A METHOD FOR THE SIMULTANEOUS MEASUREMENT OF ^{67}Ga, ^{111}In, AND ^{75}Se IN TUMORS USING A SEMICONDUCTOR DETECTOR

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Recent developments in semiconductor detector technology have caused much interest in nuclear medicine (*1*). However, the medical use of semiconductor detectors is, at the present time, restricted to certain research institutes. Flanigan et al (*2*) have compared the uptake of different simultaneously injected radiopharmaceuticals into tumor-bearing dogs with a dual NaI(Tl) detector. However, their results could not provide sufficient precision because of the difficulty inherent in detecting many radiopharmaceuticals with a conventional NaI(Tl) detector. On the other hand, the Ge(Li) semiconductor detector has a high-resolution for gamma rays compared with a conventional NaI(Tl) detector. The use of the Ge(Li) detector made it possible to detect uptakes of different simultaneously injected radiopharmaceuticals in the organ at the same time.

Numerous recent reports have indicated that ^{67}Ga-citrate is readily taken up by malignant tissues (*3–5*). In addition there has been recent evidence that ^{111}In-chloride and ^{75}Se-selenite are also preferentially incorporated into tumors (*6,7*). The authors studied the uptake of these simultaneously injected radiopharmaceuticals by Ehrlich's tumor-bearing mice with a Ge(Li) semiconductor detector.

METHODS AND MATERIALS

The experimental animals were mice (DDN-strain) 14 days after transplantation of Ehrlich's tumor cells into the femoral region. Standard solution was produced by mixing 10 μCi of each of the three radioisotopes such as ^{67}Ga-citrate (carrier-free), ^{111}In-chloride (carrier-free), and ^{75}Se-selenite (specific activity:50mCi/mg). About 0.2 cc of standard solution was injected into the abdominal cavity of each tumor-bearing mouse. The mice were sacrificed 48 hr after injection, and the tumor, liver, kidney, lungs, stomach, intestines, and vertebrae were analyzed.

The photopeaks of the three radioisotopes in each organ were measured with a 200-channel multianalyzer attached to a Ge(Li) semiconductor detector. The semiconductor detector used here is manufactured by the Ortec Company and has a capacity of 10 cc with a full width half maximum (FWHM) of 4.5 keV for ^{60}Co gamma rays (1.33 MeV).

The photopeaks of ^{67}Ga, ^{111}In, and ^{75}Se were measured at 182, 173, and 136 keV, respectively. The uptake of ^{67}Ga, ^{111}In, and ^{75}Se by each organ was measured by comparing the area of photopeaks of the standard solutions with that of the corresponding photopeaks in the organs.

RESULTS AND DISCUSSION

Figure 1 shows the gamma-ray spectra for the standard solutions obtained with NaI(Tl) detector and the Ge(Li) detector. It is obvious that the closely spaced photopeaks were more definitely resolved by the high-resolution Ge(Li) detector, and all but one of the observed photopeaks from the mixed radioisotopes was easily identified. Figure 2

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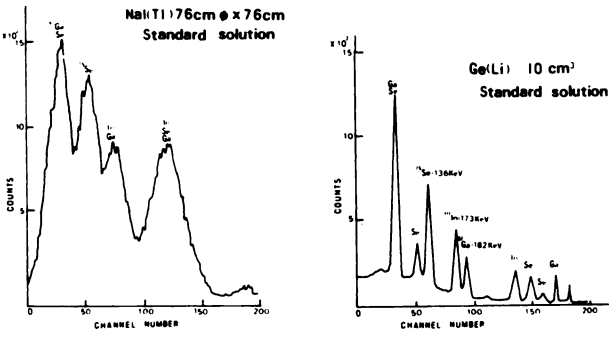

FIG. 1. Comparison between gamma-ray spectra for standard solutions as measured by NaI(Tl) and Ge(Li) detectors. Standard solution is composed of ^{67}Ga-citrate, ^{75}Se-selenite, and ^{111}In-chloride.

