Development of a User Application for Stochastic Analysis of Dose to Cell Nucleus from Alpha Particle Exposure

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1. Introduction

High-linear-energy-transfer (LET) radiation, such as alpha particles, delivers energy in a discrete manner among micron-sized target volumes. Hence, mean dose estimate for the cells *in vitro* cannot inform the real situation of cellular exposures.

Geant4 is an open-source Monte Carlo toolkit that offers several physics models of radiation interactions with matter [1]. In this study, a user-application has been developed to simulate the exposure of cells in vitro to alpha particles using the Geant4 simulation modules. The application enables doses to individual cell nuclei to be characterized by the average nucleus dose accompanied by the probability density function of the dose.

2. Methods

Geant4 toolkit with the standard electromagnetic physics processes was used to develop the user-application for simulating the α-particle tracks. The statistical estimation of nucleus dose will be evaluated by comparing with experimental observations. In experimental setup, non-homogeneous cellular doses are due to not only discrete energy depositions by alpha particles but also due to geometrically non-uniform irradiation of cells *in vitro*.

Cells are exposed to alpha particles in the alpha particle irradiator in the Radiation Bioengineering Laboratory at Seoul National University (SNU) [2], as shown in Figure 1. Geometrical parameters of cell and nucleus, cell dish, Mylar film, radiation source, and source to target distance were set as variables to be assigned by the user. Parametric values chosen for the simulation in this study are listed in Table 1. About 3.7×10^6 cells filled the bottom of the cell dish. Cells are exposed to alpha particles coming from the Am^{241} disc source. For the experiment with cells in a dish, the exposure duration can be chosen to result in up to 1 Gy of average dose to cell nuclei in the dish.

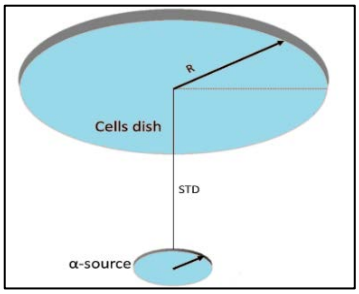

Fig. 1. Parametric illustration of the geometrical modelling of cell dish and alpha particle-emitting disc source.

Table 1: Values for geometrical parameters used in this study.

Parameter	Dimension
cell diameter	15 μm
nucleus diameter	5 μm
source diameter	9.5 mm
cell dish diameter	35 mm
Mylar film thickness	4 μm
source to target distance	24 cm

3. Results

Table 2 summarizes the fraction of alpha particles entering the dish and hitting any cell nucleus and the mean number of hits among the nuclei hit at least once, which vary depending on the mean nucleus dose. Higher mean number of nucleus hits than the ratio of hit nuclei implies that some of hit nuclei were hit more than once.

Table 2: Hit probability, mean number of nucleus hits, and ratio of hit nuclei varying with the average nucleus dose.

Average nucleus dose (Gy)	0	0.1	0.3	0.5	0.7	1
Mean number of nucleus hits	0	0.44	1.31	2.18	3.05	4.36
Ratio of nuclei hit at least once	0	0.35	0.72	0.88	0.95	0.98
Ratio of non-hit nuclei	1	0.65	0.28	0.12	0.05	0.02

The mean dose of cell nuclei was calculated using the following equation:

$$\bar{D}_{nucleus} = \int D\, p(D) dD = \sum D_n\, p(D_n)$$

Where D_n is the dose of cell nucleus and $p(D_n)$ is the fraction of cell nuclei in the cell dish with the dose D_n. The dose distribution was calculated for cell nuclei exposed to varying average doses.

