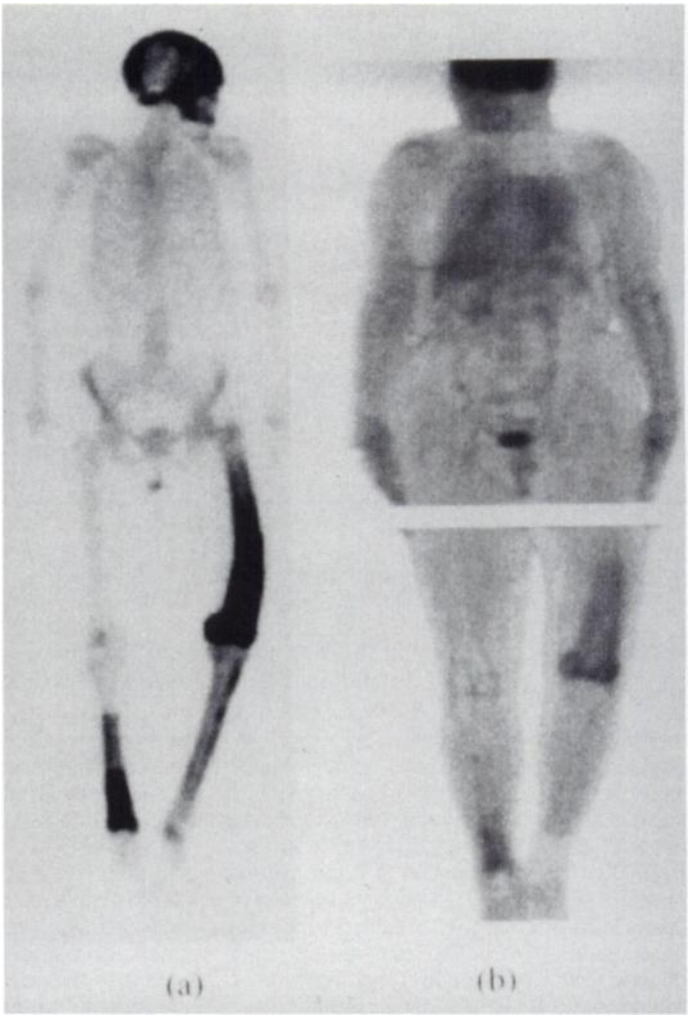


**FIGURE 2.** (A) Technetium-99m-MDP bone scan showing high activity in pagetic tibiae, left femur and skull. (B) Fluorine-18-FDG PET projection image shows corresponding uptake in the right tibia and left femur but not in the less active left tibia.

that the majority of patients with Paget's disease show no abnormal accumulation of [$^{18}$F]FDG in bones shown to be affected on MDP bone scintigraphy. Some patients with more active disease, as measured by serum ALP levels, may show increased but low-level uptake, which is lower than that which might be expected with malignant disease. A few patients may show marked uptake of [$^{18}$F]FDG at a level that could be

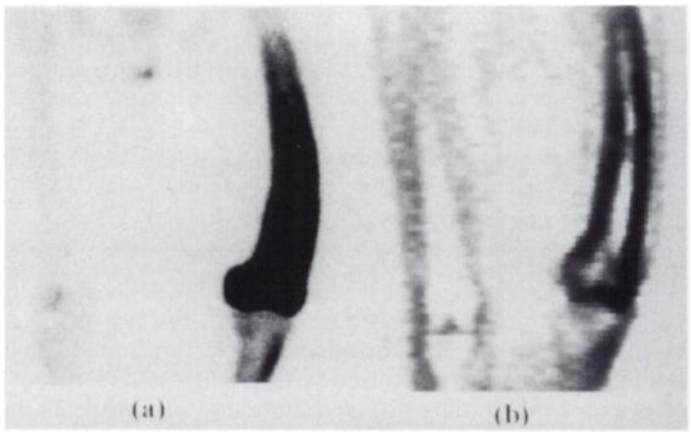


**FIGURE 3.** (A) Technetium-99m-MDP bone scan of the same patient as in Figure 2. (B) Coronal [$^{18}$F]FDG PET of femora showing the cortical distribution of tracer

