be carefully discussed with the patient and clinician. Close monitoring of the patient is essential, as well as having protamine sulfate (heparin antagonist) and blood available if needed.

The decision to use protamine sulfate is based on the presence of moderate to severe uncontrollable bleeding in a patient receiving heparin. The coagulation studies should be correlated with the clinical condition of the patient and protamine sulfate should not be administered solely on the basis of abnormal laboratory values. Because our patient showed no signs of hemorrhage while receiving the heparin infusion, the administration of protamine sulfate was not necessary. We do not recommend the routine use of protamine sulfate due to its side effects which include bradycardia and hypotension and the fact that heparin is cleared rapidly from the circulation.

If necessary, protamine sulfate should be administered by slow i.v. injection in doses not to exceed 50 mg in any 10 min period. The dose of protamine sulfate is calculated by determining the total dose of heparin administered during the previous 3 to 4 hr with each mg of protamine sulfate neutralizing 90–100 USP units of heparin.

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Uptake of Technetium-99m Diphosphonate by Metastatic Large Cell Carcinoma of the Lung

TO THE EDITOR: Although uptake of technetium-99m (^{99m}Tc) phosphate bone-scanning agents by noncalcified hepatic metastases of a number of primary malignancies has previously been described (*1–3*), we believe this to be the first reported case associated with large cell carcinoma of the lung.

A 50-yr-old female presented with a 2-mo history of cough and weight loss. Significant findings on physical examination included decreased breath sounds in the right upper chest and a slightly tender 14 cm liver. Chest roentgenogram revealed a right upper lobe mass with lobar atelectasis. Bronchoscopy and biopsy yielded a diagnosis of undifferentiated large cell carcinoma.

Neurologic signs prompted computed tomography of the brain which demonstrated a solitary posterior fossa mass. This was resected and shown to be metastatic large cell carcinoma.

At this time the patient underwent radiotherapy of the right upper lobe mass. Seven months after diagnosis the patient developed a submental soft tissue mass. Biopsy showed metastatic disease. Liver function studies revealed elevation of all liver enzymes, with normal serum bilirubin, calcium and phosphate.

Technetium-99m methylene diphosphonate ([^{99m}Tc]MDP) bone scan was performed (Fig. 1A,B). This revealed a large ovoid mass with a rim of radiotracer uptake and a prominent photopenic center. The mass occupied most of the right lobe of the liver, with inferior displacement of the right kidney. Asymmetric uptake of phosphonate was noted between the medial aspect of the ischia, but was not felt to represent metastatic disease. Uptake in the remainder of the skeleton was unremarkable. The bone scan was compared with other scans performed from the same aliquot. All showed normal biodistribution of activity.

Subsequent computed tomography of the abdomen (Fig. 1C) confirmed a 15-cm diameter lesion in the right lobe of the liver, with an inhomogeneous low attenuation center surrounded by an enhancing rim. An inhomogeneous mass was also seen in the right adrenal gland, representing metastatic disease.

The patient is currently receiving palliative care.

Localization of ^{99m}Tc-phosphate compounds within hepatic metastases from colonic adenocarcinoma (*2,3*), oat cell carcinoma of the lung, breast carcinoma, malignant melanoma, and squamous cell carcinoma of the esophagus has previously been described (*2*). In addition, focal uptake by cholangiocarcinoma (*3*) has been described.

This case of uptake within metastatic large cell carcinoma of lung has several interesting features. Uptake of radiotracer appeared to be isolated to the radiographically enhancing rim. Lyons et al. (*4*) described a case of [^{99m}Tc]pyrophosphate localization in a liver due to massive necrosis. In this case the exclusion of radiopharmaceutical from the central necrotic portion is most likely due to nonperfusion. Localization within the ischemic transition zone between viable tumor and frankly necrotic tissue is postulated.

No uptake of radiotracer could be demonstrated in the right adrenal or submental metastases, suggesting that tracer localization may be more dependent on ischemia than on tumor histology. The precise point of accumulation of phosphonate may be within mitochondrial calcium accumulations, which occur following cell membrane disruption (*5*). Phosphate binding in areas of high phophatase enzyme concentration (*6*) and ion exchange between intracellular calcium phosphate and phosphate bone-scanning agents (*7*) have been postulated as possible mechanisms of uptake.

