MICRODOSIMETRY OF ASTATINE-211 AND COMPARISON WITH THAT OF IODINE-125

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Abstract. ^{211}At is an alpha and Auger emitter radionuclide and has been frequently used for labeling of different kind of chemical agents. ^{125}I is also known as an effective Auger emitter. The radionuclides which emit short range and high LET radiations such as alpha particles and Auger electrons have high radiotoxic effectiveness on the living systems. The microdosimetric data are suitable to clarify the real radiotoxic effectiveness and to get the detail of diagnostic and therapeutic application principles of these radionuclides. In this study, the energy and dose absorptions by cell nucleus from alpha particles and Auger electrons emitted by ^{211}At have been calculated using a Monte Carlo calculation program (code: UNMOC). For these calculations two different model corresponding to the cell nucleus have been used and the data obtained were compared with the data earlier obtained for ^{125}I. As a result, the radiotoxicity of ^{211}At is in the competition with ^{125}I. In the case of a specific agent labelled with ^{211}At or ^{125}I is incorporated into the cell or cell nucleus, but non-bound to DNA or not found very close to it, ^{211}At should considerably be much more radiotoxic than ^{125}I, but in the case of the labelled agent is bound to DNA or take a place very close to it, the radiotoxicity of ^{125}I should considerably be higher than ^{211}At.

1. INTRODUCTION

^{211}At as an alpha and Auger emitter radionuclide has an extremely high potential application in cancer therapy; particularly, in molecular radiotherapy. In the literature ^{211}At has been frequently used for labeling of different kind chemical agents. As some interesting examples, the chemical agents such as Cholesterol[1], tyrosine[2], 2-methyl-1,4-naphtoquinol bis(disodium phosphate) known as synkavit[3], tamoxifen[4], deoxyuridine[5] and others have been labelled with ^{211}At. According to the chemical characters of these carrying agents ^{211}At can be directed into the different localization zones in the living systems such as intracellular, cellular or nuclear zones (for a review see Ref. 6). As is known well, the radionuclides which emit short range and high LET radiations such as alpha and/or Auger electrons should be incorporated into the nucleus of cancer cells for resulting high radiotoxic effectiveness. Especially, it is experimentally observed by several authors that high radiotoxicity of ^{125}I as an effective Auger emitter was observed when it was incorporated into the structure of DNA or found very close to it [7–9]. This means that the dose distribution within the cell nucleus at the microscopic scale is very important for comparison of real differences between the radiotoxic effectiveness of different radionuclides. It is also important to outline that the microscopic dose calculation methods should consider the real cell nucleus composition. For this reason, such a calculation method should use the cell nucleus models having practically equal elemental composition. In the literature, the water models are generally used for these calculations. In reality, the cell nucleus differs from water in the lower oxygen content, which is replaced principally by carbon and nitogen. In this context, šnak[10] recently developed a dose calculation program for Auger electrons of ^{125}I within the cell nucleus (code: UNAKNUC). In this study, the same program has been adapted to the Auger electrons and alpha particles emitted by ^{211}At.

Figure-1 shows the decay scheme of ^{211}At. According to the data given by Stepanek et al.[8], 6.3 Auger electrons and 1 alpha particle are emitted by ^{211}At per a single decay. In reality, four different alpha particles of 5.98 MeV, 7.45 MeV, 6.89 MeV, 6.57 MeV with intensities of 0.418, 0.576, 0.0033, 0.0031, respectively, are emitted by ^{211}At and its very short half-lived daughter radionuclide ^{211}Po. The Auger electron spectrum of ^{211}At has been also given by the same authors.

