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Fluorine-18 Uptake and Localization in Soft Tissue Deposits of Osteogenic Sarcoma in Rat and Man[1]

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Fluorine-18 was demonstrated by photoscanning to concentrate in the region of metastases to bone by Blau and Bender (1) and in the region of primary bone tumors in our laboratory by Dworkin *et al* (2). We have been unable to find any reports of the diagnostic or experimental use of any bone-seeking radionuclide to detect and localize primary bone tumor metastatic to soft tissues. We report here autoradiographic, well counting and photoscan data showing concentration of Fluorine-18 in osteogenic sarcoma transplanted to the subcutaneous area of the rat and photoscan and point counting demonstration of diagnostic Fluorine-18 concentration in metastases of osteogenic sarcoma to the lungs of a 17-year-old boy.

METHODS

Rat Studies:

A 265 gm rat (Simonsen strain Sprague-Dawley) with a spontaneously occurring osteogenic sarcoma (3) transplanted subcutaneously to the right neck, left scapular area and left flank was injected intraperitoneally with 1 mC of Fluorine-18 (4) in 3.7 ml of normal saline one hour prior to study. The rat was then anesthetized with an intraperitoneal injection of 1.6 ml of 3.6% chloral hydrate. When anesthetized, the rat was spread out in the prone position under the detector head of a three inch crystal photoscanner[3], fitted with a 32-hole high energy collimator, and scanned at 0.5, 1, and 4.5 hours. Immediately following each scan, point counts were made centered over several sites on the spinal column, tumor site and femoral epiphyses for a rough *in vivo* quantitation of

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[3]Picker Magna Scanner

relative tissue Flourine-18 uptake. Immediately after the scan, which was performed one hour after injection, the left flank transplant tumor was excised and measured 2.5 × 2 cm in diameter. One portion was processed for routine histopathologic examination and a second 0.12 gm portion was assayed for radioactivity concentration in a scintillation well counter. A third portion was processed for autoradiography.

The aliquot of tumor for autoradiography was quick-frozen with CO_2 vapor on a metal cutting block, sectioned into 10 micron thick strips on a hand-operated microtome, and the sections of tissue were fixed to glass slides and stained with hematoxylin and eosin. The slides were immersed briefly in Kodak NTB-2 liquid photographic emulsion in a dark room, air dried under a fan, and exposed in a light tight box for 18-24 hours. The time from excision to start of exposure to photographic emulsion was $\simeq$ 45 min. Slides were then developed in Kodak D-19 developer for 5 min, mounted with Canada Balsam and viewed under the light microscope. This specimen was compared to the aliquot of tumor submitted for routine histopathologic examination.

Patient Study:

An eighteen-year-old male underwent right lower extremity amputation for osteogenic sarcoma in July, 1966, at the University Hospital. At that time the chest roentgenogram was normal. In November, 1966, a chest roentgenogram disclosed that the patient had multiple metastatic lesions in both lungs. In April of 1967, we gave him 1.5 mC of Fluorine-18 by intravenous injection. One hour after injection, posterior and anterior scans of the chest were performed, using the same scanner, but with a 19-hole collimator. Point counts were taken over representative areas of the chest.

RESULTS

Rat Studies:

Scanning and point counting. Figure 1A is a photograph of the posterior scan of the rat 4.5 hours after intraperitoneal injection of Fluorine-18. The skull, spine, femoral heads, sacrum and left scapular and right neck tumor sites are imaged. The area of the left flank abdominal tumor excision is not visualized.

Point counting over the small osteogenic sarcoma transplants in subcutaneous sites in right neck and left scapula (sites 2 and 3 in Figure 1A) were 63% of that over the larger skull at the 4.5 hour time interval, and 58% greater than over the right scapula (#7) where there was no transplant tumor and over the left flank area from which a transplant had been excised (#8).

Fluorine-18 concentration by well counting. Tumor concentrations of ^{18}F were greater than that of surrounding soft tissue, but somewhat less than samples of normal skeleton. After corrections for background and decay, the concentration in tumor was 0.93% of the original activity of the injected aliquot (cpm/mg). In other rats without tumors the concentrations in soft tissues in liver, heart and lungs were 0.11-0.40% and in vertebrae, femoral epiphyses and tibia were 0.27%, 2.5% and 3.1%.