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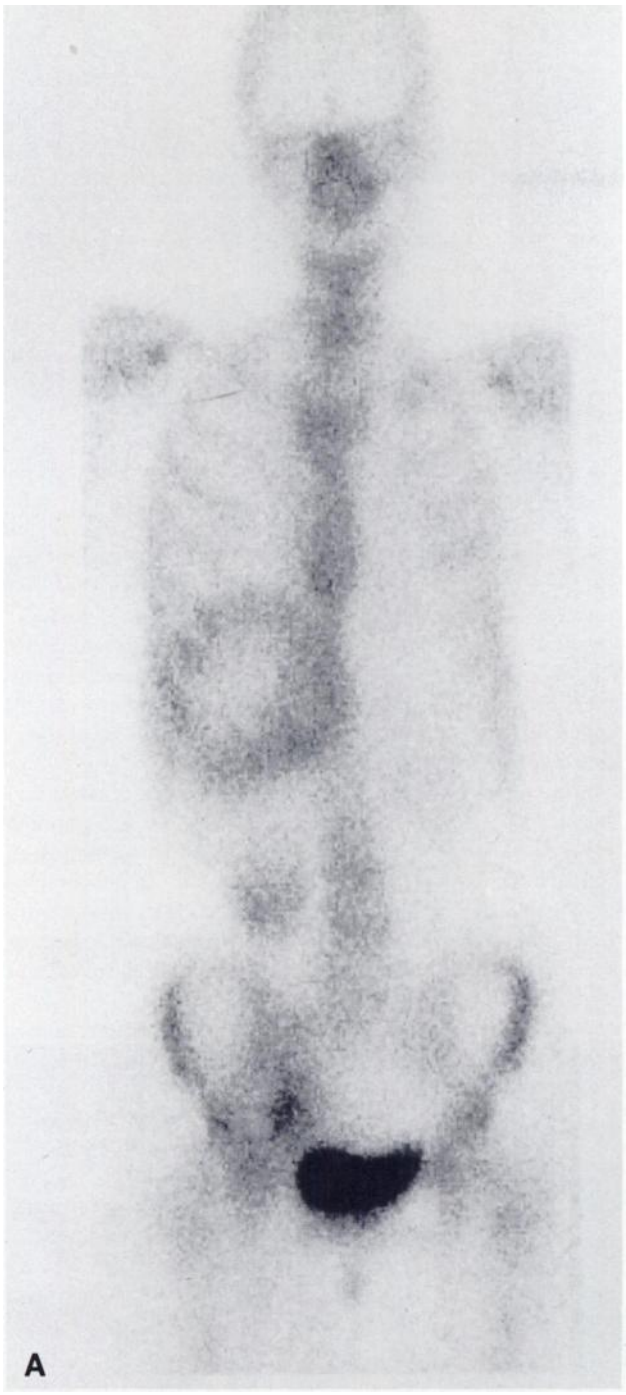

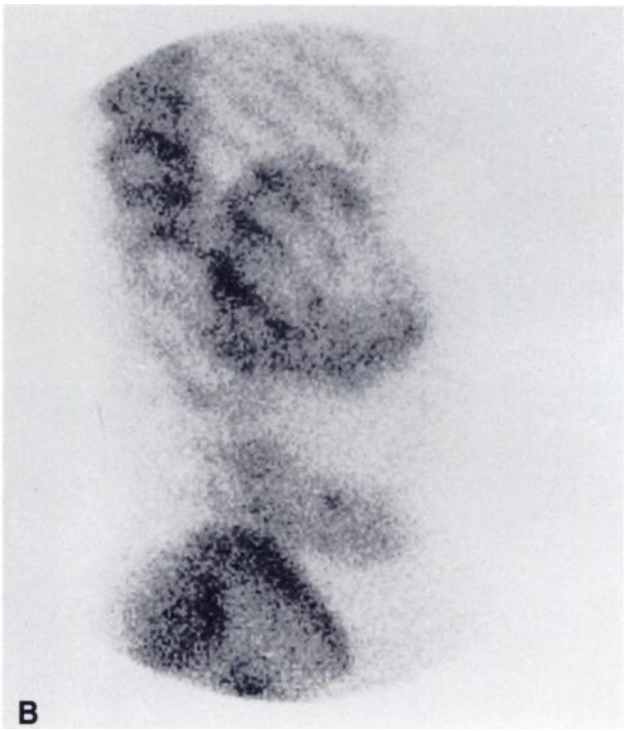

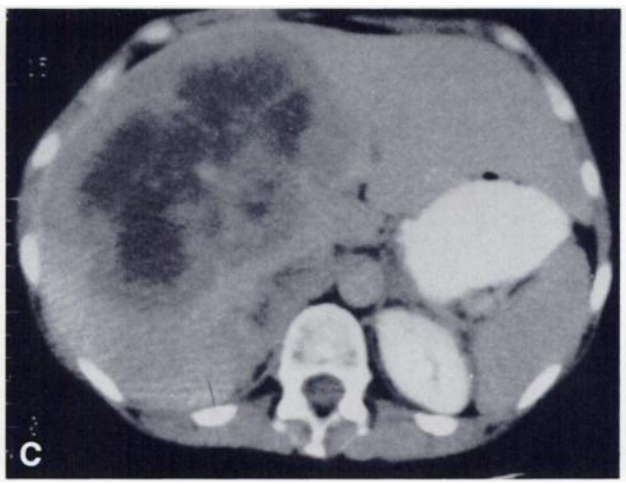

FIGURE 1
Initial anterior (A), and lateral (B) bone scan demonstrating uptake of [^{99m}Tc]MDP by hepatic metastasis. Subsequent CT scan (C) confirms large noncalcified hepatic metastasis with prominent necrotic center, and right adrenal metastasis.

