MEASURMENT OF TUMOR UPTAKE OF ^{99M} TC-DTPA – ^{10}B-CARBORANE COMPLEX IN BRAIN TO EVALUATE ^{10}B ABSORBED DOSE FOR NCT.

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ABSTRACT

Although neutron capture therapy (NCT) is a very promising technique for the treatment of brain tumors, it is very difficult to clearly evaluate the dose absorbed by the brain tumor. This paper will show how to use nuclear medicine to evalutate the ^{10}B dose aborbed by the brain tumor. ^{10}B carborane gadolinium complex was labelled with ^{99m}Tc and quality control showed 95 % of radiochemical purity. Scinticamera can tell the %uptake of ^{99m}Tc-DTPA – ^{10}B-carborane complex in brain tumor by selecting area of interest on tumor, the count rate was read and divided by the activity injected. Using %uptake of ^{99m}Tc-DTPA – ^{10}B-carborane complex of the tumor in brain, dose of ^{10}B absorbed by brain tumor can be evaluated. Nuclear medicine can be used instead of in vivo quantitation of boron using MRI only for the compound which can be labelled with suitable radionuclide. ^{99m}Tc is at the present time the most popular radionuclide for this purpose.

Keywords: BNCT, NCT, label, radionuclide, area of interest, tumor uptake.

INTRODUCTION

A factor limiting the development of NCT is the lack of drugs which will give tumor:brain uptake ratio higher than two popular compounds, Na2 B12 H11 SH (BSH) and p-dihydroxyborylphenylalanine (BPA) which have been authorised for clinical trials. So researhers from different countries are seeking ideal boron compounds which are suitable for NCT1-4. Working in nuclear medicine I can imagine, if chemists can synthesize something with optimum selectivity for cancer cells people in nuclear medicine will labell it with suitable radionuclide and inject it into the patients. Cancer can be eliminated as easy as ^{131}I has been used for some thyroid cancer.[5] Why do you still need NCT at that moment?

At present time brain tumor scan in Figure 1 shows the uptake of ^{99m}Tc-DTPA beautifully. This agent is rapidly filtered by the kidney, which is a disadvantage, so that it necessitates the injection of a larger amount of radioactivity, but its advantage is that, it provides a higher tumor-to-brain activity ratio.

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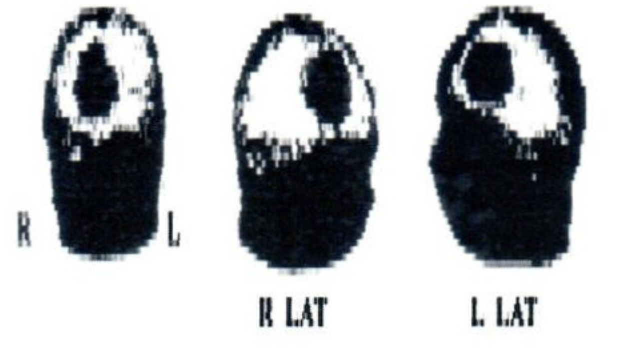

Fig. 1 Brain scintiphotographs obtained with ^{99m}Tc-DTPA in different projections 1 hour after injection. Diagnosis: glioblastoma multiforme.

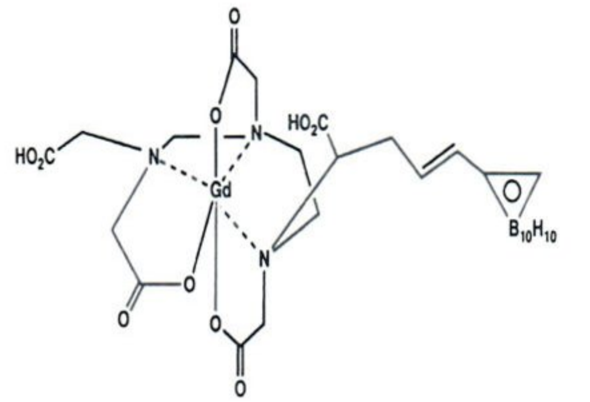

Fig. 2 ^{10}B carborane Gd-DTPA complex.

Since ^{99m}Tc-DTPA provides a higher tumor-to-brain activity ratio. Labelling ^{10}B carborane Gd-DTPA complex with ^{99m}Tc was performed aseptically. ^{10}B carborane Gd-DTPA complex can be labelled with ^{99m}Tc but it is not the same as labelling DTPA. So I would like to present this paper how to label ^{10}B carborane Gd-DTPA complex with ^{99m}Tc and how to use ^{99m}Tc-DTPA ^{10}B carborane complex in NCT.

MATERIALS

1. Cation exchange resin.
2. Sterile distilled water.
3. ^{10}B carborane Gd-DTPA complex from Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-77, Japan.
4. Stannous chloride dihydrate, E-Merck, Darmstadt, Germany.
5. Calcium chloride, Anhydrous, J.T. Baker chemical Co., Phillipsburg, N.J. 08865.
6. Sodium hydroxide pellets, E-Merck, Darmstadt, Germany.
7. Nuaire larminar flow biological safety cabinet.
8. Hetosicc Freeze dryer type CD-13.2
9. Sterile disposible syringes were used in all procedures.

