ABSORBED DOSE ESTIMATES AT THE CELLULAR LEVEL FOR ^{111}In

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ABSTRACT

Microdosimetric calculations of Auger and conversion electrons of ^{111}In have been evaluated for single cell and cell clusters. A VsBasic program has been used to calculate stopping power, LET, range values and deposited energies per decay for Auger and conversion electrons of ^{111}In. Chemical composition of cell has been taken into account in this model and results were compared with water medium. Besides, total absorbed doses have been calculated for the radionuclides distributed randomly within the cell and clusters. Cross-fire irradiation has been considered for clusters of cells. In this case, absorbed doses per cell within a cluster were found significantly higher than absorbed doses per single cell depending on the cluster size. Results were concluded that ^{111}In is a promising radionuclide for therapy of micrometatases which their width is mm or smaller.

Key Worlds: Microdosimetry, ^{111}In, Cell, Internal Conversion Electrons, Auger Electrons

1. INTRODUCTION

^{111}In is clinically used Auger electron emitting radionuclide which is 2.8 days physical half life. ^{111}In emits about 18 Auger or conversion electrons per decay with energies of approximately 2.7 eV to 532 keV.[1] The ejection of the electrons leaves the decaying atoms transiently in a state of high positive charge.[2] The burst of low energy electrons results in highly energy deposition in an extremely small volume around the decay site, and molecules immediate vicinity of decaying atoms will be irradiated by these electrons. In addition, the dissipation of the potential energy associated with the high positive charge and its neutralization may act concomitantly and lead to some of the observed biological effects.[3]

Microdosimetric approach in cellular dimension has been considered for ^{111}In in this work. Generally microdosimetric approaches assume the cell to be composed of water. However the electron stopping power properties of a cell is different from water. For that reason, the microscopic energy deposition within the cell from, Auger and conversion electrons released by ^{111}In have been calculated considering the estimated elemental composition of the cell. Model has been applied as a QBASIC program previously to other Auger emitters, alpha emitting and beta emitting radionuclides such as ^{125}I, ^{131}I, ^{201}Tl, ^{204}Tl, ^{51}Cr, $^{186/188}$Re, ^{211}At and concordant results have been obtained with the literature. [4-8] Stopping power or LET values of a chemical mixture or chemical compound largely depends on the percentage atomic weights of the medium according to this method. Ranges, total deposited energies and dose values were computed after calculations of stopping powers and LET values of medium atoms.

2. CALCULATIONAL METHOD

VsBasic program has been used in calculations. VsBasic is a friendly programming language which can be used under Windows. The program has been used to dose calculations for $^{186/188}$Re, $^{67/68}$Ga and ^{131}I previously.[7-8] Total emitted energy per decay, absorbed energy fragments per cell, stopping powers, LET (linear energy transfer) values, and ranges were calculated. Besides, absorbed energy values have been calculated for random decays per cell proportional with decay constants and results compared with other works.

Radionuclide decay data were obtained from NUDAT.[1] A cell is assumed as a sphere of 5000 nm radius filled with chemical composition mathematically. Cell volume and weight were supposed to be $5.23\ 10^{-10}$ cm^3 and $5.23\ 10^{-10}$ g, respectively.[9] Cell constitutes many organic molecules including oxygen, nitrogen, phosphorous atoms incorporated proteins, fats, sugars molecules as well as water molecules. Although cell and water consist of atoms of low atomic weights, water contains hydrogen and oxygen, cell consists of additionally some other atoms like carbon, nitrogen, phosphorous. Therefore, chemical composition of the cell was considered in this model. Data for chemical composition of the cell was taken from ICRU Report 44.[10] Radionuclides were supposed to be distributed randomly inside the cell. It was assumed that one decomposition occur in one hour at the beginning. This is the activity of 0.000278 Bq/cell. Starting from single radionuclide decay, a Monte Carlo calculation program has been applied for cumulative calculations of

the dose absorption by a cell as a function of decay time and radioactivities of ^{111}In. The basic principle of these calculations is random distribution of the radionuclides within the cell, and random determination of those radionuclides that decay within the decay period considered. For these calculations, the Monte Carlo program has randomly determined the position of each radionuclide within the nucleus. The same program also randomly chooses the decaying radionuclides. The emission direction of each particle was then randomly determined and the distance covered by each particle within the nucleus was found. So, the partial energy absorption per decay and the total absorption corresponding to the number of decayed radionuclides by the cell in decay time period have been calculated.

Cross-fire irradiation has been considered for clusters of cells. The same cluster and the same cluster sizes with Hartman and coworkers were used for our calculations.[11] However ^{111}In was suggested homogenously spread in the whole cell in our work. On the other hand, we used ^{111}In electron spectra of Nudat.

3. RESULTS AND DISCUSSION

Table-1 represents electron energy spectra, radiation intensity, cell doses, calculated and NUDAT's Δ_i (gGy/MBq-h) values of ^{111}In. Total emitted electron numbers and emitted electron energies of ^{111}In is given in Table-2. Total emitted energy is 97.069 keV. Auger electrons and conversion electrons emit 6.3764 keV and 90.6926 keV, respectively.

