^{131}I-Chlorotoxin dosimetry in liver using MCNP simulation code

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ABSTRACT

Chlorotoxin is a 36 amino acids peptide, which is able to block chloride channels isolated from mouse brain. A derivative of chlorotoxin is synthesized and it is labeled by iodine 131; then animal experiments carry out on rats. Multiple organ doses may be calculated with biological distribution results in rats with labeled compounds using simulated MCNP4C code. Human dose can be calculated using the dose distribution in rats with a conversion ratio for dose distribution. Chloramine T is our method for marking, and electrophilic substitution reactions are methods for iodize of peptides. Simulation of a human phantom to evaluate dose distribution was done using simulation code MCNP4C. To evaluate the dose distribution in the human body, using this code and the accumulated activity in each organ tissue dose is calculated. To study the biological distribution of the radiotracer 131I, 0.37 MBq radiotracer was injected into rat via the tail vein. The accumulated activity in each organ with the agent "ID / g" is determined. Biological distribution of 131I-chlorotoxine in the normal rats is obtained. Its Decay constant in the liver is 0.07h and the effective half-life of the radiotracer is 10h in rat liver. The total number of particles found in the leak from liver tissue was reported 67600. Liver tissue dosimetries originating from other sources (thyroid tissue, stomach, kidney, right & left lung, spleen, and pancreas) were examined. Then, the overall dose to the target tissue will be calculated. Leaked beta particles in liver itself (self-dose) are the most delivered dose to the liver (98%); it is for gamma rays 1.1%, while its source is adjacent tissues in addition to liver (cross-dose); Because of low atomic number of the tissue, delivered dose originated from Bremsstrahlung (braking radiation) is low (0.9%). Radiation dose to the liver in intravenous injection of 0.37 MBq ^{131}I-chlorotoxine radiotracer is 3.44 * 10-6.

Key words: Toxin Chloride; MCNP Code; ^{131}I; Liver; Dosimetry

INTRODUCTION

Chlorotoxin is a 36 amino acids peptide, which has been extracted the first from the venum of scorpion "Leiurus quinquestriatus". Synthetic type of this peptide named TM 601 commercially [1]. It has been reported that extracted toxin from venum of Israeli scorpion is able to block chloride channels isolated from mouse brain [2]. There was not an appropriate marker for definite and certain diagnosis of gliomas; it needs to tumor sampling and histological evaluations. Chlorotoxin is used in diagnosis and treatment of gliomas as a marker [3-5, 11, 12]. This peptide is able to pass through tissue & blood-brain barriers [3, 6, 10] and attach on lamellipodia of cancer cells with phosphatidyl inositide of a phosphorylated lipid [7]. Results of preclinical and clinical studies have shown that attaching of 131I to this peptide could increase therapeutic effects of the peptide [3]; they synthesized a derivative of chlorotoxin and carried out animal experiments on the rats. Multiple organ doses may be calculated with biological distribution results in rats with labeled compounds using simulated MCNP4C code [15, 16, and 17]. Human dose can be calculated using the dose distribution in rats with a conversion ratio for dose distribution.

MATERIALS AND METHODS

Chemicals were purchased from Fluka and amino acids from Novabiochem Company.

Institute of Nuclear Science and Technology provided MCNP4C simulation code. This peptide synthesized on the solid phase coloumn, based on FMOC standards. Chloramine T is our method for marking, and electrophilic substitution reactions are methods for iodize of peptides. Simulation of a human phantom to evaluate dose distribution was performed using simulation code MCNP4C. To evaluate the dose distribution in the human body, tissue dose using this code and the accumulated activity in each organ is calculated. Simulation code MCNP4C works on basis of Monte Carlo method and the transport of nuclear particles. We calculate the dose using F6 tally. To study the biological distribution of the radiotracer 131I, 0.37 MBq radiotracer was injected into rat via the tail vein. The same amount of activity as the control was excluded. After intervals of 1, 4 and 24 hours, the rat were sacrificed and dissected. The accumulated activity in each organ with the agent "ID / g" (Injected dose per gram) % is determined.

