

Letters to the Editor

Long-Lived Radioactive Contaminant of a Krypton-81m Gas Generator

TO THE EDITOR: Krypton-81m (^{81m}Kr) gas has been in use for several years in nuclear medicine for pulmonary ventilation studies. It is produced by the radioactive decay of rubidium-81 (^{81}Rb) in a 185 MBq (5 mCi) generator (Medi-Physics, Paramus, NJ) supplied to the user. The package insert clearly states that "other rubidium radioisotopes which do not decay to radioactive krypton ^{81m}Kr in their decay are present in the generator", but full details are not given.

In an effort to learn more about the contents of these generators, an investigation was conducted to determine if any long-lived radioactive contaminants were present. Since the half-life of ^{81}Rb is 4.58 hr it was decided to let the generator decay in storage long enough to eliminate any signs of this isotope from the measurements.

A 1-mo-old generator was dismantled and an exposure rate of $\sim 2.6 \times 10^{-7}$ C/kg/hr (1.0 mR/hr) was measured in contact with the glass bulb containing the generator's radioactive material. This finding confirmed the presence of a relatively long-lived radioactive isotope in the generator, so we proceeded to determine the identity and quantity of this contaminant.

The glass bulb containing the generator contents, with its associated plastic tubing attached, was placed in a 2-in. diameter by 2-in. deep NaI well detector connected to a Tracor-Northern (Econ II Model NS 710A) multichannel analyzer. An energy spectrum was acquired and the main peak identified from radionuclide decay tables. The count rate was measured over a 70-day period, with the considerable deadtime losses (that varied from 25% to 15% during this time) corrected by the multichannel analyzer circuitry. Determination of the activity of our sample from exposure rate measurements was precluded by its small value. Its calculation from well-counter data required knowledge of the detection efficiency in the sodium iodide detector, which could be calculated from the formula

$$\text{Detection Efficiency (DE)} = 1 - e^{-\mu_R t_{\text{eff}}} \quad (1)$$

where μ_R is the linear attenuation coefficient (I) in sodium iodide of 529 keV gamma rays and t_{eff} is the "effective path length" of gamma rays in the 2-in. well detector. The latter takes into account the geometric aspects of our detection system, with its nearly 4π angular acceptance.

t_{eff} was found by observing the count rates from calibrated standards of cesium-137 (^{137}Cs) and manganese-54 (^{54}Mn) and computing their detection efficiencies (DE) from the formula

$$\text{DE} = \frac{C}{I \times A} \quad (2)$$

where C is the measured count rate in counts per second, corrected for deadtime, I is the mean number of gamma

rays per decay (0.851 and 1.000 for ^{137}Cs and ^{54}Mn , respectively (2)) and A is the activity of the standard, in becquerels. The detection efficiencies thus computed were then inserted into Equation (1) with μ_R replaced by the attenuation coefficients for ^{137}Cs and ^{54}Mn (I), yielding values of $t_{\text{eff}} = 2.01$ cm and 2.02 cm, respectively. Two different standard sources for computing t_{eff} were used to illustrate the consistency of the method.

The average t_{eff} of 2.015 cm was then inserted into Equation (1) and the generator's activity found by solving for A in Equation (2).

The resultant energy spectrum (Fig. 1A) showed a single large energy peak at 528 keV (FWHM = 9.5%). The peak encompassed 14% of all channels and contained 44% of the total number of counts. The peak channel had $4.7 \times$

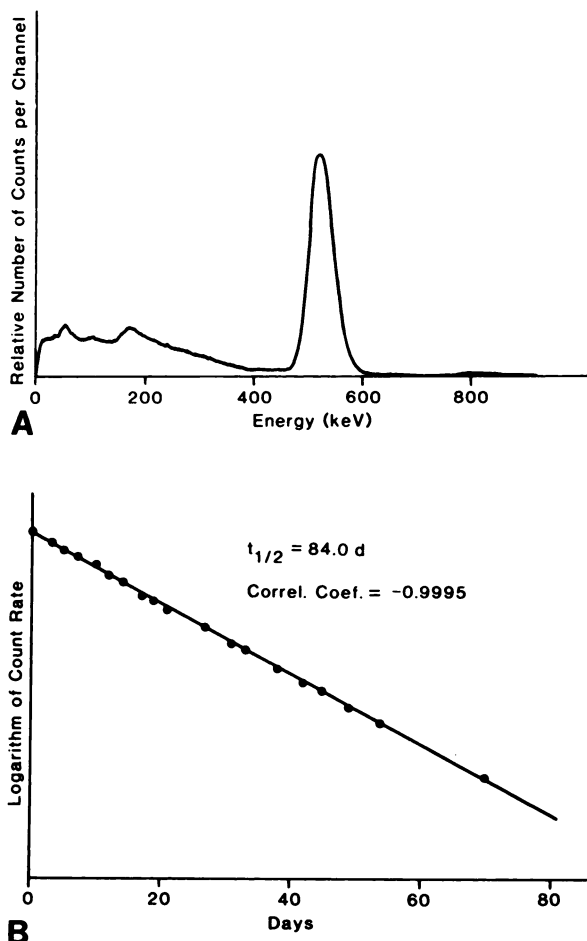


FIGURE 1

A: Energy spectrum emitted by a ^{81m}Kr gas generator, as measured with a 2-in. NaI well detector. The spectrum was taken 5 mo after the generator calibration date. B: Generator decay data and the best-fit curve. The initial count rate was 27.3 kcts/sec.

10⁴ counts. A smaller peak ~175 keV is the result of Compton backscatter.

