

## Comparison of metrezoate-labeled gallium transmission with different 50, 60 and 75% concentrations in malignant lymphatic cells

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### ABSTRACT

Radiation therapy is considered as one of the main methods in cancer treatment. In this method, determination of exact location and geometric properties of tumor is necessary for treatment planning that leads to increased accuracy and output of treatment and reduction of healthy tissue dose. For this purpose, the aim of the present study has been physiological transmission of Gallium as a pharmaceutical carrier which is bonded with an X-Ray opaque media for treatment of Lymphatic tumor via Smart Radiotherapy method (Photoelectron therapy). Using radiography or CT scan has provided determination of geometric features of tumor.

**Key words:** Pharmaceutical chemical carriers; Gallium; Lymphatic tumor; Metrezoate complex; Smart Radiotherapy

### INTRODUCTION

The Radiation therapy is considered as one of the main methods in cancer treatment. In this method, determination of tumor location and its geometry is necessary for treatment planning. The time lapse in cancer patients causes a reduction of treatment prognosis in a way the chance of treatment comes close to zero. Unavailability of tumor geometric features leads to reduction of treatment precision and an increase in the normal tissue dose, leading to the reduction of treatment output, namely causing a decrease in the dose of tumor compared to the dose of normal tissue. Many efforts have been made around the world for cancer treatment and reducing the side effects of treatment methods. Drug carriers are substances that serve as mechanisms to improve the delivery and the effectiveness of drugs. So far, some drug carriers have been used in radiotherapy, chemotherapy and photodynamic therapy and also photoelectron therapy which have newly been proposed as a radiotherapy method with high efficiency; these are treatments via accumulation of a contrast media in tumor by a

drug carrier. [1] The results of surveys have shown that drug carriers which are used in chemotherapy have increased the output up to 45% [2] while the use of specific tumor marker in photoelectron therapy as a new method has shown the better results (increase output up to 25 times). As a whole, considering the results that have been presented by researchers based on a significant increase of treatment output on laboratory animals and cultured cells at the presence of pharmaceutical substances with high atomic number, the necessity of synthesis of the proper pharmaceutical complex seems essential to the transmission the drugs with high atomic number into the tumors. [3] Chemical compounds are used in nuclear medicine for radionuclide transfer to the specific organs. Gallium is a pharmaceutical carrier which has been used in nuclear medicine for the purpose of transmission of radioisotope into the lymphatic tumor. The aim of this research has been to produce a pharmaceutical complex and study its physiological transmission into the lymphatic tumors for treatment via Smart Radiotherapy method (Photoelectron therapy).

We used Gallium as a pharmaceutical carrier which was bonded with Metrezoate as an X-Ray opaque media with high atomic number. [4] Implementation of this research aimed at identifying and analyzing effective factors in transferring metrezoate complex with gallium 67 and 69 or special tumor markers for lymphatic tumors on cultured cells. Although gallium was more absorbed in tumors with lymphatic origin, large Cell lymphoma, Small cell Lymphoma and Bourkite cell Lymphoma were chosen, which multiplied in certain colonies with culture medium of gel. [5]Metrezoate complex and gallium 69 with concentrations of 50%, 60% and 75% were prepared in water and were added to these mediums. [6]Gallium in the periodic table of elements is placed [in the third main group and its characteristics is similar to trivalent aluminum. [7]Gallium69 and 67 were used as citrate with the same composition. Though gallium uptake is more in lymphatic tumors, Large Cell Lymphoma, Small cell Lymphoma and Bourkit Lymphoma are selected because they are malignant ones. These cells were proliferated in the certain colony in gel mediums. For testing, the colony number did not matter because the measuring of uptake volume percent in the cells was desired. [8]

## MATERIALS AND METHODS

Metrezoate complex and gallium 69 were prepared with concentrations of 50%, 60% and 75% in water. Considering the X-ray, opaque agents were typically injected to target cell with volume content of 125% (permitted mean dose). In each test, ten of the same medium were prepared from each group of aforementioned cell, half cubic centimeter of the complex were added to each medium in the manner that it was distributed in all medium surface. The experiment was repeated for each individual concentration. More accurately, the same procedure was repeated for each concentration in ten of other same mediums so that mean of ten measured concentrations for each cell and each group could be used. Then, in the intervals of 1, 2, 4, 8, 24, 48, 72 hours, the absorbed volume in the cells were measured. This volume follows the initial volume (one cubic centimeter) minus remained volume with cells in culture medium. The remaining volume was

measured through minus medium volume and the left volume of complex solution; in some cases the remaining solution was sprayed with syringes. While temperature, humidity, all of physical conditions and type of culture medium for all samples were the same, it has been expected that the remaining or absorbed volume in culture medium to have no significant difference. Even for the three cell types that were examined, these amounts were very close to each other. Table [1] lists the values of ten times testing and measuring for each of three cell types at different time intervals. Since the measurements of remained volume for determining exact time of maximum accumulation of markers in the cell colony was not sufficient, gallium scan test from culture medium at intervals of 1, 4, 24 and 72 hours were carried out. At first, marker solution in which gallium 67 was used was added in the form of physiological serum with specific activity of 50 MicroCi in five drops to the gelatin medium. The utilized process was determined based on normal prescription of gallium 67 to average content of 10 mCi for tumors with approximate mass of 50 gr. Culture bed scanning after adding gallium 67 displayed the image without proper contrast or resolution which proved to be useless. For this reason, after adding the solution at aforementioned time intervals before scanning each by gama camera, culture medium was rinsed by physiological serum solution until the amount of specific activity of gallium became visible.