Autoradiography. Figure 1B is a photograph of an autoradiograph of a portion of the rat osteogenic sarcoma transplant tumor from the left flank. The maximum concentration of Fluorine-18 is seen between and on the surfaces of the malignant tumor osteoblasts at the top of the photograph. No significant concentration of Fluorine-18 was seen in the soft cartilagenous border of the tumor (bottom). Concentration of Fluorine-18 was also seen in small bony spicules immediately adjacent to the malignant osteoblasts and in areas of calcification.

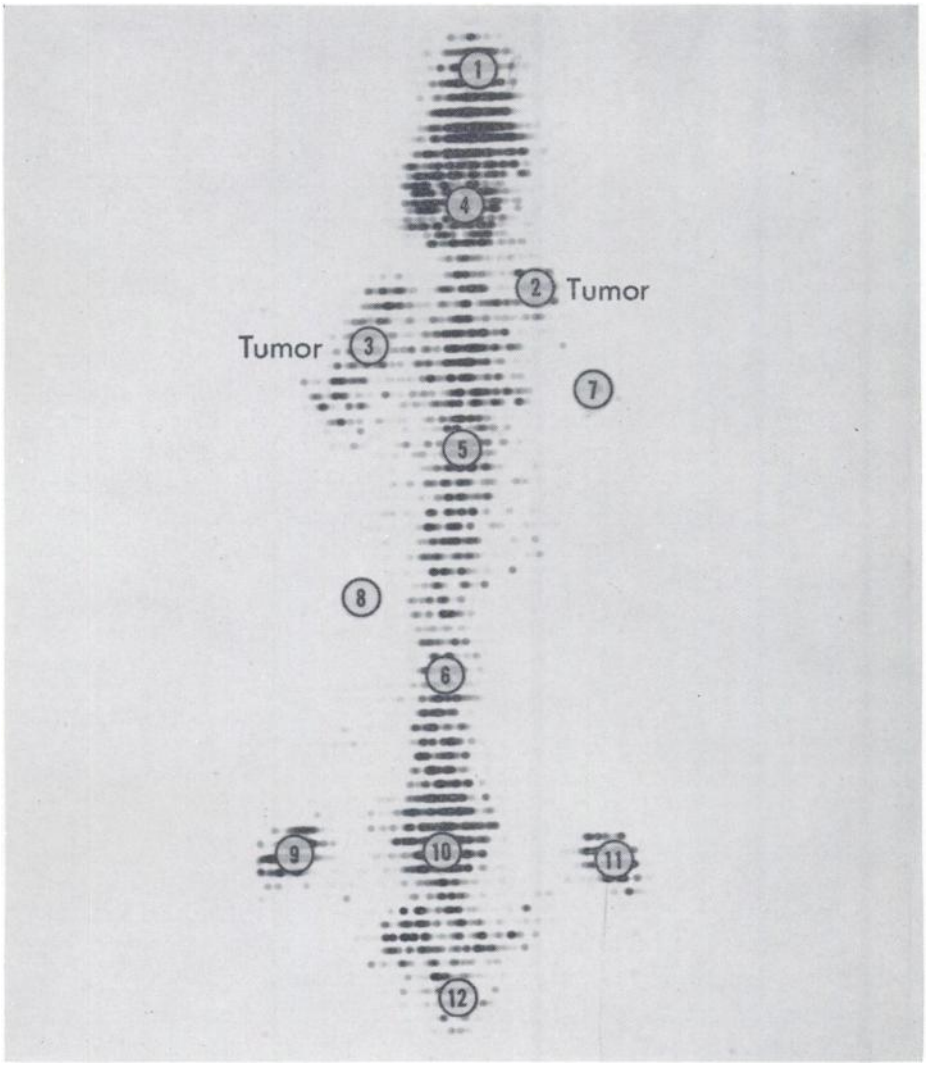

Fig. 1A. Photograph of a posterior photoscintillation scan of rat 4.5 hr after intraperitoneal injection of Fluorine-18. Concentration of Fluorine-18 is imaged over the subcutaneously growing transplanted osteogenic sarcoma over left scapula (point #3) and smaller tumor at point #2 as compared to little uptake over right scapula (point #7) and left flank where tumor had been excised (point #8).