Equation (1):

$$ID/g\% = \frac{\frac{\text{Organ Count} - \text{B.G}}{\text{Total Count} - \text{B.G}}}{W} * 100$$

Organ Count: detector counting from the organ

Total Count: detector counting from the control sample

W: The organ weight in grams

B.G: detector counting from background radiation

Basic equation of MIRD (medical internal radiation dose): The total radiation dose to the target tissue (t) can be calculated using total radiation received from the source tissues (s):

Equation (2): $D(t) = \tilde{A}s \,.S(t,s)$

Equation (3): $S(t,s) = \Sigma(\Delta i \times \varphi i / Mt)$

$\tilde{A}s$ (μCi-h): accumulation of activity in the source tissue

Mt (g): Mass of the target tissue

Δi (g.Rad /μCi.h): Fixed equivalent dose for specified type of each particle is here by the index i [8, 13]. φi: a fraction of the energy emitted by in particles of the source tissue that are absorbed in target tissue and has been set with Monte Carlo calculations [9, 14]. S-factor: The absorbed dose per activity unit is accumulated in source tissues.

In order to transfer the experimental animal data to Monte Carlo simulation that was designed for a human phantom, it is necessary that the animal data is converted to human data. In this method, data of animal organs as a percentage of the injected activity per gram of tissue have been reported. It also assumes that percentage of the injected activity in the human body is equal to the fraction of the total mass of the human body to the total mass fraction of animal organs that at %ID of animal body is multiplied. The equation is as follows:

Equation (4):

$$\%ID_{\text{Human organ}} = \%ID_{\text{Animal organ}} \times K$$

Equation (5):

$$K = \frac{\left(\frac{\text{Organ mass}}{\text{Body mass}}\text{Human}\right)}{\left(\frac{\text{Organ mass}}{\text{Body mass}}\text{Rat}\right)}$$

RESULTS

After synthesis and labeling processes, labeled compound were injected into rat. Rats were sacrificed at different times, and their considered organs were dissected. Counts were performed by counting NaI (Tl). Obtained Data about biological distribution is on diagram (1).

If we assume that a fraction of the injected activity A0 is present in the tissue, and accompanied by an exponential disposing, two processes will be effective in reducing the activity: Biological elimination with half-life Tb, physical decay constant of radionuclides with half-life Tp. These factors in the effective half-life as the following are considered.

Equation (6): $T_e = T_p \times T_b / (T_p + T_b)$

Equation (7): $T_e = Ln2/\lambda_e$

Data were fitted with an exponential function. Figure 2 shows the counting results for liver tissue. Curve, that is $A = A0\ e^{-\lambda t}$. Thus, the effective decay constant in the liver 1 – 0.07h is obtained. And using equation (7), effective half-life of the radiotracer in rat liver is 10h. Integrating the surface under the curve count – time at the total time period represents the total number of Leaked particles in the tissue.

Table 1: Radius of the sphere on the tissues

Cell no.	Tissue	Radius (cm)
1600	Stomach	4
2200	Liver	9
2500	Pancreas	10
2600	Spleen	3

This process was performed for all considered tissues; the result was a count of 67,600 for liver tissue. Using MCNP simulation program, mass of human tissues from human phantom is obtained; mass of similar animal tissues using average tissue of rats was applied in the calculations. Accumulate counts in tissues of human phantom in figure 3 is given. Simulation calculations were performed using MCNP code. In this program, the beta energy of 0.61 MeV and gamma of 0.38 MeV related to ^{131}I were considered as the source of radioactive. Using enclosing sphere rejection method, complex tissues in terms of geometry, were defined as the source. Radius of the sphere on the tissues was calculated using Exceed software version 11.0.0; some results are given in Table (1). F6 Tally is used at program to obtain the amount of leakage energy by beta particles, Bremsstrahlung (braking radiation), and Gamma photons in target tissue. In order to increase the quality factor, the programs were run for 30 minutes. Because of low energy electrons less the 1keV do not provide any direction, energy threshold of 10-3 MeV were considered in MCNP program for exclusion these particles.