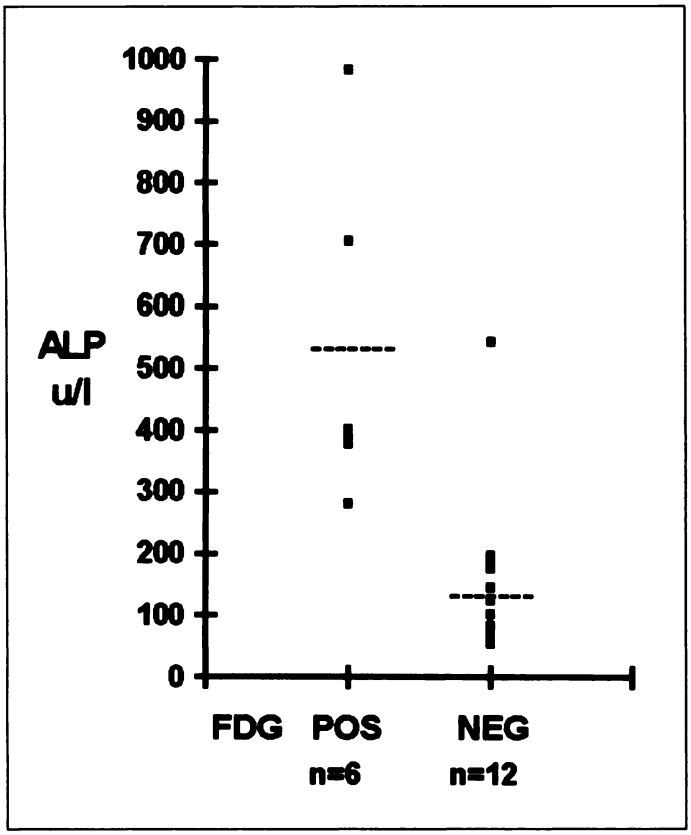


**FIGURE 4.** Graph displaying distribution of ALP in [$^{18}$F]FDG-positive and negative patients. There is a significant difference in ALP levels between the two groups ($p < 0.05$) (hatched lines = mean ALP value).

mistaken for malignant tissue. In some patients, [$^{18}$F]FDG uptake may have a cortical distribution, however, allowing differentiation from metastases, which are usually medullary. We observed variable levels of uptake in Paget's disease and [$^{18}$F]FDG PET may have varied appearances in metastatic disease of bone depending on the disease type (*4,5*), creating an overlap of features. Therefore, semiquantitative indices such as standardized uptake values may not be helpful in differentiating pagetic bone from metastatic bone lesions.

There has been no substantial work on osteosarcomas and no reports of Paget's sarcoma with [$^{18}$F]FDG PET, but a high glycolytic rate and uptake of [$^{18}$F]FDG would be expected as in the majority of soft-tissue sarcomas (*6*). Therefore, there is potential for discriminating between benign Paget's disease and associated sarcoma. A positive scan would require further investigation but a negative study would be reassuring that no malignancy was present.

It is interesting to note that, even when positive, uptake of [$^{18}$F]FDG often is not consistent throughout affected bones in individual patients. Five of six [$^{18}$F]FDG-positive patients show fewer [$^{18}$F]FDG-avid bones than were positive on MDP scintigraphy. This is in accordance with data from Ryan et al. (*7*) who described different responses to bisphosphonate therapy between different sites in affected individuals as measured by MDP scintigraphy. Five of six of our [$^{18}$F]FDG-positive patients had received previous disodium pamidronate therapy. Of the six [$^{18}$F]FDG-positive patients, five showed no discernible difference in MDP uptake into affected bones to mirror the heterogeneity seen with [$^{18}$F]FDG within individual patients. One patient, who had been treated previously with disodium pamidronate, showed relatively lower uptake of MDP into areas that appeared less active on [$^{18}$F]FDG scans. There does not appear to be a consistent relationship between [$^{18}$F]FDG and MDP uptake in pagetic bone. In addition, no difference was observed in radiological appearances in bones with high [$^{18}$F]FDG activity compared to those without. One other factor that may lead to a discrepancy between bone scintigraphy and [$^{18}$F]FDG PET is due to high accumulation of [$^{18}$F]FDG in the brain. This is likely to make accumulation of [$^{18}$F]FDG into active Paget's disease of the skull invisible.

There does not appear to be a consistent relationship between presence or absence of [$^{18}$F]FDG uptake and history or time since disodium pamidronate therapy. Although we have no serial studies, it is likely, however, that the effect of successful bisphosphonate treatment is to reduce [$^{18}$F]FDG accumulation in parallel to the effect seen on ALP levels.

## CONCLUSION

Paget's disease of bone is not associated with abnormal [$^{18}$F]FDG uptake in the majority of patients and there is potential for discriminating between benign Paget's disease and associated sarcomas. However, uptake may be seen in patients with more active disease as measured by ALP. On occasion, marked uptake of [$^{18}$F]FDG can occur and incidental Paget's disease rarely could cause false-positive scans in elderly patients who are being assessed for metastatic disease with [$^{18}$F]FDG PET.

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