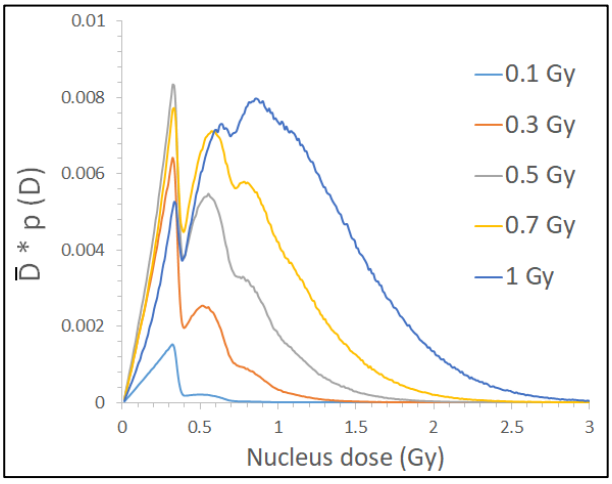

Fig. 2. Distributions of nucleus dose for a group of cells exposed to varying average doses. To better distinguish the profiles, individual probability densities were multiplied by their average doses.

The variation in nucleus dose was caused by varying chance of cells being hit depending on their location. Cells near the center had greater chance of being hit and received more energy than cells near the edge of the cell dish. Doses of cell nuclei in the cell dish differed by about 30% as shown in Figure 3.

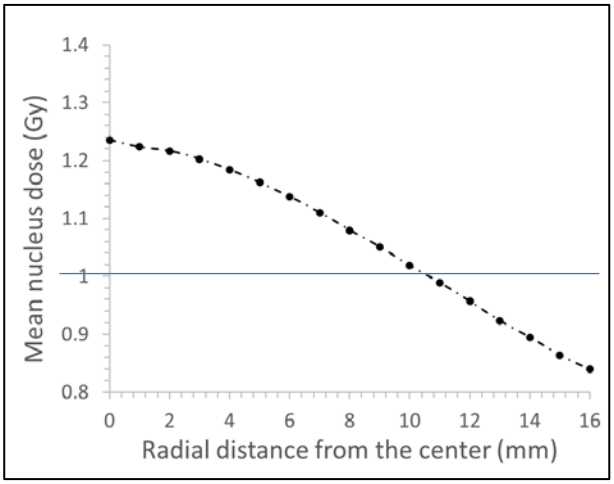

Fig. 3. Calculated mean nucleus dose as a function of the radial distance of cell from the cell dish center.

Additional variation in nucleus dose resulted from varying initial kinetic energy of alpha particles entering the cell nucleus. This is due to the stochastic energy loss of particles travelling from the source, entering the cell cytoplasm, and reaching the nucleus. The probability distribution of the energy alpha particles entering energy is presented in Figure 4.

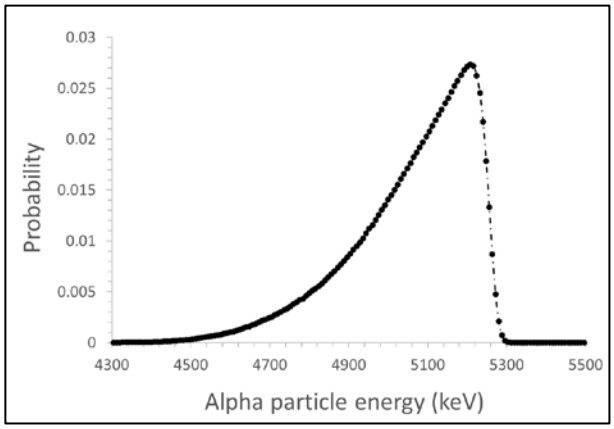

Fig. 4. Probability distribution of the initial kinetic energy of alpha particles entering the cell nuclei in the cell dish.

4. Conclusion

A GEANT4-based user application has been developed to calculate statistical variations in dose of cell nucleus. This application will be utilized in future-studies correlating the biological observations of alpha particle irradiated cells *in vitro* with computational estimates of physical damage to the cells.

REFERENCES

[1] Agostinelli, S. et al. GEANT4—a simulation toolkit. Nuclear instruments and methods in physics research section A: Accelerators, Spectrometers, Detectors and Associated Equipment 506, 250-303 (2003).

[2] Lee, K. M., Lee, U. S. & Kim, E. H. A practical alpha particle irradiator for studying internal alpha particle exposure. Appl Radiat Isot 115, 304-311 (2016).