Analysis of Dose-Rate Effect at Alpha Particle Exposure Based on Statistical Variability of Radiation Interaction with Cellular Targets

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1. Introduction

Macroscopic quantities such as mean dose, dose rate, and LET have traditionally been used to analyze the impact of radiation on exposed targets. From macroscopic point of view, cellular response becomes more evident with increasing dose, dose rate and LET of radiation [1, 2]. Hence, the dose and dose rate effectiveness is recommended to be considered in radiation risk or bio-effect assessment. In our earlier studies on dose rate effectiveness in cellular targets [3, 4], conflicting data were obtained from X-ray and alpha particle exposure at doses of less than 1 Gy. From X-ray exposure, hyper-radiosensitivity was observed at doses below 0.4 Gy and was diminished with an increasing dose rate. From alpha particle exposure, cells better survived as dose rate increased at dose below 0.5 Gy.

In this study, we simulated the interaction of alpha particles with cellular targets in a microdosimetric framework, focusing on the distribution of particle hits on cells. By calculating the probability of non-hit cells and the distribution of energy deposition to hit cells under different irradiation conditions, we have clarified the mechanisms underlying the observed contradictions.

2. Methods

2.1 Experimental setup for test data

The α-particle irradiation system at the Radiation Bioengineering Laboratory of Seoul National University (SNU) was implemented in Geant4 to replicate the experimental conditions. Alpha particles emitted from an Am-241 disk source were transported through a helium medium, passed through the 4-μm-thick Mylar bottom of the cell dish (35 mm in diameter), and subsequently reached the cell layer, which was modeled as a 35-mm-diameter layer with a nominal thickness of 5 μm.

Table I summarized the specifications of alpha particles entering the cell layer in the experiment to implement mean doses of 0.5 and 1 Gy delivered at two different dose rates [5].

Table I: Irradiation conditions of experiments in [5]

Dose rate (Gy/min)	Mean Energy of alpha particles entering cell dish (MeV)	Mean LET of alpha particles entering cell dish ($keV/\mu m$)	Activity-time* (μCi-sec) Dose (Gy)	
			0.5	1
0.05	3.54	113	2.23E8	4.45E8
0.1	1.99	164	1.13E8	2.23E8
0.5	3.54	113	2.28E8	4.55E8
1.0	1.99	164	1.14E8	2.28E8

* Total disintegration of Am-241 nuclei during exposure

2.2 Geant4 Simulation of Alpha Tracks in Cells

The G4EmStandardPhysics_option4 physics list in Geant4 was used to model particle interactions. This high-precision electromagnetic physics package is optimized for low-energy charged particle transport and provides accurate treatment of multiple scattering, ionization, and secondary electron generation. Its use ensured reliable tracking of α-particles through the helium medium, Mylar layers, and the cell layer, thereby enabling precise estimation of energy deposition patterns under the experimental irradiation conditions.

2.3 Calculation of Specific Energy

Particle tracking data from Geant4 were analyzed in MATLAB to evaluate the interactions in each ensemble of N cells randomly distributed on a circular disk. For each traversal through a cell located at radial distance *r*, the imparted energy was calculated as the product of the particle's intracellular path length and the corresponding LET at that position within the cell. This deposited energy was normalized by the cell's mass to obtain the position-dependent single-event density $f_1(z;r)$.

For a cell located at radial distance *r* from the disk center and under an irradiation time *T*, the mean number of hits per cell, $\mu(r,T)$, was estimated from the fluence reaching the cell layer. Hit probabilities for 0, 1, or multiple events were then derived according to the Poisson distribution (Eq. 1).

$$(1)\ f(z;D) = \frac{1}{N}\sum_{n=1}^{N}\sum_{k=0}^{\infty}\frac{\mu(r_n,T)^k}{k!}e^{-\mu(r,T)}[f_1(z_n;r_n)]^{*k}$$

In particular, the case $k = 0$ corresponds to a Dirac delta function at $z = 0$, representing cells with no energy deposition. For $k \geq 1$, the distribution of deposited specific energy was obtained from the k-fold convolution of the single event density $f_1(z; r)$.

Here, D denotes the macroscopic mean dose delivered to the entire cell population, obtained as the average energy imparted to all cells divided by the total mass of the population. Thus, although energy deposition in every individual cells statistically varies, the distribution $f(z; D)$ is normalized such that its expectation value corresponds to the prescribed mean dose D (Eq. 2).

$$(2)\ \bar{z} = \int_0^\infty z f(z; D) dz = D$$

3. Results

3.1 Microdosimetric Quantities

Table II summarizes the non-hit probability (p_0), representing the fraction of cells that received no particle traversal. As expected, p_0 decreases with increasing dose, reflecting the reduced likelihood of cells remaining untraversed at higher dose. At the same mean dose, however, the values showed little dependence on dose rate when the geometrical setup of irradiation was identical. Furthermore, difference in non-hit probability was obvious due to different geometrical setup of irradiation, regardless of dose rate. Different geometrical setups are responsible for different energy and corresponding LET of alpha particles hitting cells.