## RESULTS

Results of tests on the lymph cells are shown in Table (1). A comparison of initial volume (one cubic centimeter) and residual volume at different time intervals showed that the total volume was not equal to absorbed volume in the cells plus the residual volume, as it absorbs some solutions in the culture medium, and this medium was the same for all cultures; consequently the different concentration (three type of concentration) did not have a significant effect on absorption percentage, yet more concentration caused more effective atomic number. Absorbed volume of field was determined using medium without cells. Cell test Results manifested that physicochemical property of gallium complex was similar to

gallium itself. Gallium played the role of carrier in this collection. The maximum amount of

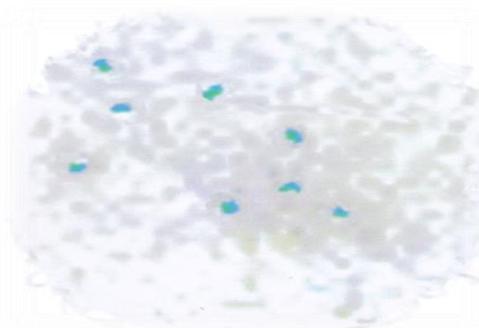
<b>Time interval measurement of residual complex size</b>	72	48	24	8	4	2	1
<b>The remaining volume</b>	.43	.425	.425	.405	.44	.4	.405
<b>The percent of remaining volume</b>	86%	85%	85%	81%	88%	79/5%	81%

complex which was added to culture medium after two hours conveyed 20% absorption in

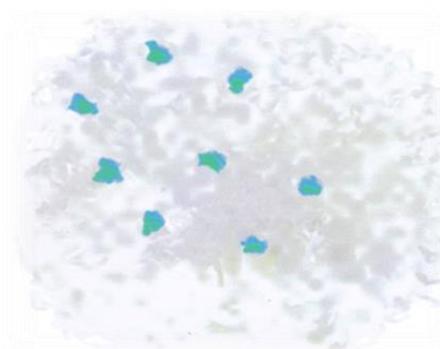
**Table 1.** residual volume values of complex markers (not absorbed) specified for lymphatic tumors in culture medium at different times.

cells and consequently effective atomic number of these cells achieved 20% more than adjacent cells. This process provides planning for treatment with new radiation therapy technique that has been the ultimate goal of this drug complex. Density of neoplasm's cell colony with lymphoid origin can be seen in scan images of Gallium 67 (Figure 1 to 4). This figure showed that the marker accumulation in the cell culture medium reaches a maximum after 4 hours. Colony activity measurement showed the following values: Diameter containers for neoplasm cultured colonies were 10 cm.

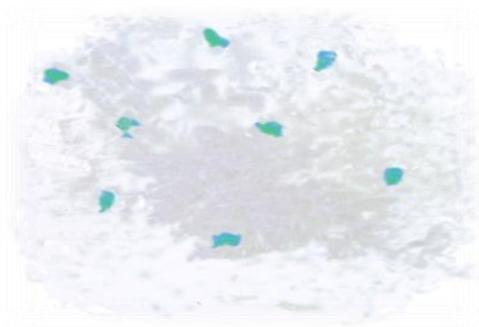
- 1 - 1-hour samples: 16 mCi: about 21 440 Kant.
- 2 - 4-hour samples: 29 mCi: about 36 250 Kant.
- 3 - 24-hour samples: 23 mCi: about 27 600 Kant
- .4 - 72-hour samples: 20 mCi: about 26 400 Kant Demonstrated.



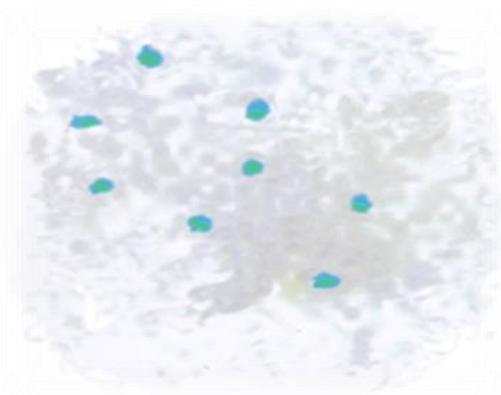
**Figure 1.** Image Scan of culture cells with lymphoid neoplasm origin with the marker solution of gallium 67, using a gamma camera hours after adding the solution



**Figure 2.** Image scan cell culture origin lymphoid neoplasm associated with a marker solution of gallium 67 with gamma camera used four hours after adding the solution



**Figure 3.** Image scan cell culture origin lymphoid neoplasm associated with a marker solution of gallium 67 using gamma camera 24 h after adding solution using Gallium metrozoate complex



**Figur 4.** Image scan cell culture origin lymphoid neoplasm associated with a marker solution of gallium 67 using gamma camera 72 h after adding solution

**Summary of final Results are as follows:**

1. It's better to use drug complex of gallium with Metrezoate in highest concentration of 75%. 2. Proper time for designing new treatment was between 24 to 48 hours after injection. 3. With a simple X-ray radiography more accurate time for each specific patient can be determined after 24 hours.

**DISCUSSION**

A research was conducted in oncology department of Minnesota University and the results were published in 2001. Since gallium absorption is more in neoplasm cells (about 40% higher than the average rate of other cells) and this property was more within lymphatic cells, result of using this complex on patients increased the efficiency to 45%. [8,9] Our calculation in the present study, which is in line with the findings of the aforementioned research, shows the efficiency increase to more than two thousand percent. [9,10]

*“The authors declare no conflict of interest”*

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