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^{165}Er: AN "IDEAL" RADIONUCLIDE FOR IMAGING WITH PRESSURIZED MULTIWIRE PROPORTIONAL GAMMA CAMERAS

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From consideration of tissue penetration, spatial resolution, and detector efficiency, radionuclides for imaging with multiwire proportional gamma cameras should emit photons in the range of 35–50 keV. We have obtained reactor-produced ^{165}Er, half-life of 10.3 hr, which emits only photons of 48 and 54 keV. As to its biologic behavior, this isotope is primarily a bone-seeker as expected. We found that it can be used as a tumor-localizing agent. Absorbed doses were calculated and found to be no greater than those from ^{99m}Tc. We have also shown that this radionuclide can be used satisfactorily with the present scintillation cameras.

It has been shown recently (*1–4*) that multiwire proportional cameras (MWPC) can give excellent spatial resolution (better than 1 mm). The only disadvantage of these detectors is that they are limited to photons of energy less than 100 keV although several attempts are underway to improve these detectors so that they can be effectively used up to the ^{99m}Tc energy.

The MWPC developed by Kaufman, et al (*2*), which was pressurized to 60 psi with 93% xenon and 7% CO_2 gas, has maximum detection efficiency for photons of energy just above the xenon K-edge (35 keV). It was also shown by them that as the energy of the photon increases, not only the detection efficiency drops rapidly but also the spatial resolution deteriorates. For these reasons, radionuclides which emit photons of energy around 40 keV but not less than 35 keV should be extremely useful if they are clinically valuable. The relatively simple and inexpensive MWPC might play an increasingly significant role in nuclear medicine if radionuclides and pharmaceuticals particularly suitable for this imaging device are studied and developed.

PRODUCTION

Erbium-165 with 10.3-hr physical half-life decays completely by electron capture to the ground state of stable ^{165}Ho. The only photons expected are K x-rays with an average energy of about 50 keV. We have obtained 67% enriched stable ^{164}Er in the form of Er_2O_3 from Oak Ridge National Laboratories at a moderate cost. About 8 mg of this sample have been irradiated with neutrons (6.7×10^{13} neutrons/cm^2/sec) in the Union Carbide nuclear reactor at Tuxedo Park, New York. After 16 hr of irradiation, about 50 mCi of ^{165}Er has been obtained and dissolved in concentrated nitric acid to dryness. Ten percent citric acid was then added and allowed to dry to obtain erbium citrate.

There are two other radionuclides produced during this process due to impurities in stable ^{164}Er. These are ^{169}Er and ^{171}Er with 9.4 days and 7.5 hr half-life, respectively. The radionuclide ^{169}Er is a pure beta-emitter with an end-point energy of about 0.34 MeV while ^{171}Er emits beta-gamma radiations. There was approximately 10% of ^{169}Er and 5% of ^{171}Er in the amount we produced. These impurities are not desirable for clinical use but the resulting radiations do not interfere with animal or phantom studies. A gamma-ray spectrum taken with a germanium detector immediately after the production is shown in Fig. 1. Although 99% enriched stable ^{164}Er is not available at this time, custom enrichment is possible at extra expense.

BIOLOGIC DISTRIBUTION

Hisada and Ando (*5*) in their study of radiolanthanides as tumor-scanning agents predicted that erbium will have tumor affinity. O'Mara and Subra-

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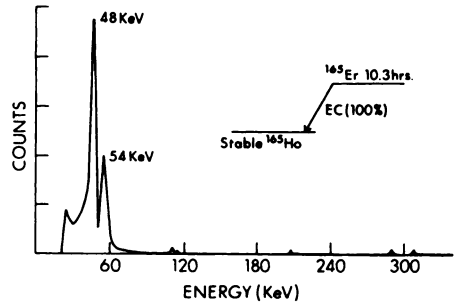

FIG. 1. Gamma-ray spectrum of ^{165}Er, 1 hr after production of neutron irradiation of 67% enriched stable ^{161}Er. Gamma rays of 111 keV and above come from ^{171}Er produced because of 2% ^{170}Er present.

manian (*6*) have obtained bone images of patients with ^{171}Er. We have injected intraperitoneally about 10 μCi of ^{165}Er-citrate at a pH of about 5 into male Buffalo strain rats with subcutaneous transplantation of Hepatoma 9618A2 2 weeks prior to the administration of the radionuclide. The histology and growth properties of the tumor were described previously (*7,8*). These rats were sacrificed at different times and several organs were taken and counted in a scintillation counter and the results are given in Table 1. The tumor/muscle and tumor/blood ratios at 6 hr are observed to be 20 and 10, respectively. The uptake in bone is maximum and considerable activity is observed in kidneys and liver. The distribution of erbium in rats is in general similar to the results obtained by Hisada and Ando (*5*) with ^{169}Yb-citrate.

About 1 mCi of ^{165}Er-citrate has been injected intravenously into a normal rabbit and about 30 μCi intraperitoneally into a mouse with an implanted tumor in the right thigh. A scintillation camera image of the inferior half of the rabbit shown in Fig. 2A has been obtained 6 hr after the administration of the radionuclide. Figure 2B shows the scintillation image of the pelvis of the mouse taken 3 hr after the injection using a pinhole collimator. This illustrates the use of this radionuclide with the present scintillation cameras although one would expect poor resolution when compared with ^{99m}Tc but not much different from what we get with ^{197}Hg. We wish to continue our studies with chelates to reduce the uptake by liver and kidneys. An attempt will be made to obtain images with pressurized MWPC at one of the available centers in the near future.

