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A Gallium[68] Positron Cow for Medical Use[1]

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INTRODUCTION

The Ge^{68}-Ga^{68} positron cow (1) is a convenient and economical source of Ga^{68}-EDTA (ethylenediamine tetra-acetic acid). The parent isotope Ge^{68} decays with a half life of 280 days to provide a continuous supply of the daughter isotope Ga^{68}. The daughter is a positron emitter and has a half life of 68 minutes. The cow, which makes use of the ion-exchange properties of activated alumina (Al_2O_3), (2) is milked of the Ga^{68} in a simple and rapid manner. It requires only the addition of the EDTA solution at the top of the column and collection of the effluent solution at the bottom. The Ge^{68} is strongly retained by the alumina so that the contamination of the Ga^{68}-EDTA by the Ge^{68} is extremely low. A reliable separation of the Ga^{68}-EDTA is obtained with little possibility of contamination due to faulty technique. The technique for obtaining a sterile and isotonic solution for intravenous injection is also rapid and simple.

By maintaining one millicurie of Ge^{68} on the alumina column, about 350 microcuries of Ga^{68} can be obtained for injection after the collection and processing. The decay equilibrium in the cow is established in about two hours so that a near maximum amount of Ga^{68} can be obtained from the column every two or there hours. When the cow is used several times per week, the cost per dose becomes very low, because the usual charge for the isotope and the shipping charges are saved. The cost of the cow is prorated over several months.

The new tracer compound, when used with the positron scintillation camera, has given a good record of brain tumor localization (3). To date more than 100 patients have been examined with only a small number of false positives and few known missed tumors. The radiation dose delivered to the patient is very low compared to that given by other isotopes. For a dose of 250 microcuries, the

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whole body radiation is less than 7 millirad, and the renal dose is less than 50 millirad.

PREPARATION OF THE COLUMN

The alumina column is prepared by a method similar to that previously suggested (4). A glass column 25 mm in diameter, 10 cm in length, and fitted with a medium porosity fritted glass disc is loaded with 10 grams of Fisher's chromatographic grade alumina. The alumina in the column is held in place at the top with a filter paper disc and plastic ring.

The alumina column is first washed with distilled water to remove fine particles and then washed with 0.005 *M* EDTA solution at a neutral pH. The washing of the column is continued until the pH of the effluent is near 7.

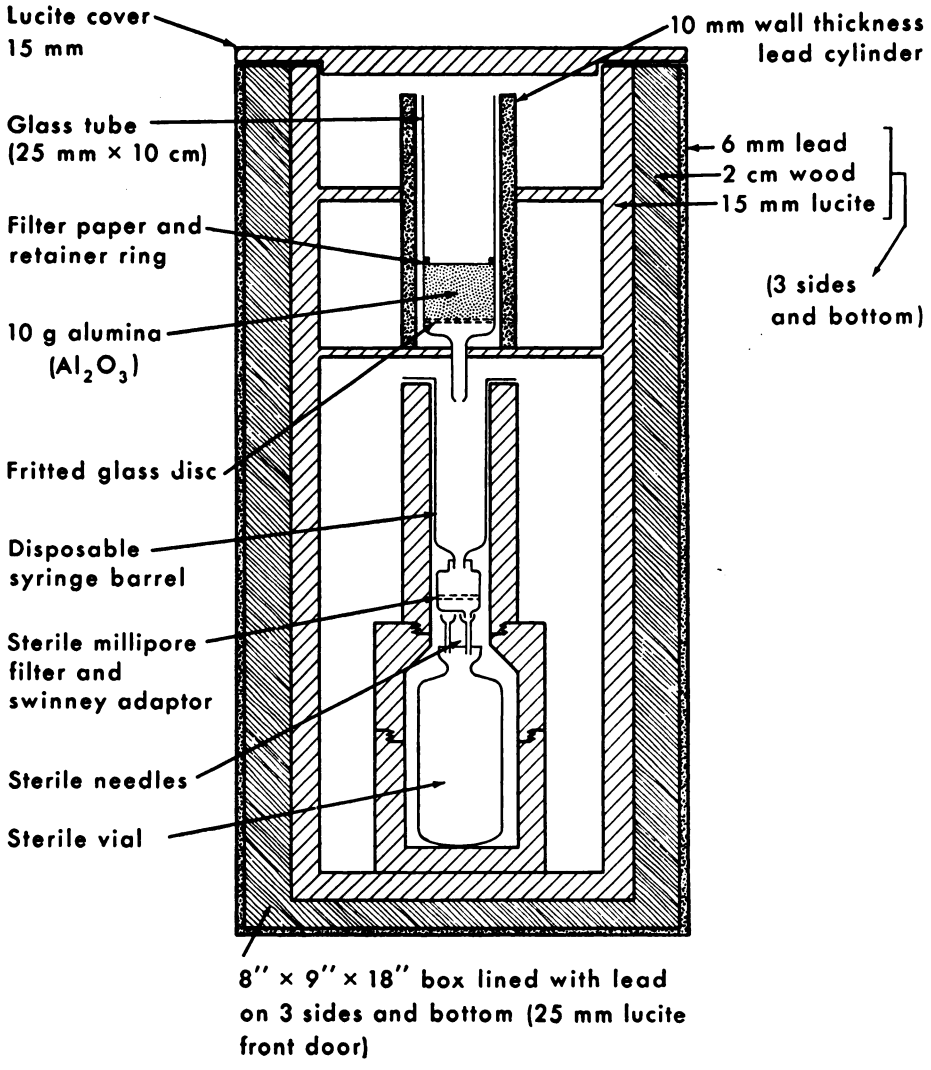

Fig. 1. Positron cow with shield and collecting apparatus.

