jnm / CASE REPORT

# ENHANCED DETECTION OF A SKELETAL LESION WITH DELAYED $^{99m}$Tc-POLYPHOSPHATE BONE SCANNING

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***In a patient with histologically proven neoplastic involvement of the skeleton, a $^{99m}$Tc-polyphosphate bone scan performed 5 hr after intravenous administration showed only a subtle increase in activity. At 10 hr the concentration of activity relative to background was greatly enhanced. On a subsequent $^{18}$F bone scan, there was a slight increase in activity similar to the initial (5-hr) $^{99m}$Tc-polyphosphate scan. Delayed blood clearance and/or altered uptake of the radiopharmaceutical may have played a role in the enhanced delayed images.***

Radiopharmaceutical investigation based on early observations of phosphate incorporation in bone (*1,2*) has led to the development of $^{99m}$Tc-polyphosphate, a new agent for skeletal imaging (*3,4*). Formulation of a lyophylized kit method of preparation (*5*) has made this agent available for widespread clinical use.

Blood clearance studies of $^{99m}$Tc-polyphosphate in humans and animals suggest that imaging be performed at 4–6 hr after injection (*4,6*). The following case presents a patient with histologically proven neoplastic involvement of the skeleton in which delayed imaging significantly enhanced detection of a lesion.

## CASE REPORT

This 68-year-old white woman presented with hepatomegaly and low back pain. Radiographs of the lumbosacral spine in 1966 and 1971 had shown degenerative changes only. For the month before hospitalization her pain had become more severe and had radiated to the right buttock.

Her admission chest x-ray revealed right hilar and paratracheal masses; subsequent liver biopsy showed poorly differentiated carcinoma. In a further effort to determine the extent of her disease and delineate a course of palliative therapy, skeletal radiographs and a bone scan were obtained. The x-ray survey was normal.

The posterior image of the initial rectilinear scan at 5 hr after administration of $^{99m}$Tc-polyphosphate (15.0 mCi i.v.) was minimally suspicious at the left lateral rib margin (Fig. 1). A scintillation camera image at 5 hr again showed only a subtle focus of isotope concentration in this area (Fig. 2, top). It was elected to have the patient return for a third image at 10 hr to further delineate this region (Fig. 2, bottom); the abnormal focus of increased activity was easily visualized and considerably enhanced compared with the early images.

The entire examination was repeated 2 days later using 12.0 mCi of $^{99m}$Tc-polyphosphate; 5- and

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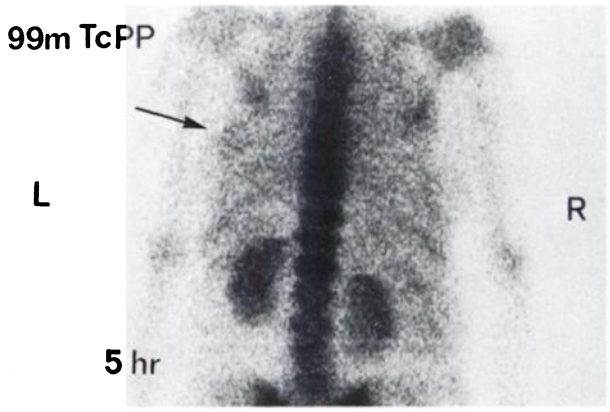


**FIG. 1.** Posterior rectilinear bone scan obtained 5 hr after intravenous administration of 15.0 mCi of $^{99m}$Tc-polyphosphate. Arrow indicates region of subtle accumulation of radioactivity at left lateral rib margin.

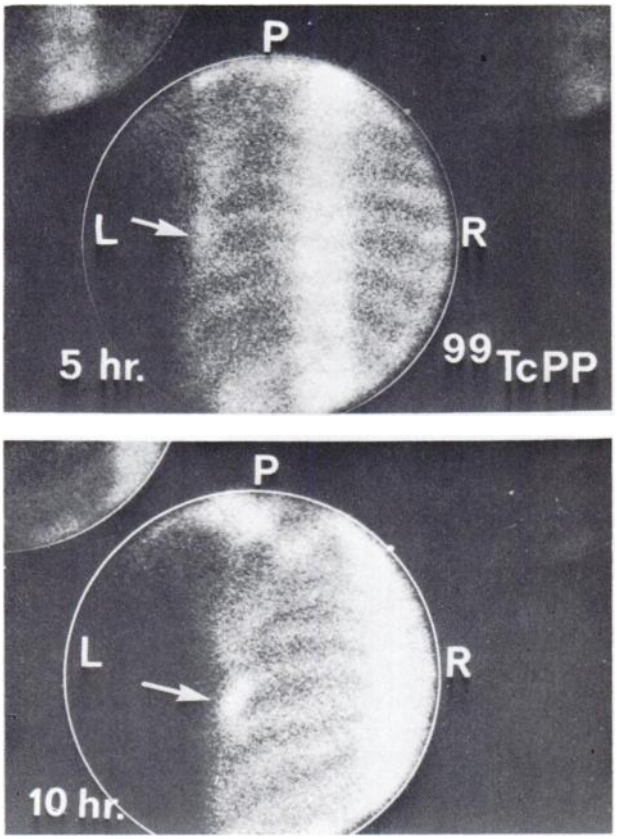


**FIG. 2.** Posterior gamma camera images obtained 5 hr (top) and 10 hr (bottom) after intravenous administration of 15.0 mCi of $^{99m}$Tc-polyphosphate. Arrows indicate regions of interest in left lateral rib margin. Marked increase in activity is seen on delayed study.