A review of radionuclide decay tables (2) indicated that the spectrum is consistent with that from ⁸³Rb, which has a half-life of 86.2 days and decays by electron capture, emitting gamma rays with an average energy of 529 keV. The primary gamma rays include 520.41 keV (46%), 529.64 keV (30.3%), and 552.65 keV (16.4%).

Measurement of the declining count rate over a 70-day period, corrected for deadtime losses, yielded a half-life of 84.0 days, thus confirming the identity of the source as ⁸³Rb (Fig. 1B). The initial count rate was 2.7 × 10⁴ cts/sec. Counting time was 200 sec in all cases. The correlation coefficient of the best-fit exponential curve to the data was -0.9995.

The activity of ⁸³Rb in the generator, decayed backward to the latter's calibration date, was calculated to be 149 MBq (4.0 μCi), or 0.080% of the total activity. For comparison, a second spent generator was dismantled and found to contain 117 MBq (3.2 μCi) of ⁸³Rb (0.062% contamination) at its calibration date.

Rubidium-83 is not listed in the NRC's table of exempt concentrations (3) and therefore only concentrations not exceeding 1 × 10⁶ μCi/g (37.0 Bq/kg) of solids are exempt from disposal regulations. Furthermore, NRC rules preclude disposal via decay-in storage for a radionuclide with a half-life greater than 65 days, (4). In conclusion, although the quantity of ⁸³Rb in the generators is quite small and is consistent with the information provided in the package insert, its presence must nevertheless be taken into account when methods of disposal are considered.

References

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3. Code of Federal Regulations, 10 CFR 30.14, Revised January 1, 1988.
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On the Accumulation in Liver of ¹¹¹In Following Administration of the B72.3 Antibody

TO THE EDITOR: A recent issue of the *Journal of Nuclear Medicine* contains two reports on the biodistribution of indium-111 (¹¹¹In) following i.v. administration of the B72.3 antibody radiolabeled with essentially the same p-isothiocyanatobenzyl-diethylenetriaminepentaacetic acid (SCN-Bz-DTPA) chelator. Both the work of Carney et al., which was conducted in nude mice (1), and that of Yokoyama et al., performed in eight patients (2), included a comparison with the B72.3 antibody radioiodinated via chloramine-T or Iodogen. With respect to the accumulation of ¹¹¹In in the liver,

strikingly different results were obtained in these two investigations with higher levels of ¹¹¹In in liver being observed in patients.

One obvious conclusion from these observations is that a radiolabel and/or a radiolabeled antibody may behave differently in animals and in patients with regard, at least, to the liver. This is not surprising since mechanisms exist in patients but not in mice which encourage antibody localization in liver. For example, the formation in patients of circulating antigen-antibody complexes, HAMA and the recognition by the liver of foreign proteins will all contribute to antibody accumulation in this organ (3).

The low ¹¹¹In liver levels observed in mice by Carney et al., have been previously reported for B72.3 when radiolabeled via SCN-Bz-DTPA (4). Higher liver levels were observed when the antibody was radiolabeled with ¹¹¹In using the cyclic anhydride of DTPA (CDTPA). In our view, an explanation of these differences based on the higher denticity of the SCN-Bz-DTPA chelator is unconvincing especially in light of recent results showing identical biodistributions in mice of ¹¹¹In following i.v. administration of the B72.3 antibody radiolabeled both via SCN-Bz-EDTA and SCN-Bz-DTPA (5). Furthermore, explanations based on the increased stability of ¹¹¹In towards transchelation to transferrin when chelated via SCN-Bz-DTPA are also unsatisfying since at early times, equivalent accumulation in liver of ¹¹¹In attached via CDTPA and iodine-125 (¹²⁵I) have been reported following i.v. administration of the 10-3D2 antibody to mice (3). Furthermore, a recent investigation of three antibodies radiolabeled with ¹¹¹In via CDTPA and internally with ⁷⁵Se report similar accumulations of both labels in mouse liver over 96 hr (6). In addition, recent studies using rat livers show that the major radiolabeled catabolic product of the B6.2 antibody labeled with ¹¹¹In via CDTPA is a low molecular weight species in which ¹¹¹In is probably present in its DTPA chelate (7). In our view, the most likely explanation of reduced ¹¹¹In levels in mice following administration of SCN-Bz-DTPA conjugated antibodies is instability of the thiourea bond whereby this chelator is conjugated (8). Some evidence has recently been presented in support of this suggestion in that ¹¹¹In in urine was found to be present as the Bz-EDTA chelate following administration to mice of the Lym-1 antibody radiolabeled with SCN-Bz-EDTA (9).

One remarkable observation of Carney et al. is the identical biodistributions obtained in mice for ¹¹¹In and ¹²⁵I in all organs, including liver, and at all time points. Previous comparison studies have shown lower radioiodine levels in liver when CDTPA was used to attach ¹¹¹In (10). The similarities observed by Carney et al., however, do not necessarily reflect either improved integrity of the B72.3 antibody or increased stability of its ¹¹¹In label when the SCN-Bz-DTPA chelator is used. To argue thus ignores the fact that radioiodine, when attached to antibodies via conventional techniques, is itself unstable in vivo by the process of dehalogenation. The extent to which this process occurs is undoubtedly dependent on the antibody but must have been prominent in the study of Carney et al. judging by the high (38% ID/day) urine excretion of ¹²⁵I. If thyroid and stomach had been sampled, it is most likely that additional evidence of dehalogenation would have been apparent. If, as is likely, significant instabilities of ¹²⁵I as a result of dehalogenation occurred and since identical biodistributions of ¹²⁵I and ¹¹¹In were observed, some process of