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A Preliminary Report on the Use of Gallium⁷² in Clinical Tracer Studies¹

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DUDLEY (1-5) AND King (6, 7) have reported on the distribution of radiogallium in animals and on its excretion by both man and animals, while Mulry and Dudley (8), in 18 patients with radiographic evidence of malignant bone tumors, demonstrated increased deposition of gallium⁷² in the affected skeletal areas in 15. Conclusions based on these studies may be summarized as follows:

(1) Gallium⁷² is a short-half-life isotope (14.3 hours) with energetic gamma emissions (the value for I_{γ} is 13.3 compared with 8.47 for radium) and moderately energetic beta particles, with an average energy of 0.45 mev.

(2) Biological studies indicate that gallium⁷² has an early deposition in growing bone and that the more rapidly growing the bone the more rapid the uptake. It is excreted almost primarily by way of the kidneys, with a very small amount in the feces.

It is apparent from the data presented that this isotope might be employed as a diagnostic tracer in studying the spread and extent of certain types of bone tumor.

The purpose of this report is to present the preliminary results of a project utilizing gallium⁷² for clinical tracer studies. The objective was to evaluate this isotope as a possible diagnostic tool (a) in the determination of the spread of primary bone tumors to areas other than the primary site and (b) in the determination of the site and extent of early bone metastasis from malignant lesions in the soft tissues. The results presented here concern the preliminary part of this project, during which

72 tracer studies were performed on 63 patients. The advanced portion of the study is now under way with a simplified and improved technic and a more careful selection of patients. It is anticipated that the results will be more conclusive than those to be reported here.

A continuous study was made of a group of patients with proved cancer of a type likely to metastasize to bone. Gallium⁷²-tracer studies were repeated at three- to six-month intervals along with routine bone surveys at corresponding periods. The final evaluation cannot be made until sufficient time has elapsed for radiographic evidence of bone metastases to develop in a significant number of the patients. When this significant number is available, an attempt will be made to correlate the gallium studies with the radiographic findings.

PROCEDURE

A tracer dose (0.5 millicurie) of gallium⁷² citrate, prepared as described by Dudley (4), was administered intravenously. Counts were made by means of an end-window Geiger tube (1/2-inch diameter window with 3 1/2-mg./cm.² window thickness) shielded by 1 inch of lead. The distance between the window and end of the lead collimator, or the sleeve, was 1 inch. With the patient supine, skin surface counts were made at thirty-seven points over the skeleton, as indicated in Figure 1. Counts were made at six, twenty-four, and forty-eight hours following injection. A "body background" was determined at the six-hour interval by

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placing the collimator perpendicular to and at the same height as the mid-portion of the patient and parallel to the floor, at a distance of two meters from the patient. All counts were corrected for radioactive decay back to the time of administration of the radiogallium.

Fourteen patients (Table I) had definite bone metastases. Eight of this number showed increased gallium deposition in the metastatic areas, while in 3 cases the results were doubtful. In 2 of these latter cases (Nos. 12 and 19) there was involvement of one or more ribs with no

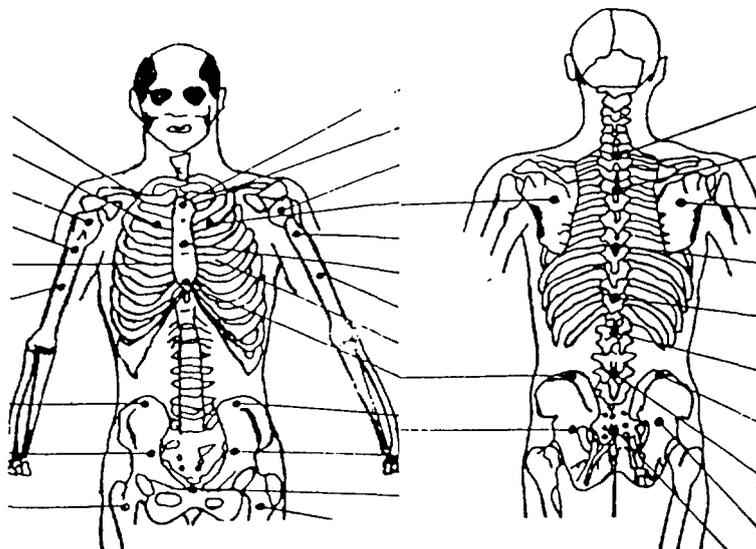


Fig. 1. Points routinely counted in radiogallium tracer studies. Additional points are counted when it is deemed necessary.

