

MEMORANDUM

DATE: July 19, 1954

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COLLECTION Protocols - Clinical  
BOX No. 4  
FOLDER Human Protocols 1950-1963

TO: BNL Committee on Use of Radioactive Isotopes in Humans  
FROM: Charles G. Foster, M. D.  
SUBJECT: Project H-34: Use of radiogallium (Ga-72) of high specific activity for the therapy of widespread metastatic malignancies involving bone.

It is proposed that radiogallium (Ga-72) of high specific activity be used in therapeutic amounts as a means of palliation in patients having pain from widespread osseous metastatic malignancies.

I. Proposed Procedure

Enriched gallium (98% Ga-71) in the form of metallic gallium or as gallium oxide ( $Ga_2O_3$ ) be irradiated in the Brookhaven National Laboratory Reactor for a period of three days, converted into gallium citrate and administered intravenously at once.  
Estimated activity: 3.31 mc/mg of enriched metallic Ga-71  
2.48 mc/mg of enriched  $Ga_2O_3$

Above calculations based on a flux of  $3.4 \times 10^{12}$  neutrons/sec/cm<sup>2</sup>, a thermal neutron cross section of 4.5 barns, an irradiation time of three days.

- II. From animal and human studies it has been shown that the concentration of radiogallium is greater in bone than in any other tissue. Furthermore, it has been demonstrated in humans utilizing tracer amounts of radiogallium that those portions of bone with metastatic deposits have concentrations of radiogallium which are four or more times greater than normal bone.

Previous investigations with stable gallium citrate in animals disclosed that gallium was toxic only when given parenterally. The LD<sub>50</sub> varied from species to species. In all species a cumulative effect was observed.

Clinical trials of radiogallium (Ga-72) citrate at the Oak Ridge Institute of Nuclear Studies in 21 patients and at the United States Naval Hospital, Bethesda, Maryland in four patients disclosed that the effects of metallic gallium were both toxic and cumulative as had been observed in animals.

In the aforementioned patients, the specific activity of the administered Ga-72 was 0.2 mc/mg of gallium. Approximately 60 mg. of

carrier gallium were given with each radiogallium treatment. Toxic manifestations due to metallic gallium were observed following the administration of a total of 300 to 1,920 mg. of gallium. From the above studies it was concluded that stable gallium toxicity was the limiting factor in the use of radiogallium (Ga-72) citrate as a therapeutic agent.

III. In the aforementioned investigations, natural gallium composed of 60% Ga-69 and 40% Ga-71 was irradiated in the Oak Ridge Pile, resulting specific activity being only 0.2 mc/mg of gallium.

The combination of enriched gallium and the greater flux of the Brookhaven Reactor will produce radiogallium (Ga-72) having a specific activity of 2.48 to 3.31 mc/mg of Ga<sub>2</sub>O<sub>3</sub> or metallic gallium respectively. Thus, the amount of radiogallium (Ga-72) citrate which can be given to a patient will be limited, not by stable gallium, but by whole body radiation, a limitation imposed by all radioactive preparations used in clinical medicine.

#### IV. Dosage Calculations

Assuming no excretion, the dosage in terms of equivalent roentgens/microcurie destroyed/gram is as follows:

$$\begin{aligned} \bar{B} &= 0.401 \text{ MEV} \\ T-1/2 &= 14.1 \text{ hours (0.59 days)} \\ I &= 13.22 \\ \frac{\gamma}{g} &= 200 \\ \frac{D}{B} &= 88 \times 0.401 \times 0.59 \times 1 \\ &= 20.8 \text{ er or } 19.3 \text{ rad/ucd/gram} \\ &= 20.8 \text{ er or } 19.3 \text{ rad/mcd/kilogram} \\ \frac{D}{\gamma} &= 1.44 \times 14.1 \times 13.22 \times 200 \times 1 \times 10^{-3} \\ &= 53.7 \text{ er or } 49.9 \text{ rad/ucd/gram} \\ &= 53.7 \text{ er or } 49.9 \text{ rad/mcd/kilogram} \\ D &= 20.8 + 53.7 = 74.5 \text{ er (69.2 rad)/ucd/gram} \\ B + \gamma &= 74.5 \text{ er (69.2 rad)/mcd/kg} \end{aligned}$$

Sample Calculation

If 117 millicuries of Ga-72 were administered intravenously to a patient weighing 56.8 kg, the whole body radiation dose (assuming no excretion) would be:

$$\frac{D}{B + \gamma} = \frac{117}{56.8} \times 74.5 = 153.5 \text{ er (142.6 rad)}$$

Assuming that the above patient had an osseous metastatic deposit which concentrated four times as much Ga-72 as the normal skeleton and that 50% of the administered Ga-72 was deposited in the skeleton, the dose delivered to the lesion would be as follows:

$$14.3\% \text{ of body weight} = \text{skeletal weight}$$

$$56.8 \times 0.143 = 8.1 \text{ kg (skeletal weight)}$$

$$\text{Amount of Ga-72 in skeleton} = 117 \times 0.5 = 58.5 \text{ mc}$$

$$\text{Concentration of Ga-72 in skeleton} = \frac{58,500}{8,100}$$

$$= 7.22 \text{ } \mu\text{c/gram of normal bone}$$

$$\frac{D}{B} = 20.8 \times (7.22 \times 4) = 600.7 \text{ er (558.7 rad)/gram}$$

$$\frac{D}{\gamma} = \frac{117}{56.8} \times 53.7 = 111.0 \text{ er (103.2 rad)/gram}$$

$$\frac{D}{B + \gamma} = 711.7 \text{ er (661.9 rad)/gram}$$

- V. It is proposed that the whole body radiation from a single dose of radiogallium (Ga-72) citrate shall not exceed 125 er in a patient with normal hematopoiesis not previously treated by other means. In patients who have received previous X-ray therapy or such agents as nitrogen mustard, triethylene melamine, urethane, folic acid antagonists, the effects from such therapy should be stabilized before radiogallium therapy is administered. For such patients, not more than 80 to 100 er whole body radiation should be delivered from a single dose of radiogallium even in the presence of normal hematopoiesis. In all instances, repeat courses of radiogallium should not be given until the effects from the previous dose have been observed. No patient with

a platelet count under 100,000/cm<sup>3</sup>, a white blood count less than 2,000/cm<sup>3</sup> or with a low hemoglobin which can be corrected only by means of frequent blood transfusions should be treated with radio-gallium except under unusual circumstances on an individual basis.

Approved:

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