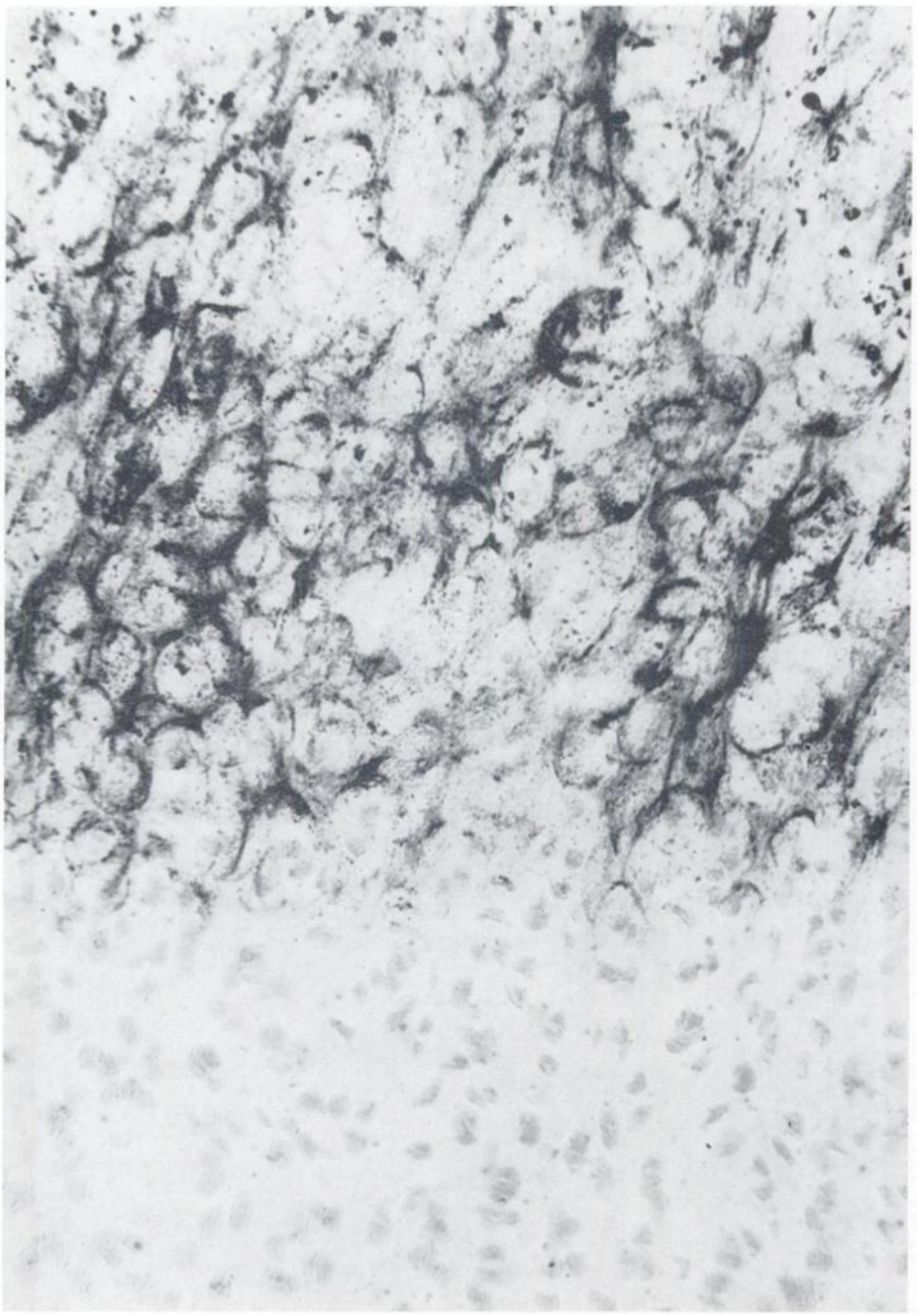

Fig. 1B. Photograph of high power view of autoradiograph of a portion of the rat osteogenic sarcoma transplant tumor from the left flank. The maximum concentration of Fluorine-18 is seen between and on the surfaces of the malignant tumor osteoblasts.