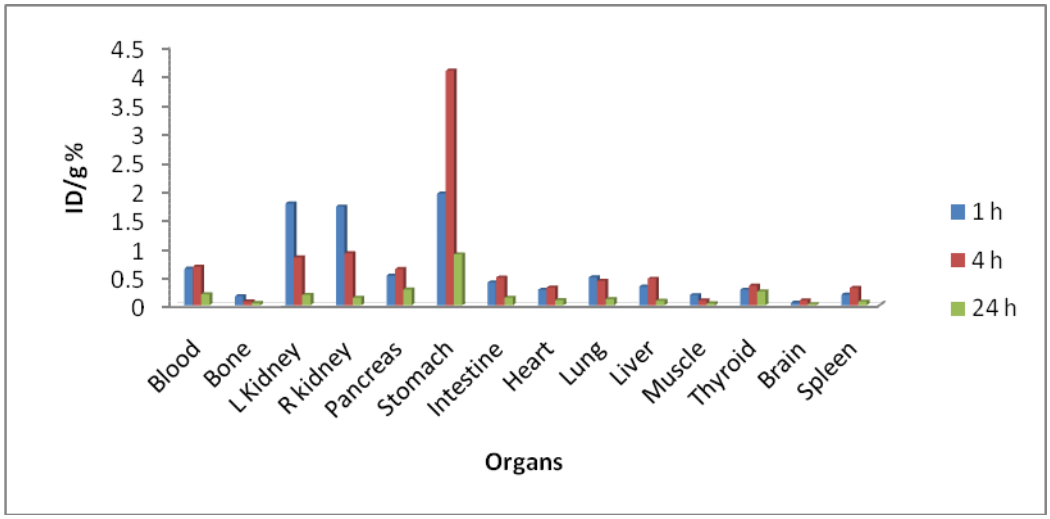

Figure 1. Biologicad distribution of 131I-chlorotoxine in body of normal rats

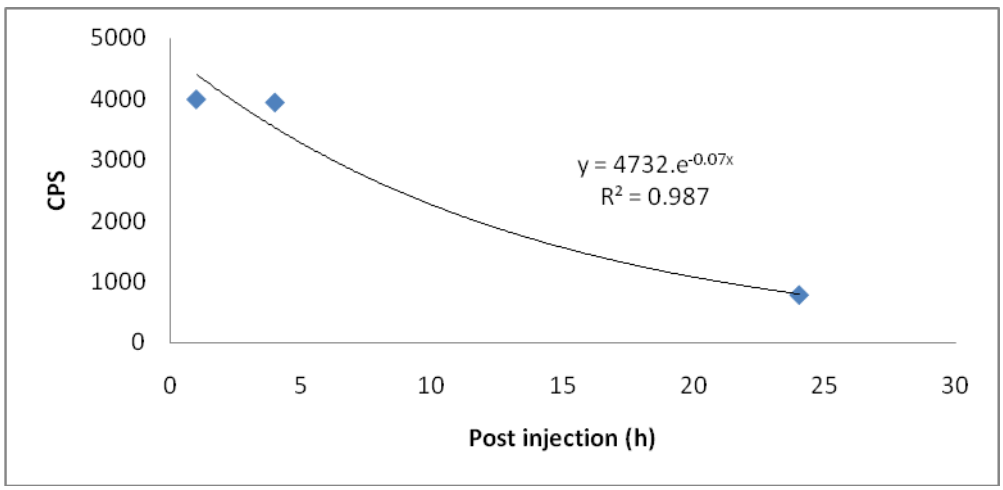

Figure 2. Calculation of decay constant for the liver tissues

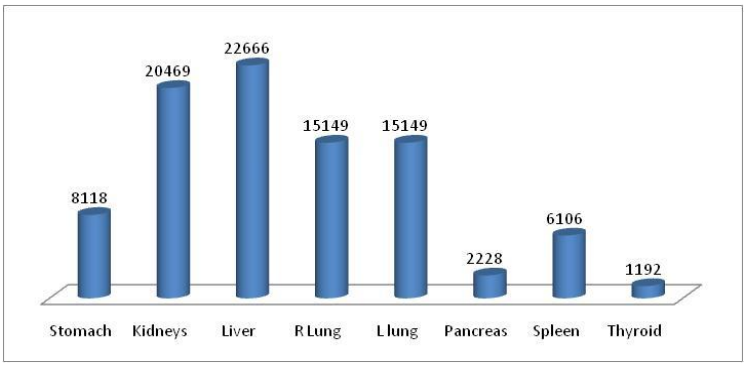

Figure 3: Counting of accumulate in human tissues

In present study, Liver tissue dosimetries originating from other sources (thyroid tissue, stomach, kidney, right & left lung, spleen, and pancreas) were examined. Entering the command FM6 1.602E-7, the energy accumulated in the target tissue for a particle accumulated in the source was converted to mGy; with effecting aggregate counting of the total tissues, Total dose to target tissue could be calculated. Table 2 shows the output of the MCNP program.

Table 2- F6 tally output in liver tissue for beta particles, gamma rays and braking radiation (MeV/g)

Cell no.	Tissue	X -Ray	Beta	Gamma
1600	Stomach	6.46E-05	6.46E-05	6.46E-05
2100	Kidneys	7.75E-05	7.75E-05	7.75E-05
2200	Liver	6.61E-03	7.04E+00	8.18E-01
2300	R Lung	1.96E-04	1.53E-04	3.79E-02
2301	L lung	9.07E-07	1.83E-05	8.23E-03
2500	Pancreas	4.49E-05	5.34E-05	1.45E-02
2600	Spleen	1.99E-05	1.68E-05	8.58E-03
2900	Thyroid	7.55E-06	3.60E-06	2.23E-03

DISCUSSION

Beta particles of ^{131}I have 0.61Mev maximum energy and range of them is approximately millimeter [10, 11].

If the beta sources located in tissue, the particles deposit their energies in tissue because the beta particle have millimeter rang therefore the source located in liver can deposit whole beta energies in it. The gamma rays in liver tissue may not