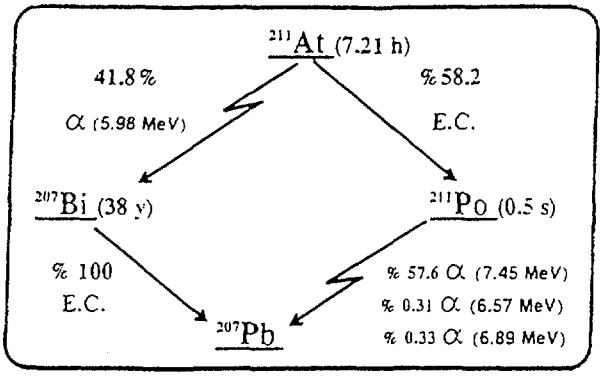

FIG. 1. Decay scheme of ^{211}At.

In this study, two different models of cell nucleus have been used for microdosimetric calculations of ^{211}At and these were compared with that of ^{125}I.

2. CALCULATION METHOD

2.1. Total energy absorption per a single decay of ^{211}At

The basic calculation method for microscopic dose distribution from Auger electrons in a cell nucleus per a single decay of ^{125}I placed at the nucleus center was earlier described in detail by šnak [10]. In that method a calculation program coded as UNAKNUK was used. The same calculation method has been also used in this study for the Auger electrons emitted during the decay of ^{211}At, and this method has been also adapted to the microscopic dose calculations from alpha particles. Finally, the total energy absorption by a cell nucleus per a single decay of ^{211}At could similarly be calculated. The principle of this method was based on the use of the real chemical compositions of radiation absorbing media. For this reason, the dose absorption differences between similar absorbing media, but having a little chemical composition difference can easily be distinguished by this calculation method. So, the energy absorption by a cell nucleus model representing the approximate elemental composition can be distinguished than that of a water model of cell nucleus. In the first model, a sphere of 4000 nm radius filled with a chemical material having approximately the real chemical composition of cell nucleus was used. In the second model, the same sphere was considered as filled only with water (Fig.-2).

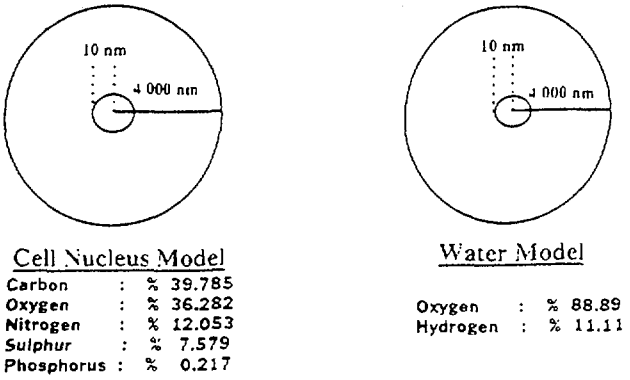

FIG. 2. Schematic representation of the cell nucleus models used in this study.

The Auger electron spectra given by Stepanek et al.[11] and Charlton and Booz [12] were used for ^{211}At and ^{125}I, respectively.

2.2 Monte Carlo calculations

Starting from the single radionuclide decay, a Monte Carlo calculation program (code:UNMOC) has been developed for cumulative dose absorption calculations by cell nucleus as a function of radionuclide decay time and radionuclide activity. The basic principle of these calculations is randomly distribution of radionuclides within the cell nucleus, and randomly determination of radionuclides decayed within the decay period considered. The number of radionuclides randomly distributed within the cell nucleus is, of course, depended on the corresponding radionuclide activity incorporated directly into the cell nucleus. For a given activity of ^{211}At and ^{125}I the dose absorptions as function of decay times have been calculated. For these calculations the position of each radionuclide within the nucleus has been randomly determined by the Monte Carlo program. The decayed radionuclides have been also randomly chosen by the same program. Then, the emission directions of each alpha particle or Auger electron have been again randomly determined and the distance covered by each particle within the nucleus has been found. So, the partial energy absorption per decay and the total absorption corresponding to the number of decayed radionuclides by the nucleus in a decay time have been calculated.

The accuracy of Monte Carlo data is, of course, depended on the number of the probability events repeated during the calculation procedures and the most accurate results can only be obtained when the number of probability events is as high as possible. For this reason, in this study the number of probability events was fixed as about 1000. Nevertheless, as is seen in Fig. 3, the data have practically been stabilized after about 300–400 events, and became sufficiently reliable.