TABLE 1. PERCENTAGE UPTAKE OF ERBIUM-CITRATE PER GRAM OF TISSUE IN RATS*

Organ	1 hr	3 hr	6 hr	24 hr
Blood	0.59	0.17	0.04	0.005
Muscle	0.08	0.03	0.02	0.01
Spleen	0.22	0.17	0.13	0.07
Liver	0.33	0.34	0.31	0.14
Tumor	0.32	0.45	0.39	0.24
Kidneys	0.97	1.15	0.90	0.48
Bone	0.92	1.56	1.45	1.04

* Each figure is a mean value of data of three animals. The average weight of these rats is about 180 gm.

DISCUSSION

Because we are mainly interested in using this radionuclide with MWPC, we will consider only photons of energy up to 140 keV above which the efficiency of the detector is extremely poor. We have calculated the penetration in water-equivalent tissue for different energies at different depths up to 15 cm. Taking the stopping power of pressurized xenon gas detector described by Kaufman, et al (*2*) for different energies, we have multiplied these by the tissue penetration to obtain relative efficiency, which is shown in Fig. 3. At all these practical depths, ^{165}Er seems to be superior to other radionuclides.

As usual, the absorbed dose is another important factor to be considered for the clinical use of any radionuclide. For the sake of comparison, absorbed doses to skeleton and whole body were calculated for ^{99m}Tc as well as ^{165}Er assuming 50% bone uptake for both radionuclides and no biologic excretion. The dose from ^{165}Er to the whole body is 0.12 rads and to the skeleton 0.33 rads whereas from ^{99m}Tc the whole-body dose is 0.15 rads and the skeleton receives 0.45 rads for an administered dose of 10 mCi in each case. Thus, the absorbed dose is about 25% less with ^{165}Er, which has a physical half-life longer than that of ^{99m}Tc.

The radionuclide ^{165}Er not only has a simple decay scheme emitting 50-keV photons but also has a

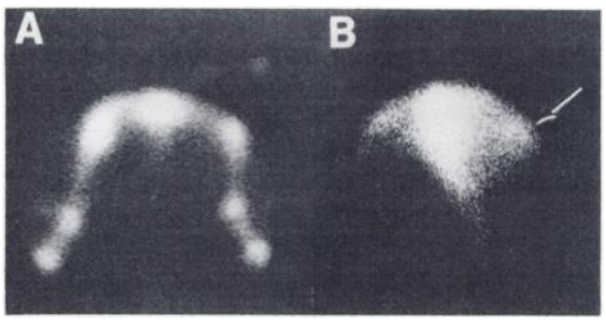

FIG. 2. (A) Scintillation image of inferior half of normal rabbit taken 6 hr postinjection. (B) Scintillation image using pinhole collimator of pelvis of mouse with implanted tumor in right thigh taken 3 hr after i.p. injection. More uptake at tumor site when compared with left side can be noticed.

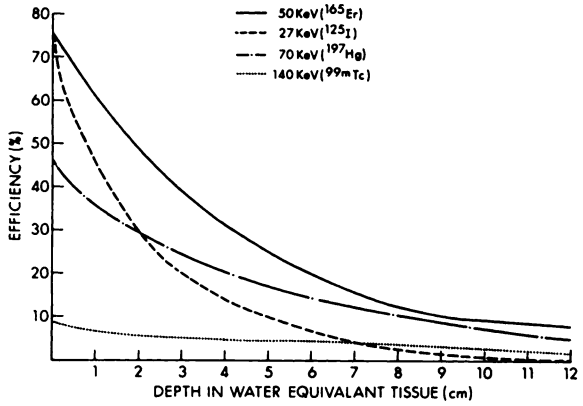

FIG. 3. Product of percent detection efficiency of xenon-pressurized multiwire proportional camera (2) and percent transmission through tissue for different photon sources at various depths in tissue. Erbium-165 is seen to provide highest values at all depths.

convenient half-life for shipping and quality control. It is also worth noting that the radionuclide ^{165}Tm, the parent of ^{165}Er, has a physical half-life of 30 hr and therefore offers the possibility for a generator. The low-energy photons from ^{165}Er reduce problems of collimation and shielding. Since this radionuclide can be reactor-produced, it can be obtained at a reasonable cost. Finally, this radionuclide can also be used satisfactorily for imaging with existing scintillation cameras whereas it is vitally important for imaging with pressurized MWPC, which are presently under development at several centers.

Erbium-165 may be the "ideal" radionuclide for imaging with MWPC on the basis of spatial resolution, detector efficiency, tissue penetration, and absorbed dose. Imaging is also possible with scintillation cameras as demonstrated in these studies. Preliminary studies with animals indicated that this radionuclide can be used for bone imaging and tumor localization. The excellent spatial resolution offered by MWPC together with the use of this radionuclide might help to localize small tumors with good accuracy.

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