fully deposit their energies in liver but gamma rays in surrounding tissue reach to liver and can deliver their energies to liver. The bremsstrahlung radiation is low because the components of liver have low effective atomic number. Evaluation of delivered dose to the liver tissue for beta particles, Bremsstrahlung (braking radiation), and gamma rays shows that leaked beta particles in liver itself (self-dose) are the most delivered dose to the liver (98%); it is for gamma rays 1.1%, while its source is adjacent tissues in addition to liver (cross-dose); Because of low atomic number of the tissue, delivered dose originated from Bremsstrahlung (braking radiation) is low (0.9%).

Radiation dose to the liver in intravenous injection of 0.37 MBq ^{131}I-chlorotoxine radiotracer is $3.44 * 10^{-6}$. Human phantom dosimetry extrapolation also showed that excreting organs such as the liver, will not receive a significant radiation dose. Radiation dose of iodine-131 is more by the non-penetrating radiations; contribution of penetrating radiation is little; because of high-energy photons for the radionuclide and the small size of the rat.

CONCLUSION

The MCNP simulation code is useful program to simulate the absorbed dose in the liver and other similar tissues. Basic equation of MIRD was done by MCNP code for calculation of liver dose. By intravenous injection 0.37MBq of therapeutic radioisotope in animal, the contribution of percent absorbed dose in liver for beta, gamma rays and bremesstrahlung was 98, 1.1 and 0.9 respectivley.

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