TUMOR SCANNING WITH ^{67}Ga CITRATE

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The need for a good tumor-specific scanning agent has promoted a wide search for such materials but, as yet, success has been limited (1). Recently we have observed an unusual affinity of certain soft-tissue tumors for carrier-free ^{67}Ga administered as citrate. This has enabled us to visualize several types of neoplasms with unusual contrast. We believe that the results of these early observations with ^{67}Ga are sufficiently encouraging to warrant a preliminary report.

The radionuclides of gallium have been of clinical interest both for therapy and as diagnostic scanning agents for bone and brain. Hayes *et al* demonstrated rapid localization (2 hr) of ^{68}Ga citrate in the skeleton of rats and rabbits (2,3). To obtain favorable concentration ratios of bone-to-blood and bone-to-muscle and to avoid an undesirable deposition in the liver and spleen, they needed to give objectionably high doses of stable carrier gallium. Further animal studies, however, did show that with scanning intervals increased to 24 or 48 hr, favorable bone ratios could be achieved with little or no carrier although the relatively high liver and spleen deposition was still present with carrier-free doses (4). On the basis of these results a longer half-life appeared desirable, and we obtained a carrier-free preparation of ^{67}Ga (half-life, 78 hr) for clinical trial to find out whether favorable bone ratios could be obtained in humans. Patients with malignant disorders and known or suspected bone lesions were selected for study. Localization of radiogallium in soft-tissue tumor of one of the original patients was an unexpected bonus (Case 1). This observation prompted further trials and constitutes the subject of this preliminary report.

Gallium-67 has many characteristics of an ideal radionuclide for scanning. Because it is accelerator-produced, it is available in a carrier-free state. It has a half-life of 78 hr and decays by electron capture with the emission of four main gamma rays having energies of 93, 184, 296 and 388 keV. The 388-keV photon accounts for only 7% while the

184- and 296-keV photons comprise 46% of the gamma emissions. These moderate gamma energies are suitable for scanning not only with commercially available rectilinear scanners, but also with scintillation cameras. The total-body radiation dose for ^{67}Ga is estimated to be 0.34 rads/mCi. For human trials the ^{67}Ga —after previous pyrogen testing—was administered intravenously together with 7 mg of sodium citrate (Eli Lilly Co.) per kilogram of body weight.

Case 1. This 73-year-old woman had enlarged cervical lymph nodes for 2 months. A lymph-node biopsy showed Hodgkin's disease. No other lymph nodes were palpably enlarged. A whole-body scan

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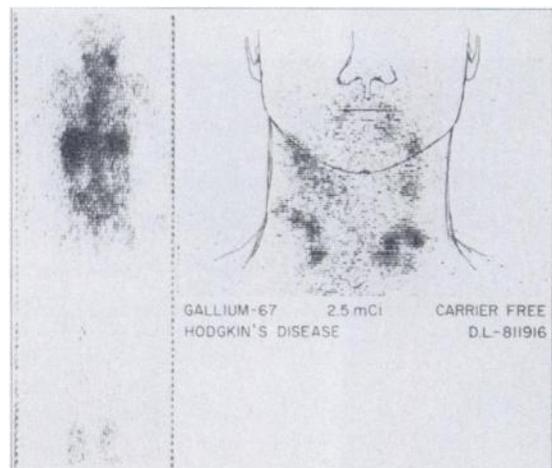


FIG. 1. Case 1. (Left) Posterior whole-body photoscan at 6 days after 2.5 mCi of ^{67}Ga citrate. Scan was made with ORAU whole-body scanner which has $5\frac{1}{4} \times 3$ -in. NaI crystal and 88-hole focusing collimator. (Right) Anterior photoscan of patient's neck 72 hr after ^{67}Ga citrate administration, using Picker 5-in. Magnascanner with 265-hole fine-focusing collimator. No contrast enhancement was used in either scan.