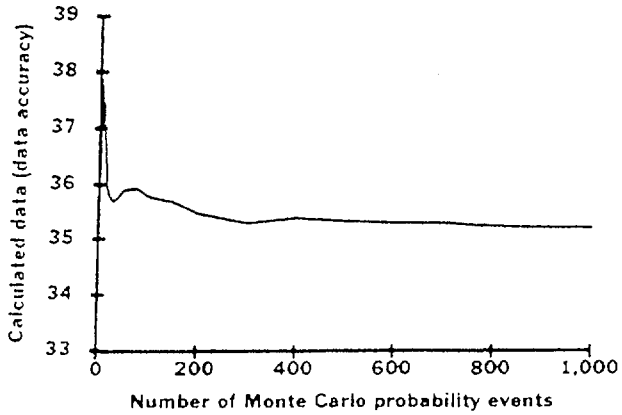

FIG. 3. Data accuracy as a function of Monte Carlo probability events repeated during the calculation procedures.

3. RESULTS AND DISCUSSION

3.1 Comparison of energy and dose absorptions by a cell nucleus per a single decay of ^{211}At or ^{125}I

Figure-4 shows the dose absorption in a cell nucleus as a function of distance from the decay center of a single ^{211}At or ^{125}I radionuclide just placed at the center of the nucleus. As is seen well, the dose absorption within the cell nucleus is not homogeneous and is very high at the decay vicinity, but rapidly decreases with the distance from the decay center. The absorbed dose by a spherical volume having the radius of about 10 nm that means at the DNA scale, is about 19382 Gy per a single decay of ^{211}At; but, this is much more higher for ^{125}I as being about 27042 Gy. Contrarily, the total energy absorption by the whole nucleus is 27.62 mGy for ^{211}At while this is about 5.65 mGy for ^{125}I.

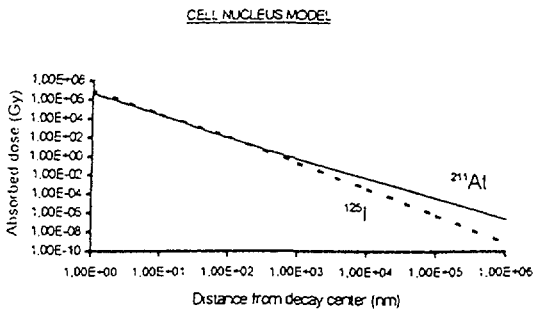

FIG. 4. Dose absorption variations as a function of distance from decay center of ^{211}At or ^{125}I radionuclides.

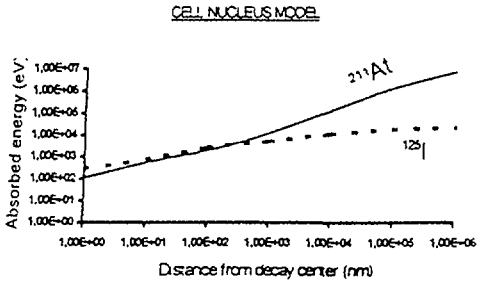

FIG. 5. Energy absorption variations as a function of distance from decay center of ^{211}At and ^{125}I radionuclides.

Figure 5 shows the similar energy absorptions from ^{211}At and ^{125}I. The total energy absorbed by the whole nucleus is about 50.84 keV for ^{211}At and 10.40 keV for ^{125}I. At the DNA scale these are 557 eV and 777 eV for ^{211}At and ^{125}I, respectively.

3.2 Comparison of the partial influence of alpha particles and Auger electrons of ^{211}At

The data given in Figs 4 and 5 are the total energy and dose values of ^{211}At. During the decay of this radionuclide alpha particles and Auger electrons are emitted simultaneously. Either alpha particles or Auger electrons are short range and high LET radiations. For this reason, it is difficult to judge which is more effective on the radiotoxicity of ^{211}At. Figs 6 and 7 show the individual influence of alpha particles and Auger electrons of ^{211}At. As is seen, the alpha particles are much more effective than the Auger electrons for whole cell nucleus; but contrarily, the influence of Auger electrons are more effective than alpha particles at the DNA scale.