Figure 1 presents the probability density functions (pdfs) of specific energy in a cellular target and corresponding cumulative distribution functions at mean doses of 0.5 Gy and 1.0 Gy. The distributions were nearly identical across cell groups that are hit by alpha particles at the same energy and LET, regardless of dose level. The cell groups that are hit by alpha particles at the other energy and LET corresponded to the separate, but common, distribution curves.

Table II. Non-hit probability (p_0) from exposure to alpha parti cles at different dose rates for the same dose.

	0.5 Gy	1.0 Gy
0.05 Gy/min	0.394	0.156
0.5 Gy/min	0.385	0.149
0.1 Gy/min	0.528	0.280
1.0 Gy/min	0.512	0.272

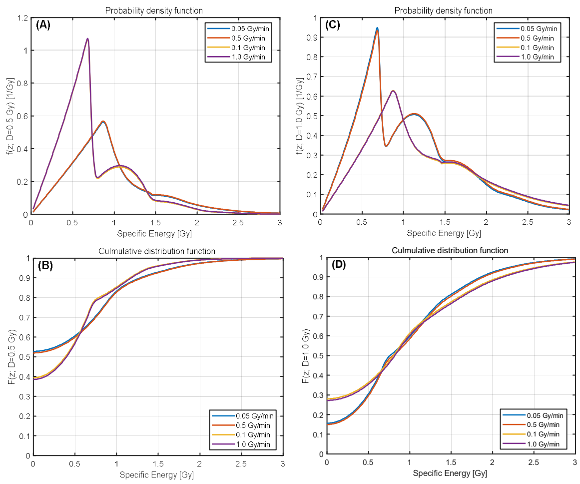

Figure 1. Specific-energy distributions among cellular targets at mean doses of 0.5 Gy and 1.0 Gy: (A) PDF *f(z; D = 0.5 Gy)*, (B) CDF *F(z; D = 0.5 Gy)*. (C) PDF *f(z; D = 1.0 Gy)*. (D) CDF *F(z; D = 1.0 Gy)*. For visibility, the δ-peaks at z = 0 (non-hit probability p_0) is omitted from the PDF plots. CDFs includes $F(0) = p_0$.

3.2 Surviving Fraction

Figure 2 was drawn with the experimental data reported by Lee in his Master's thesis [5]. Within-group comparisons—0.05 vs 0.5 Gy/min for 0.5 and 1.0 Gy showed no statistically significant difference in survival, despite the nearly tenfold difference in dose rate [Figs. 2(A) and (B)]. This outcome can be explained by the identical energy and LET of alpha particles hit cells, even at different particle hit rates but for the same total energy deposition. The same applies to the comparison between cell groups exposed at 0.1 vs 1.0 Gy/min for 0.5 and 1.0 Gy. By contrast, statistically significant differences were observed between the cell groups exposed to alpha particles of different LET (0.05/0.5 vs 0.1/1.0 Gy/min) at both dose levels. The cell groups exposed to higher-LET alpha particles at 0.1 and 1.0 Gy/min exhibited higher p_0 value, indicating a greater fraction of non-hit cells, and consequently a higher survival chance as compared to the cell groups exposed to lower-LET alpha particles at 0.05 and 0.5 Gy/min, for mean dose of 0.5 Gy and 1.0 Gy, respectively. Cells survived by a lower chance from exposure to a higher dose, regardless of dose rate within the groups exposed to alpha particles of the same LET [Figs. 2(C) and (D)].

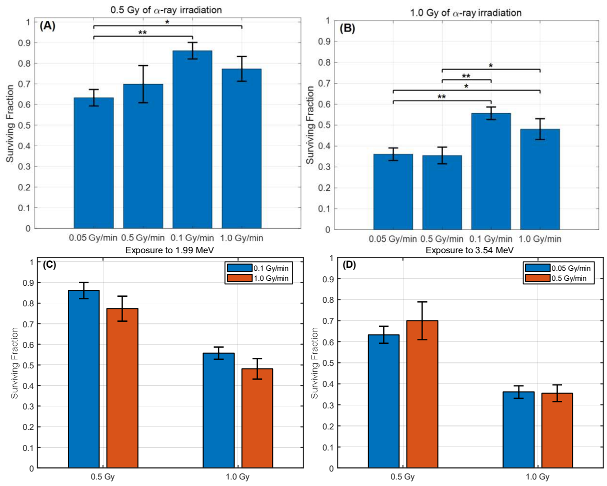

Figure 2. Surviving fractions of normal rat diencephalon cells from α-particle exposure at different dose rates for mean doses of 0.5 Gy (A) and 1.0 Gy (B) [5]. Surviving fractions from exposure to alpha particle of 1.99 MeV (C) and 3.54 MeV (D). Each bar indicates one standard error of SF.

3. Conclusions

This study demonstrated that dose-rate effects observed in cells exposed to alpha particles can be better explained by employing stochastic analysis of statistically varying events of target (cell) selection by high-LET radiation. Even at mean doses of 0.5 and 1.0 Gy, a substantial proportion of cells remained unhit by high-LET radiation such as alpha particles. These non-hit portion of cells played a decisive role in survival outcome. LET and dose rate still affect the chance of survival among hit cells, but their influence was secondary to the statistical variability among cells in the chance of hit. This perspective is consistent with the observation that there is a lack of dose rate effect in cells exposed to high-LET alpha particles at doses below 1.0 Gy.

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