Patient Studies:

Figure 2 is a photograph of the chest roentgenogram of the patient four days before lung scanning with superimposition of the posterior lung scan. The scan demonstrates concentration of Fluorine-18 in the majority of the opaque areas caused by metastatic osteogenic sarcoma. Point counts over metastatic tumor sites (#4 and #8) over left lung are 21% higher than those recorded over points #1 and #9 over the vertebral column; and 44% higher than over points

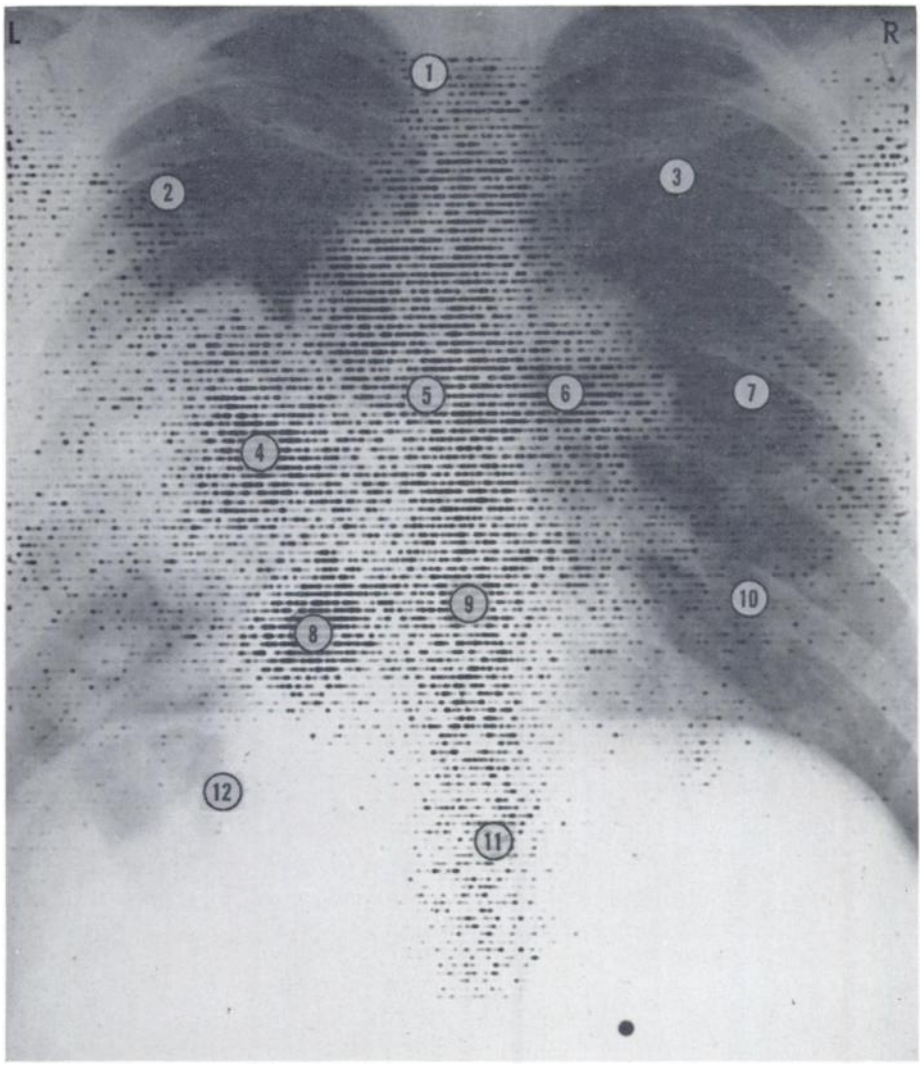

Fig. 2. Photograph of a P-A chest roentgenogram of a 17-year-old boy with osteogenic sarcoma (right lower leg amputation) metastatic to lung, with a superimposed posterior photoscintiscan with Fluorine-18. Concentration of radionuclide is seen in the majority of metastases visualized by chest roentgenogram.

#3 and #7 in right lung. Apparently, there are small metastases visualized faintly by the chest roentgenogram in the vicinity of points #7 and #10 (and may be elsewhere) showing no localized concentration of Fluorine-18. It is possible that these areas might have been imaged with the scanner if the settings were not adjusted to image primarily the larger collections of radionuclide in the osteogenic sarcoma.

DISCUSSION

Radioiodine ^{131}I has been used successfully to demonstrate metastatic carcinoma of the thyroid to lung (5), and Fluorine-18 has been used to demonstrate metastatic neoplasm to bone (2) while conventional roentgenograms of these areas are still non-diagnostic. We are now exploring the efficacy of Fluorine-18 for lung scanning before surgical amputation for primary bone tumors to detect metastases to lung in the presence of normal chest roentgenograms.

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