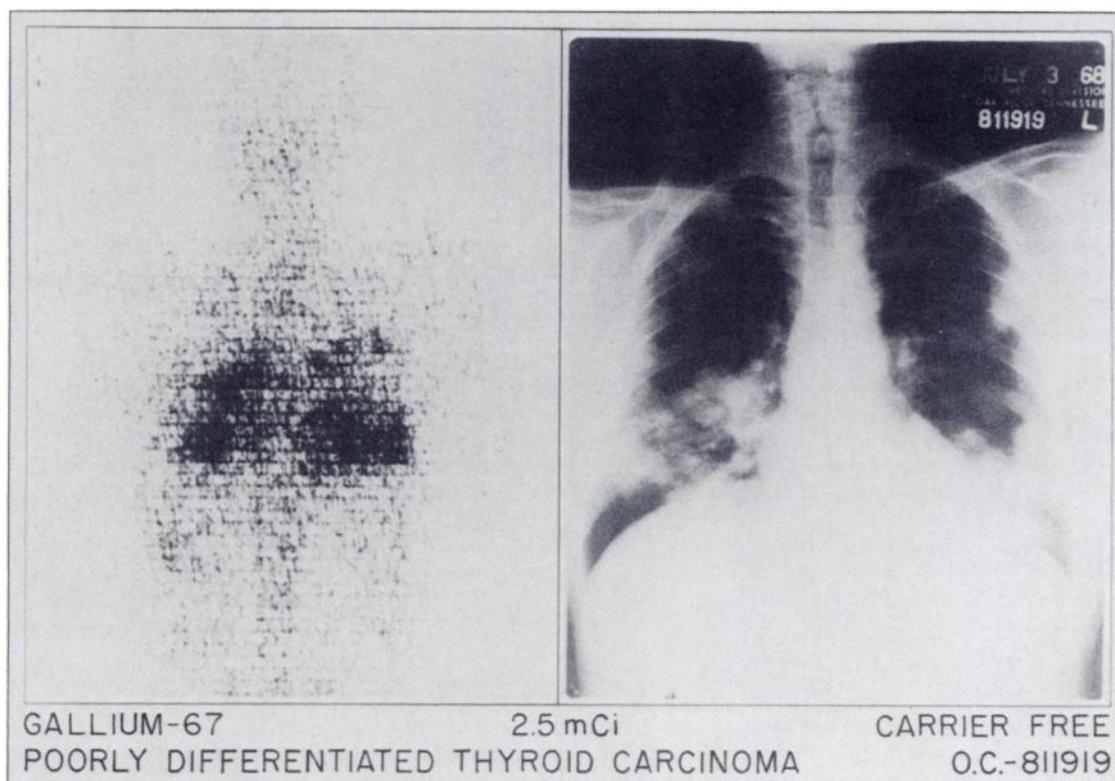


FIG. 2. Case 2. (Left) Posterior photoscan of upper torso made on ORAU whole-body scanner 19 hr after administration of 2.5 mCi of ^{67}Ga citrate. No contrast enhancement was used. (Right) P-A chest x-ray of patient at time of scan.

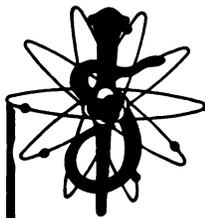
24 hr after the intravenous injection of 2.5 mCi of ^{67}Ga revealed no bone lesions, but an unexpected concentration of the isotope in the neck persisted during the entire study (7 days). A more detailed scan showed that the distribution of the isotope corresponded to the location of the palpable cervical lymph nodes (Fig. 1).

To determine whether this was a unique case, nine additional patients with soft-tissue tumors have been studied. Distinct localization of ^{67}Ga in known and presumed tumor was seen in three of four patients with Hodgkin's disease, and three of four patients with other types of lymphoma. In a number of these patients, in addition to known tumor, we detected tumor not known to be present at the time of scan but which was later confirmed on x-rays or by physical examination and also tumor not detectable by other means but consistent with symptoms. A negative scan was obtained in only one patient with Hodgkin's disease. This patient had just completed a course of chemotherapy (vinblastine) and at the time of the scan had no known tumor. The other

negative or borderline study was in a patient with chronic lymphocytic leukemia and massive nodes. The nodes could be detected on the scans but the contrast was insufficient to justify a classification as definitely positive. Unlike the patients in whom the tumors were distinctly seen, he was on a maintenance course of chemotherapy (cyclophosphamide and prednisone) at the time of the scans.

Case 2. One additional patient with a poorly differentiated carcinoma of the thyroid with pulmonary metastases was studied to test the ^{67}Ga preparation in nonlymphomatous tumor. This 64-year-old man had hoarseness and a rapidly enlarging goiter which was found to be a poorly differentiated carcinoma. A scan with ^{131}I before thyroidectomy and assay of the excised tumor revealed no localization of the iodine in the tumor. Subsequent scans likewise failed to reveal any concentration of iodine in the known pulmonary metastases. A whole-body scan 24 hr after the intravenous administration of 2.5 mCi of carrier-free ^{67}Ga showed that most of the isotope was present in the pulmonary metastases (Fig. 2). Further scans and external counting over the patient's body indicated no appreciable loss of the isotope from the tumor during the study (9 days).

These preliminary findings suggest that ^{67}Ga may be a valuable scanning agent for the detection of



soft-tissue tumors. At this time the mechanism for isotope localization within the tumor is unknown, but it may be related to the protein-binding properties of gallium (5). However, ^{113m}In , another nuclide known to be bound by plasma proteins, failed to localize in the tumors of two patients with positive ^{67}Ga scans (Case 2 and a patient with Hodgkin's disease). In addition ^{75}Se -selenomethionine was not concentrated in the carcinoma of Case 2. Obviously further experience in patients and appropriate animal experiments are needed to evaluate this agent and the mechanism involved.

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