Table-3 shows percentage of absorbed electron energies within cell and water from conversion electrons and Auger electrons of ^{111}In. The absorbed energy per decay of ^{111}In is 6.6527 keV/cell (6.85% of the total released energy). On the other hand, if the cell composition is accepted as water, absorbed energy is 4.2432 keV/water (4.37% of the total released energy). Deposited energy is 1.56 times higher in cell comparing to water composition. For example, 79.28% (5.2740 keV) of absorbed energy comes from Auger electrons, 20.72% (1.3786 keV) of absorbed energy comes from conversion electrons within cell. If the cell volume is assumed as water 93.69% (3.9753 keV) of absorbed energy comes from Auger electrons, 6.31% (0.2679 keV) of absorbed energy comes from conversion electrons. Consequently, cell deposits higher energy than water according to our model.

Figures 1-2 represent energies versus to distance for conversion electrons and Auger electrons of ^{111}In. Conversion electrons give 1.52% and 0.30%, while Auger electrons deposit 82.71% and 62.34% of energies in cellular dimension and water in the same volume of the cell, respectively. Results show that cellular dose is low according to total emitted electron energies for ^{111}In however dose distribution is not homogenous in the cell, while Auger electrons deposit most of their energy within cell; conversion electrons deposit a lesser amount of their energies according to Auger electrons. On the other hand, there is heterogeneity of dose distribution since Auger electrons give a considerable dose in cellular dimension. Consequently, 6.85% and 4.37% of the total emitted energy of ^{111}In is absorbed within a single cell and water as the same volume of cell, respectively.

Cross-fire effect provides considerable doses to adjacent cell in radionuclide therapy. It follows that the radiation dose received by any individual cell is a resultant of cross-fire radiation emitted from radionuclide targeted to adjacent cells as well as radiation from radionuclide taken up by the cell itself. Hartman and coworkers investigated dose distributions of subcellular ^{131}I and influence of the cell size and cross-fire irradiation in clusters of cells. They reported that cross-fire irradiation can be major contributor to the nuclear dose in clusters of more than six cells.[11] While absorbed doses did not change for Auger electrons, they increased 8 – 15 times for internal conversion electrons if the cluster size goes up 51 to 800 cells in our work (fig. 3).

The dimension of tumor is very important in cross-fire effect. For very small tumors (micrometastases) whose diameter is less than particle range, absorption of radiation energy is inefficient, a proportion of this energy being deposited outside the tumor. This implies that very small microtumors may be underdosed (and hence less easily cured) than slightly larger ones.[12] O'Donoghue and coworkers have shown that the optimal tumor size (diameter) is slightly grater than the mean particle range for each radionuclide.[13]

4. CONCLUSION

Conversion and Auger electrons contribute considerable doses to total absorbed doses. Though most of the absorbed doses come from Auger electrons inside the cell. Though we found significant differences between water and cell according to calculations that have supposed the chemical compositions of cell as water. On

the other hand, cross-fire irradiation supplied significant amount doses for clusters especially for conversion electrons.

Consequently, ^{111}In has a good potential for radionuclide tumor therapy. However since the particular ranges of the internal conversion electrons are within mm dimension it may be better for therapy of tumors which are width of mm and smaller micrometastases. Although conversion electrons contributions to total cellular doses are minor, it should be considered especially in larger dimensions because of crossfire effect.

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ACKNOWLEDGEMENT

Author have been granted by the Abdus Salam ICTP regular associateship during a part of the work. The author thank to the Abdus Salam ICTP for the support.

Rad. Type	*Energy (E)* (eV)	*Radiation Intensity (W)*	*E x W* (eV)	*Given energy to cell* (eV)	*Δi (cell)* (gGy/MBq-h)	*Δi (water)* (gGy/MBq-h)	*NUDAT Δi* (gGy/MBq-h)
1 AU	2720	1	2720	2673.7269004	0.0015622	0.001589263	0.001567568
2 AU	19300	0.1566	3022.38	2077.0316065	0.0012136	0.00176594	0.00172973
3 CE	124100	0.000044	5.4604	0.3296546	$1.926x10^{-07}$	$3.19045x10^{-06}$	0
4 CE	144570	0.079	11421.03	535.8858374	0.0003131	0.006673171	0.006540541
5 CE	146790	0.000021	3.08259	0.1413055	$8.256x10^{-08}$	$1.80112x10^{-06}$	0
6 CE	150040	0.0000041	0.615164	0.0270461	$1.58x10^{-08}$	$3.59433x10^{-07}$	0
7 CE	150700	0.0000008	0.12056	0.0052709	$3.08x10^{-09}$	$7.04418x10^{-08}$	0
8 CE	167260	0.01	1672.6	61.9532627	$3.62x10^{-05}$	0.00097728	0.000972973
9 CE	170510	0.0019	323.969	11.5595690	$6.754x10^{-06}$	0.000189291	0.000189189
10 CE	171170	0.000426	72.91842	2.5967365	$1.517x10^{-06}$	$4.26054x10^{-05}$	$5.40541x10^{-05}$
11 CE	218640	0.0494	10800.816	261.2588269	0.0001527	0.006310787	0.006216216
12 CE	241330	0.00781	1884.7873	39.0480077	$2.282x10^{-05}$	0.001101259	0.001081081
13 CE	244580	0.00151	369.3158	7.4832087	$4.372x10^{-06}$	0.000215787	0.000216216
14 CE	245240	0.000301	73.81724	1.4927818	$8.722x10^{-07}$	$4.31305x10^{-05}$	$5.40541x10^{-05}$
15 AU	2840	0.11	312.4	306.7357419	0.0001792	0.000182532	0.000189189
16 AU	20100	0.016	321.6	216.5266857	0.0001265	0.000187907	0.000189189
17 CE	509100	0.107	54473.7	392.1397086	0.0002291	0.031828328	0.031351351
18 CE	532800	0.018	9590.4	64.7103336	$3.781x10^{-05}$	0.005603555	0.005540541
Total		1.5580	97069.012	6652.65	0.0038871	0.056716257	0.055891892