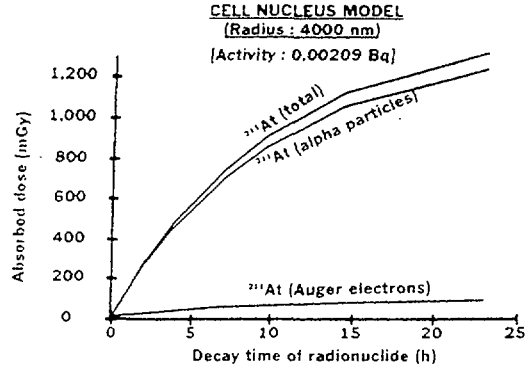

FIG. 6. Partial and total dose absorptions from alpha particles and Auger electrons of ^{211}At in a cell nucleus of a radius 4000 nm.

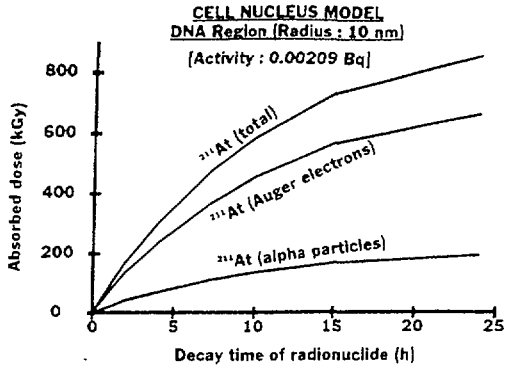

FIG. 7. Partial and total dose absorptions from alpha particles and Auger electrons of ^{211}At in a spherical volume of 10 nm radius corresponding to the DNA region.

3.3 Dose absorption data as a function of decay time of radionuclide

In practical applications many radionuclides can simultaneously be incorporated into the cell nucleus and are, of course, non-homogeneously distributed within the nucleus depending on the chemical properties of carrying radiopharmaceuticals. For this reason, the total dose absorption as a function of decay time or activity of the radionuclide is important for diagnostic and therapeutic applications. Figs 8 and 9 show the variations of dose absorption for having the equal activity of

0.00209 Bq in the first 24 h for whole nucleus and DNA scale. This activity corresponds to the ^{125}I activity which has been given by Humm and Charlton [13] as the initial activity per cell, to reduce the cell population to 37 % survival, and produces an average 100 single strand break (dsb) within two cell divisions (48 h). As is seen, the dose absorption increases rapidly as a function of decay time either for ^{211}At or ^{125}I, but after 24 h dose absorption rate is considerably slowing down for ^{211}At, while it is continuing to increase for ^{125}I. It is also important to outline that at the DNA scale, i.e. in a sphere of 10 nm radius the dose absorption from ^{125}I is considerably higher than that of ^{211}At.

3.4 Comparison of data for cell nucleus and water models

The energy absorption per a single decay of ^{211}At or ^{125}I, and the dose absorption as a function of decay time have been also repeated using the water model corresponding to a cell nucleus. As is noted in the introduction section, the water vapor or liquid water has been generally used in the literature as a radiation absorbing medium corresponding to cell or cell nucleus structure (for a short review of these microdosimetric approaches see the introduction section of Ref. 10). The comparison of our cell nucleus model with the water model was earlier done by Ünak [10] for ^{125}I. In this study the similar comparison was also repeated for the dose absorption calculations of ^{211}At. Figs 10 and 11 show these comparisons. Briefly, the chemical structure of water has the ability of higher energy absorption from the radiation than the real cell nucleus structure, while its density is slowly lower than that of a cell nucleus structure. Of course, this is a result of a lower oxygen content of cell nucleus than water, which is replaced principally by carbon and nitrogen.