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Streptavidin and Biotin as Potential Tumor Imaging Agents

TO THE EDITOR: We have read with interest the recent article by Hnatowich et al. (*1*) who have reported imaging of conjugated beads with indium-111-labeled streptavidin and biotin. We also have recent experience using these two agents and the purpose of our experimental study was to use the strong affinity of streptavidin to biotin ($K_d = 10^{-15}M$) to improve tumor imaging.

TABLE 1
Tumor/Organ Ratios in Nude Rats with Solid HeLa Cell Tumors 48 hr After Injection of [^{125}I]Streptavidin

Group*	1	2	3
Tumor/blood	2:2	1:0	1:9
Tumor/kidney	0:1	0:2	0:1
Tumor/liver	0:7	0:3	0:6
Tumor/lung	2:6	1:8	1:8
Tumor/heart	4:1	2:8	2:9
Tumor/intestine	4:4	3:1	3:1
Tumor/muscle	9:1	5:4	5:6

* Two rats per group.
Group 1: Anticytokeratin-biotin, [^{125}I]streptavidin.
Group 2: Nonspecific IgG-biotin, [^{125}I]streptavidin.
Group 3: [^{125}I]streptavidin.

Biotin was conjugated to anticytokeratin antibodies and injected i.v. into rats with solid HeLa cell tumors containing cytokeratin as a tumor-associated antigen. Three days later, ^{125}I-labeled streptavidin was injected i.v. The uptake of radioactivity was detected by scintigraphy as well as by radioactivity determination in tumor and various organ tissues by means of a well counter. Tumor/tissue ratios from the bled and

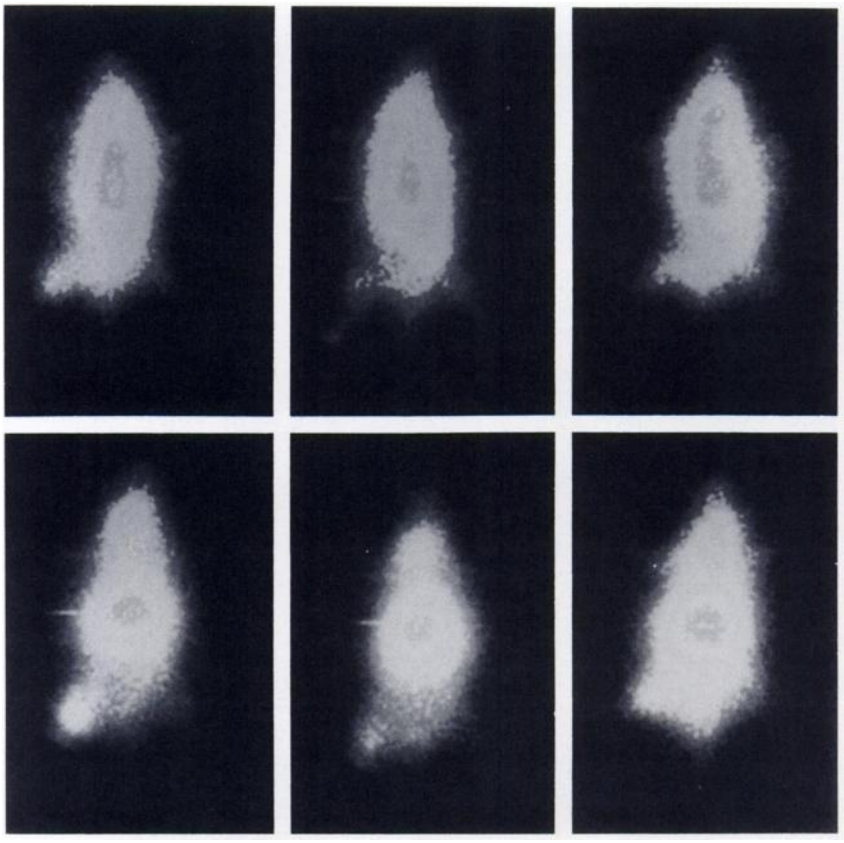

FIGURE 1
Whole-body images of nude rats bearing HeLa cell tumors on their left hind leg and injected i.v. with (125I) streptavidin. Images obtained 1 hr and 48 hr after injection of the radiolabeled streptavidin. A: Anti-cytokeratin-biotin, (125I) streptavidin—1 hr postadm. B: Nonspecific IgG-biotin, (125I) streptavidin—1 hr. C: (125I) streptavidin,—1 hr, D: see A—48 hr, E: see B—48 hr, F: see C—48 hr.