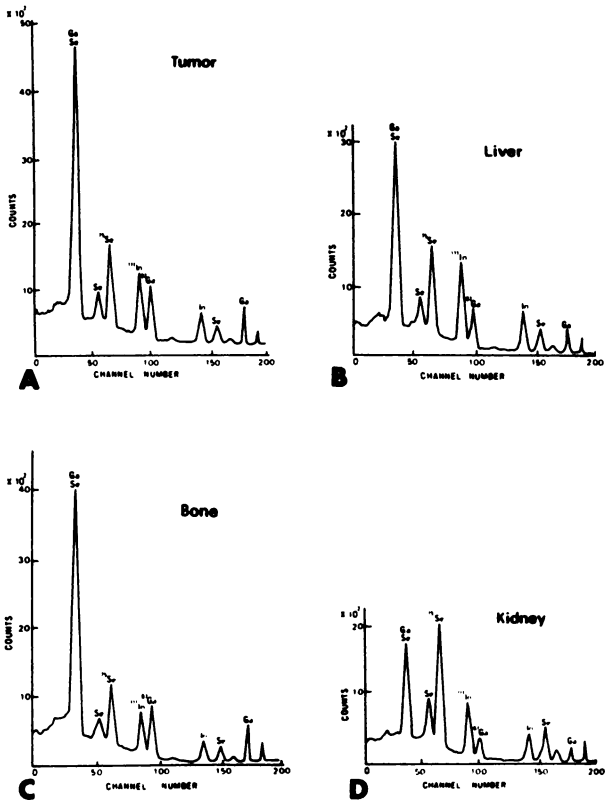

FIG. 2. Spectra of ^{67}Ga, ^{111}In, and ^{75}Se in tumor (A), liver (B), bone (C), and kidney (D) with the Ge(Li) detector. Photopeaks of ^{67}Ga, ^{111}In, and ^{75}Se were measured at 182, 173, and 136 keV, respectively.

TABLE 1. COMPARISON OF UPTAKES OF ^{67}Ga, ^{111}In, AND ^{75}Se TRACERS IN EHRLICH'S TUMOR-BEARING MICE 48 HR AFTER INTRAPERITONEAL ADMINISTRATION

Tissues	^{67}Ga-citrate (% dose/gm)	^{111}In-chloride (% dose/gm)	^{75}Se-selenite (% dose/gm)
Tumor	4.60 ± 0.86*	3.31 ± 0.49*	3.32 ± 0.83*
Liver	8.43 ± 2.67	8.96 ± 2.08	8.44 ± 2.79
Bone	4.49 ± 1.70	2.81 ± 0.55	2.70 ± 1.51
Kidney	7.74 ± 2.61	16.42 ± 6.23	16.55 ± 5.75
Lung	1.94 ± 0.29	2.17 ± 0.88	3.51 ± 0.86
Stomach	3.70 ± 1.29	3.34 ± 1.03	2.79 ± 0.88
Intestine	4.39 ± 1.68	4.63 ± 2.01	5.51 ± 1.67

* Values are given ± the standard error (number of animals is 5).

shows the gamma-ray spectra for the tumor, liver, bone, and kidney at 48 hr after intraperitoneal administration. The distribution of the three radioisotopes into the different organs is shown in Table 1. The following results at 48 hr after simultaneously intraperitoneal administration were obtained: (A) ^{67}Ga-citrate is most readily incorporated into the tumor with ^{111}In-chloride and ^{75}Se-selenite having similar but lower uptakes; (B) ^{67}Ga-citrate had the lowest kidney uptake; (C) ^{67}Ga-citrate uptake by the bone marrow-bearing vertebrae was high whereas uptake of the other isotopes was low; (D) the other organs studied had similar uptakes for all three isotopes. Edwards et al (*3*) have reported that both ^{114m}In-chloride and ^{75}Se-selenomethionine uptakes in animal tumors had been lower than ^{67}Ga-citrate uptake. Goodwin (*8*) reported that both ^{111}In-chloride and ^{111}In-citrate gave tumor uptakes similar to ^{67}Ga-citrate, although the tumor-to-background ratios were not so high. However, Serafini (*9*) found that ^{111}In-chloride was more readily taken up by lymphosarcoma than was ^{67}Ga-chloride. These differences may be due to the different experimental tumors used or to different routes of injection or transferrin binding. Our experiments show that the ^{67}Ga-citrate uptake by Ehrlich's tumor tissue was somewhat higher than the ^{111}In-chloride and ^{75}Se-selenite uptakes at 48 hr after intraperitoneal injection. The period of 48 hr was used because it correlates well with the usual clinical situation in humans. It is interesting to note that ^{111}In and ^{67}Ga are different in uptake despite their similar position on the periodic law table. This may be due to the differences between the citrate and chloride agents. The actual mechanism of uptake of these metal elements into the tumor cells and the biological behavior of these metal elements into the tumor cells are still unknown.

In this experiment the authors could detect three radioisotopes (^{67}Ga, ^{111}In, and ^{75}Se) in organs at the same time with a Ge(Li) detector which has a high resolution for gamma rays. For this purpose we assumed that these carrier-free radionuclides did not interfere with each other. No data are available to use which would contradict this statement.

In conclusion, this method made it possible to detect many isotopes simultaneously and to estimate their relative uptakes, and thus minimize the differences due to individual variations in experimental animals.

SUMMARY

The use of a Ge(Li) semiconductor detector made it possible to detect uptakes of ^{67}Ga-citrate, ^{111}In-chloride, and ^{75}Se-selenite in the same tumor-bearing mice at the same time. The results showed that ^{67}Ga-citrate uptake in Ehrlich's tumor tissue at 48 hr after intraperitoneal administration was highest of the three radioisotopes used. The authors believe that this detecting method will prove very useful for this purpose in the future.

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