4. CONCLUSION

The data obtained in this study show clearly that the radiotoxicity of ^{211}At as known as an alpha and Auger emitter radionuclide is in the competition with that of ^{125}I. In the case of a specific agent labelled with ^{211}At or ^{125}I is incorporated into the cell or cell nucleus, but non-bound to DNA or not found very close to it, ^{211}At should considerably be much more radiotoxic than ^{125}I, but in the case of the labelled agent with ^{211}At or ^{125}I is bound to DNA or take a place very close to it, the radiotoxicity of ^{125}I should considerably be higher than that of ^{211}At (see Figs 8 and 9).

On the other hand, in practical diagnostic and therapeutic applications of a radionuclide the critical dose calculations should be done using as really as possible chemical compositions of the target materials of body, if not, the serious mistakes between the real and calculated doses will be inevitable.

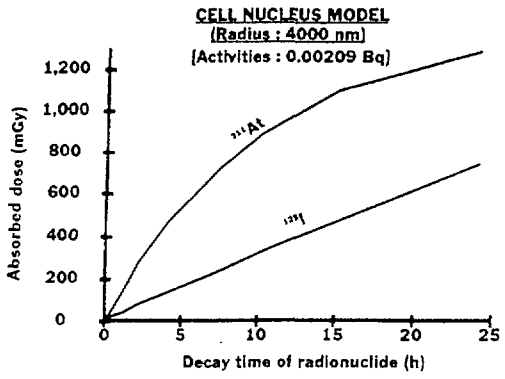

FIG. 8. Comparison of dose absorptions from ^{211}At and ^{125}I in a cell nucleus of 4000 nm adius.

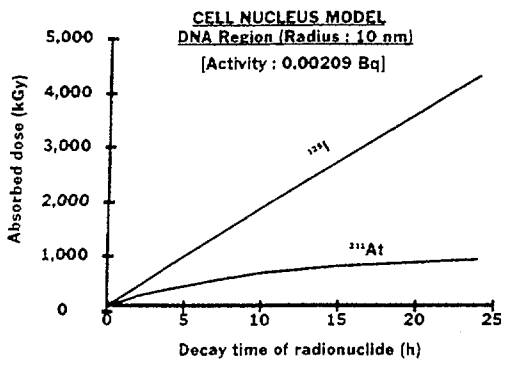

FIG. 9. Comparison of the dose absorptions from ^{211}At and ^{125}I in a spherical volume of 10 nm radius corresponding to the DNA region.

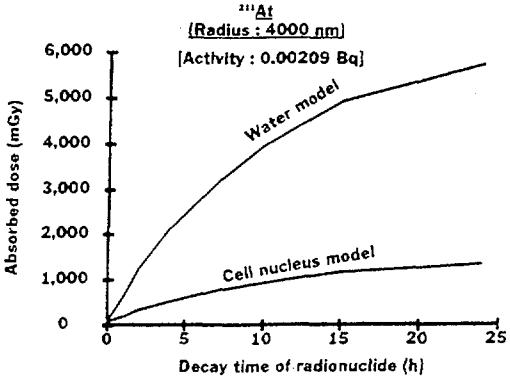

FIG. 10. Comparison of dose absorptions from ^{211}At in a cell nucleus of 4000 nm radius for two different cell nucleus models.

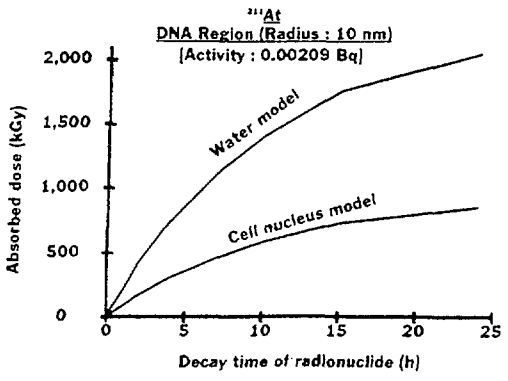

FIG. 11. Comparison of dose absorptions from ^{211}At in a spherical volume of 10 nm radius corresponding to the DNA region for two different cell nucleus models.

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