Table. 1. Electron energy spectra, radiation intensity, cell doses and Δi (gGy/MBq-h) values of ^{111}In

Table. 2. Total emitted electron numbers and emitted electron energies for ^{111}In

	Tot. Auger	**Total $E_{Auger}W_{Auger}$ (keV)**	**Total Conversion**	**Total $E_{con}W_{con}$ (keV)**	**Total Electron**	**Total EW (keV)**
^{111}In	1.2826 82.32%	6.3764 6.57%	0.2754 17.68%	90.6926 93.43%	1.5580	97.0690

Table. 3. Absorbed electron energies and per cent ratios of absorbed energies within cell and water medium of ^{111}In

	Cell			**Water**		
	Auger	*CE*	*Total*	*Auger*	*CE*	*Total*
Absorbed Energy (keV)	5.2740	1.3786	6.6527	3.9753	0.2679	4.2432
%	79.28%	20.72%	100.0%	93.69%	6.31%	100.0%

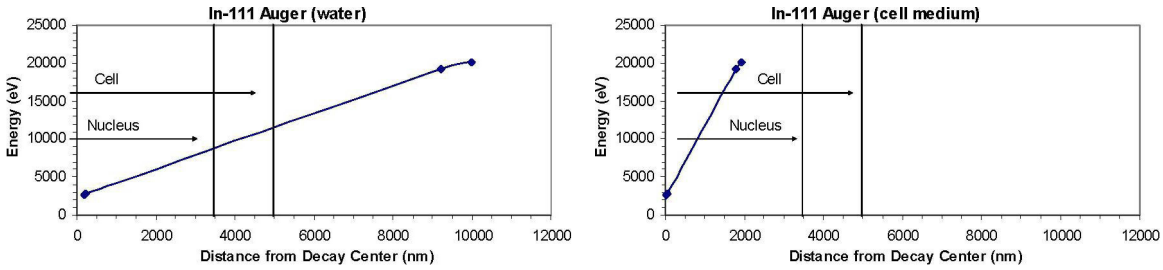

Figure. 1. Auger electron energies as a function of distance from decay center for Auger electrons of ^{111}In

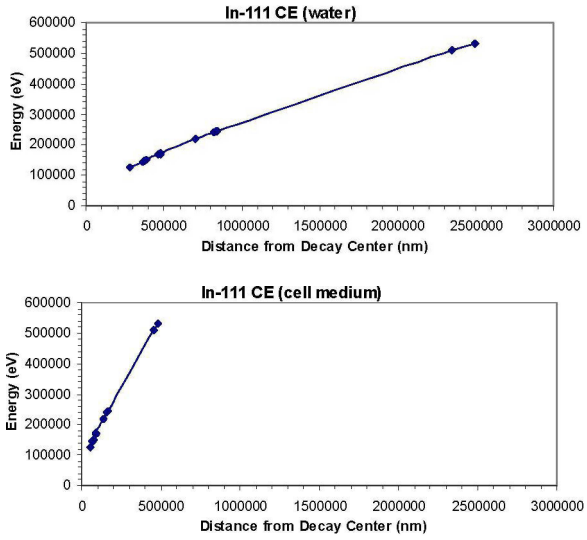

Figure. 2. CE electron energies as a function of distance from decay center for CE electrons of ^{111}In

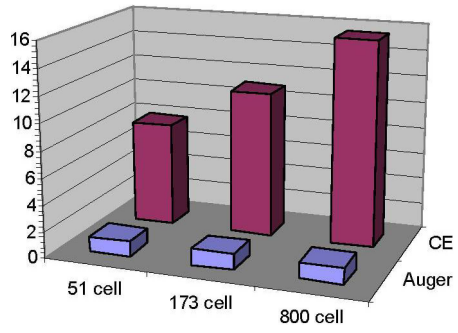

Figure. 3. Cross-fire irradiation effect for several cluster sizes for Auger and conversion electrons of ^{111}In