METHODS

1. Cleaned glassware and equipment were wrapped in wrapping paper, and sterilized in autoclave.
2. Dissolve ^{10}B carborane Gd-DTPA complex 0.5 g in 50 ml of Sterile distilled water and let it stand in room temperature for 6 hours then pass the solution through cation exchange resin.
3. Put 0.55 g of $CaCl_2$ in the solution from 2, stir until the solution is clear. Add 40% NaOH 0.35 ml pH = 8
4. Dissolve $SnCl_2.2H_2O$ 1 g in 5 ml of concentrated HCl. Filter the solution through 0.22 mm millipore filter. Stir the filtered solution at least 30 minutes.
5. To the solution in 3, add 0.15 ml of solution from 4, the pH is 4
6. Sterilize the solution by 0.22 mm membrane filtration into pre-sterilized evacuated vials. Aseptically transfer 1 ml each of this solution to sterile 7 ml serum vials. Freeze dry for 24 hour, seal under vacuum after freeze drying, each vial contains 0.6 mg stannous chloride.
7. Take one vial from 6 and add 1.5 ml=35 mCi of ^{99m}Tc, shake well.
8. Find the radiochemical purity using instant thin-layer chromatography (ITLC-SG) as shown in Figure 3

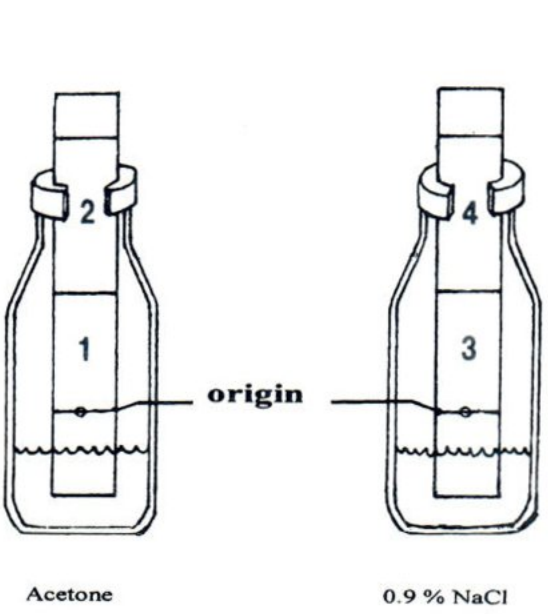

Fig. 3 Two strip mini- instant thinlayer chromatography system (Left) $^{99m}TcO_4^-$ sepa ration, (right) ^{99m}Tc-hydro lyzed reduced technetium (R-^{99m}Tc) separation.

A. Put about 1 ml of acetone into the left vial and 1 ml of 0.9% NaCl into the right vial.
B. Spot 2 μl of solution from 7 at the bottom pencil lines of the two strips.
C. Immediately place the bottom of the strips in the appropriate solvents and allow the solvents to migrate until they reach the top pencil lines.
D. Cut each strips at its central pencil line into sections1, 2, 3 and 4.
E. Count each section in a well scintillation counter.
F. Calculate % $^{99m}TcO_4^-$:

$$= \frac{\text{net activity of section 2}}{\text{(net activity of section 1) +(net activity of section 2)}} \times 100$$

Calculate % R-^{99m}Tc:

$$= \frac{\text{net activity of section 3}}{\text{(net activity of section 3) +(net activity of section 4)}} \times 100$$

Calculate %bound

$= 100 - (\%^{99m}TcO_4^- + \%\ R\text{-}^{99m}Tc)$.

RESULT AND DISCUSSION

After labellingThe ^{99m}Tc be in place of ^{157}Gd as shown in Figure 4.

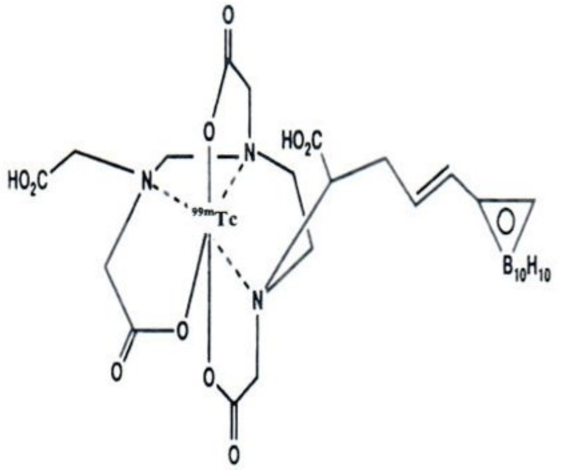

Fig. 4 Shows structure of ^{99m}Tc-DTPA-^{10}B-carborane complex.

When ^{99m}Tc-DTPA-^{10}B-carborane complex 20 mCi is injected to glioma patients the doctor can tell which patient is suitable for NCT. So it will be very useful. After injection the counts from the camera should be recorded not only at the brain, but also the counts of the wholebody should be recorded in order to get % brain tumor uptake.

A key requirement of NCT is the selective delivery of an adequate concentration of ^{10}B to tumors (15-30 mg ^{10}B/ g tumor).[6] For the 7 gram tumor need at least 105 mg of ^{10}B, if % brain tumor uptake is 1% at least 10.5 g of ^{10}B must be given to the patients. So the key requirement of NCT can be solved by nuclear medicine method.

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