RESULTS

The results were expressed as a ratio between each individual count and the "body background." Evaluation of the results of each tracer study depended on the following arbitrarily chosen standards, each of which was deemed significant: (1) points having a ratio value of over 22 in the six-hour period; (2) points having an increase in the ratio value between the twenty-four- and forty-eight-hour interval.

Thirteen of the patients studied had breast carcinoma and had undergone radical mastectomy. There were 11 cases of carcinoma of the prostate and 5 cases each of carcinoma of the cervix, malignant tumor of the testis, and carcinoma of the urinary bladder. The remaining cases comprised malignant lung tumors, carcinoma of the colon, penis, tonsil, and skin, malignant melanoma, synovial sarcoma, liposarcoma, Hodgkin's disease, multiple myeloma, and 3 metastatic tumors of unknown origin.

other evident metastases. In 3 of the 14 patients, increased deposition in the bone lesions could not be demonstrated. Of these 3, No. 32 had a single, small lesion in the upper femur and No. 61 had involvement of the seventh cervical and first thoracic vertebra. The latter case was recently proved at autopsy to have been a case of bone erosion rather than bone metastasis.

In addition to cases with definite bone involvement by metastasis, 11 patients were demonstrated by x-ray to have hypertrophic arthritis (Table II). In some of these cases the arthritis was severe enough to mask any possible metastases. In 8 of this group, deposition of gallium⁷² was found to be definitely increased over the areas affected by the arthritis, which in every instance included the lower lumbar spine.

Five other patients had bone lesions which can only be listed as questionably metastatic in origin. In 2 of these patients

TABLE I: RESULTS OF GA⁷²-TRACER STUDIES IN PATIENTS WITH DEFINITE BONE METASTASIS

Diagnosis	Total Points of Increased Uptake*	Increased Uptake in Metastasis Areas	Diagnosis of Metastasis by
Carcinoma of Breast			
Case 1	13-2	Yes	X-ray and autopsy
Case 5	20-4	Yes	X-ray and autopsy
Case 10	4-8	Yes	X-ray
Case 12	9-7	?	X-ray
Carcinoma of Cervix			
Case 19	9-7	?	X-ray and biopsy
Case 23	8-5	Yes	X-ray and autopsy
Carcinoma of Prostate			
Case 29	7-6	Yes	X-ray
Case 32	4-2	No	X-ray
Case 33	3-3	Yes	X-ray and autopsy
Bronchogenic Carcinoma			
Case 34	0-6	No	X-ray
Carcinoma of Large Bowel			
Case 40	0-4	?	X-ray and autopsy
Synovial Sarcoma			
Case 58	0-5	Yes	X-ray and biopsy
Malignant Melanoma			
Case 61	1-2	No	X-ray
Carcinoma of Urinary Bladder			
Case 62	4-5	Yes	X-ray and autopsy

* The first row of figures in this column refers to points with a ratio value of over 22 six hours following gallium⁷² administration. The second row refers to points with an increased deposition of gallium between 24-hour and 48-hour counts.

there was increased gallium localization at the site of involvement; 2 showed no increase, and in the other the result was doubtful.