The alumina column is now ready for loading with Ge^{68}. First, the column is placed in a box lined with Lucite and lead shielding (shown in Fig. 1). Then the Ge^{68}, in a near neutral solution of EDTA, is added to the column. Finally the column is washed with about 60 ml of 0.005 *M* EDTA solution. Ga^{68}-EDTA can now be milked from the column at desired intervals with 0.005 *M* EDTA solution. The Ga^{68}-EDTA collected from the column is at a neutral pH. It is contaminated with less than 1.4×10^{-5} parts of Ge^{68}.

STERILIZING AND COLLECTING APPARATUS

Ga^{68}-EDTA is sterilized for injection as follows. As the Ga^{68} elutes from the column, it is collected in a 10 ml syringe barrel attached to a previously autoclaved Millipore filter (pore size 0.22 microns) contained in a Swinney hypodermic adaptor. The other end of the Swinney adaptor is attached to a sterile syringe needle. The needle is stuck through the rubber stopper of a sterile serum vial, which also has a sterile venting needle. All the collecting and sterilizing apparatus is held in a vertical position above the serum vial by a Lucite holder and shield.

MILKING THE COW

To milk the column, the collecting apparatus is first introduced into the shielded box and placed beneath the column. Then 10 ml of 0.005 *M* EDTA solution is added to the top of the column. The resulting Ga^{68}-EDTA solution is collected in the barrel of the syringe. The entire collection apparatus with its Lucite shielding is then removed and placed outside the shielded box. The 10 ml of Ga^{68}-EDTA is made isotonic by adding 0.5 ml of 18 per cent sodium chloride solution. The pH of the solution is checked with pHydrion paper. A 100 lambda aliquot is taken for assaying the Ga^{68} activity against a Ge^{68} standard. The plunger is now replaced in the syringe barrel and the Ga^{68}-EDTA is forced under pressure through the Millipore filter into the sterile serum vial. Finally the upper portion of the collecting apparatus is separated from the serum vial by disconnecting the Lucite shielding above the serum vial and withdrawing the injection needles from the rubber stopper.

The serum vial contains the sterile solution of Ga^{68}-EDTA ready for injection. The total time required for the procedure is 20 to 25 minutes.

PREPARATION OF GA^{68} IN OTHER CHEMICAL FORMS

Because of the many advantages associated with Ga^{68}, attempts are being made to use it for other diagnostic purposes. The Ga^{68} can be freed from the EDTA complex by the following procedure.

1. The cow is milked with 10 ml of 0.005 *M* EDTA solution, and the Ga^{68}-EDTA is collected in a 40 ml centrifuge tube.
2. 10 to 20 mg of carrier $GaCl_3$ in HCL solution is added.
3. Then 0.5 ml of saturated ammonium acetate solution is added.
4. Concentrated NH_4OH is added dropwise (about 1 ml) to precipitate $Ga(OH)_3$ at pH 6.0.

5. The solution is heated in a boiling water bath for 10 minutes to coagulate the $Ga(OH)_3$.

6. The solution is centrifuged, and the supernatant solution is discarded.

7. The $Ga(OH)_3$ is dissolved with a minimum volume of hot 20% NaOH.

8. The solution is acidified with about 1 ml of concentrated HCl.

The time required for the procedure is about 30 minutes. With 10 mg of carrier Ga about 60 per cent of Ga^{68} from the EDTA solution is obtained. With 20 mg of carrier 70 per cent recovery is obtained.

ACKNOWLEDGEMENT

Mr. Edward A. Heilstad and Mr. Will D. Phillips of the Health Chemistry Department, Lawrence Radiation Laboratory, assisted in the development of the shielding and hardware.

REFERENCES

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LETTER TO THE EDITOR

TO THE EDITOR:

I have had a chance to read Mr. Harris's and Dr. Blau's letters to the editor. The nuclear physicists who co-operated with me in the 197 calculations took all available literature into their calculations and did not utilize the information supplied by Mr. Harris. Five months before the publication of our scientific letter to the editor, the published form of the Mercury-197 dosimetry was forwarded to Mr. Harris. In the time period until the publication of the dosimetry of Mercury-197 in the Journal of Nuclear Medicine, there had been no comment from Mr. Harris and Dr. Ross's laboratory. I am sure that Dr. Roerer, Dr. Ross and Mr. Harris did put thought into their version of the calculations about Mercury-197, however we stand by our calculations. It would also like to point out that there are others than the major supplier of Mercury-197, and the other suppliers have been helpful to us in verifying our calculations. I believe the confusion as to the decay scheme of Mercury-197 should have been discussed between the physicist and the supplier of the isotope before they presented the isotope to the clinician. It will be noted, however, that even with Mr. Harris's and Dr. Roerer's calculated figures for E_B and the specific gamma-ray emission that the calculated dose of Mercury-197 still falls far below the calculated dose of Mercury-203.

In Dr. Blau's letter to the editor, it is obvious that statements out of context can be explained in many ways. It is difficult in a letter to enlarge on factual information. The tissue-to-background ratio mentioned in Dr. Blau's first paragraph was a misprint and should have been tumor-to-background ratio, and these were facts ascertained *in vitro* and *in vivo*. Dr. Blau's collimation comments are well-taken; however, it is a fact that 68-77 Kev is much easier to