10-hr scintillation camera images produced results comparable to the previous examination. One week later, a $^{18}$F scan performed 2 hr after the i.v. administration of 4 mCi of Na$^{18}$F (Fig. 3) showed only the most subtle collection of activity in the area of the abnormal rib, similar to the results obtained on the initial 5-hr rectilinear image using $^{99m}$Tc-polyphosphate. Radiographs and soft-tissue examination of this region were normal.

The patient evidenced a rapid decline, dying 8 weeks after her initial presentation. An autopsy determined the primary cause of death to be pneumonia secondary to the obstruction of a bronchus by a bronchogenic carcinoma (oat cell type). Attention was directed to the left lateral hemithorax where an obvious region of expanded rib was seen. In its greatest diameter it was at least twice that of the adjacent rib. Histologic sections of both expanded and normal appearing rib showed massive replacement of marrow elements by tumor cells with a prominent fibrous reaction. In addition there was diffuse involvement of the vertebral marrow, an area normal both by radiograph and scan.

## DISCUSSION

Blood clearance studies in humans indicate that within 30–60 min, between 45 and 50% of the $^{99m}$Tc-polyphosphate is associated with bone; the remaining circulating isotope is cleared gradually by the kidneys (*7*). Background activity decreases to levels adequate for skeletal imaging within 4–6 hr.

In this case, the 5-hr rectilinear image showed only the most subtle suggestion of asymmetric isotope concentration, and, given this finding alone, the examination might have been considered within normal limits. The patient was re-examined on two separate occasions at 5 and 10 hr using the identical instrument and identical techniques. The discrepancy in the images at these two time intervals was striking, with marked enhancement of the lesion on the delayed examination.

A number of possibilities exist which could explain the findings in this case. Gradual and continuous uptake of $^{99m}$Tc-polyphosphate in this bone lesion, a pattern opposite from that of the usual rapid accumulation of this agent, may have occurred, suggesting an idiosyncratic response based upon an altered metabolic state of the patient.

The administration of Cytoxan (1.4 gm i.v.) and Methyl CCNU (300 mg p.o.) given as palliative therapy 4 days before her first bone scan may have altered the usual mechanisms of isotope concentration within the lesion. This effect has not been previously reported, and the problem of scintigraphic imaging in patients receiving antimetabolites has not to our knowledge been fully investigated.

The patient's renal function appeared altered with her serum creatinine 1.4 mg% (normal, 0.7–1.2 mg%) at the time of initial imaging. As well, her degree of hydration was suboptimal with a moderately decreased fluid input. The ultimate scintigraphic

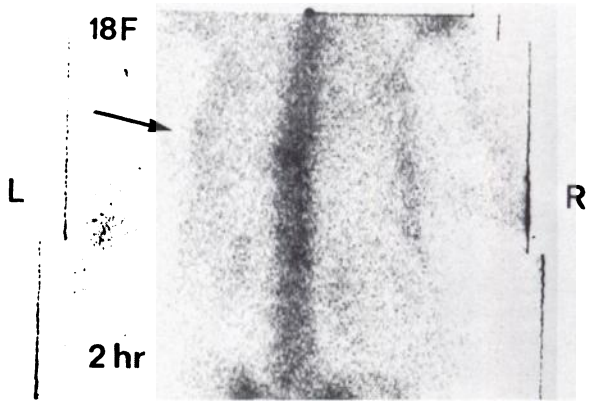


**FIG. 3.** Posterior rectilinear bone scan obtained 2 hr after intravenous administration of 4.0 mCi of $^{18}$F. Arrow denotes area of interest which is comparable in intensity to that indicated in Fig. 1.

intensity of the lesion was such that the additional background activity eliminated by delayed renal clearance could account for the increased ease of identification of the neoplastic focus at 10 hr. This factor is probably the most significant contributor to the improved clarity of the images with time (*4*).

In this case, $^{18}$F compared unfavorably with $^{99m}$Tc-polyphosphate. The 2-hr $^{18}$F and the initial 5-hr $^{99m}$Tc-polyphosphate scans were similar; however, the shorter half-life of the $^{18}$F bone agent precluded a clinically practical delayed study, and consequently yielded information essentially identical to that obtained on the 5-hr $^{99m}$Tc-polyphosphate study.

The optimal time for performing the $^{99m}$Tc-polyphosphate bone scan has not yet been fully explored. For the most part, data have been generated from animal models and humans with skeletal neoplasms of a limited number of cell types. (*4,8*). The potential role of delayed bone imaging needs to be evaluated not only by blood clearance studies but by serial total-body images as well. It is possible that delayed skeletal imaging may enhance the sensitivity of the bone scan, particularly in those patients with impaired renal function.

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