Unfortunately, no studies could be performed on normal individuals. In an attempt to compare the above results with cases without demonstrable bone involvement, the remaining 42 tracer studies were averaged as to the total points of increased uptake per study, using standards previously mentioned. The average for these cases was 4 points for the first standard, that is a ratio value of over 22 at the six-hour count, and 4 points for the second standard, namely, an increase in deposition between the twenty-four- and forty-eight-hour count. It should be emphasized that these results were on patients with proved diagnoses of malignant tumor.

All of the patients studied showed high values over the sternum, due no doubt to its superficial position. Also, in all of the breast cases high values were obtained over the site of the original lesion. As has been mentioned, these patients had

all undergone a radical mastectomy and it was recognized that the high value was probably due to the absence of the soft-tissue mass of the breast on the affected side.

TABLE II: CLINICAL TRACER STUDIES WITH GA⁷² IN PATIENTS WITH HYPERTROPHIC ARTHRITIS IN ADDITION TO CANCER

Diagnosis	Total Points of Increased Uptake*	Increased Uptake in Hypertrophic Areas
Carcinoma of Breast		
Case 13	4-2	?
Carcinoma of Urinary Bladder		
Case 14	6-5	Yes
Case 15	5-2	Yes
Case 16	0-6	Yes
Case 18	2-6	Yes
Carcinoma of Cervix		
Case 20	17-2	Yes
Carcinoma of Prostate		
Case 25	0-6	Yes
Case 31	12-3	?
Carcinoma of Penis		
Case 42	2-6	?
Hypertrophic Arthritis		
Case 46	0-8	Yes
Benign Prostatic Hypertrophy		
Case 47	8-14	Yes

* The first row of figures in this column refers to points with a ratio value of over 22 six hours following gallium⁷² administration. The second row refers to points with an increased deposition of gallium between 24-hour and 48-hour counts.

DISCUSSION

The increased gallium⁷² deposition in 8 of 14 patients with bone metastases observed in this study does not seem as significant as the results of Mulry and Dudley (8), who demonstrated increased deposition in 15 of 18 cases. This discrepancy may be due partially to the fact that in the majority of the cases in the present study bone involvement was still in an early phase, while those cases presented by Mulry and Dudley were more extensive.

It is also to be noted that the total points of increased uptake in patients not having radiographic evidence of bone involvement are higher (4-4) than some of the similar values for patients listed in Table I. We shall not attempt to explain this variation, although it should be stated that some of the former group of patients

might at the time of study have had actual bone metastases not yet evident radiographically.

In only 1 case thus far studied (No. 10) have metastases, discernible roentgenographically, developed following gallium tracer studies. In this case gallium⁷² studies performed five months prior to the first radiographic evidence of a metastasis demonstrated increased gallium deposition in nearly all of the metastatic areas evident at the time of the writing of this article.

In those cases in which more than one observation was made there was usually a discrepancy in areas of increased deposition. This may have been due to faulty technic or to actual changes in a particular area in the as yet unknown mechanism of gallium deposition in bone.

The fact that the patients with hypertrophic arthritis showed an increase in gallium deposition over the affected areas is compatible with the accepted belief that deposition of this element is greatest in areas of increased osteoblastic activity, such as bone proliferation, areas of bone repair, and areas of rapid bone growth.

In the second phase of this study now under way, the counting technic has been changed by using a more sensitive Geiger tube with a heavier collimator which has a more acute solid angle, and counts are now being made for a longer predetermined count interval. Patient selection has also been improved, and only those types of tumor that are known to metastasize to bone in a high percentage of cases are being studied. It is hoped that these changes of procedure will produce results which will be more conclusive than those presented here.

SUMMARY

1. Clinical tracer studies utilizing gallium⁷² have demonstrated increased gallium localization in 8 out of 14 patients with definite bone metastases.

2. Eleven patients with proved malignant growth showed no definite radiographic evidence of bone metastases but did have advanced hypertrophic arthritis. In 8 of these 11 cases there was increased deposition of gallium over the arthritic areas.

3. On the basis of these results, gallium⁷² does not appear too promising as a clinical diagnostic tool. It is anticipated that further studies will present more conclusive results.

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