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Radiosensitivity of rat diencephalon cells to low-dose alpha particles at different dose rates

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1. Introduction

Hyper radiosensitivity (HRS) is the phenomenon that cells are more sensitive to lower-dose radiation, which is contrary to the linear-non-threshold (LNT) hypothesis for cellular response at low dose exposure [1]. The HRS weakens as dose increases and the cellular response turns accordant to the LNT hypothesis due to induced radioresistance (IRR) in cells [2]. The dependence of HRS/IRR on the quality and the exposure rate has been reported [3]. The HRS/IRR phenomena are supported by massive experimental data from X-ray exposure, but have been rarely reported from alpha particle exposure [4]. This study was performed to investigate the HRS/IRR phenomena with cells exposed to alpha particles at varying dose and dose rate.

2. Materials and Methods

2.1. Cell culture and irradiation

Normal rat diencephalon cells (DI TNC 1, CRL-2005, ATCC) were cultured with 90% Dulbecco's Modified Eagle's Medium(DMEM, Gibco) and 10% Fetal Bovine Serum(FBS, ATCC) and incubated at 37 ℃ with 10% CO2. Cells were exposed in the alpha particle irradiator installed with Am-241 in the Radiation Bioengineering Laboratory at Seoul National University [5]. Cells were exposed to alpha particles at dose rates of 0.05, 0.5, and 1 Gy/min for total doses of up to 2 Gy.

2.2. Clonogenic assay

After exposure to alpha particles, cells were seeded in the six-well plates and incubated for 10 days in culture medium before colony counting. Cells were fixed and stained with crystal violet. Colonies with more than 50 cells were counted as survivors.

3. Results

Fig. 1 shows the surviving fractions of diencephalon cells. The HRS response does not appear clearly in Fig. 1. Moreover, more colonies were counted at dose rates of 0.05 and 0.5 Gy/min than the background in the low dose region (< 0.2 Gy). Considering that alpha particles are high-LET radiation, data points were fitted to the following linear-quadratic curve with β = 0:

$$SF(D)=\exp(-\alpha D-\beta D^2), \quad (1)$$

where SF(D) is the cell surviving fraction at dose D.

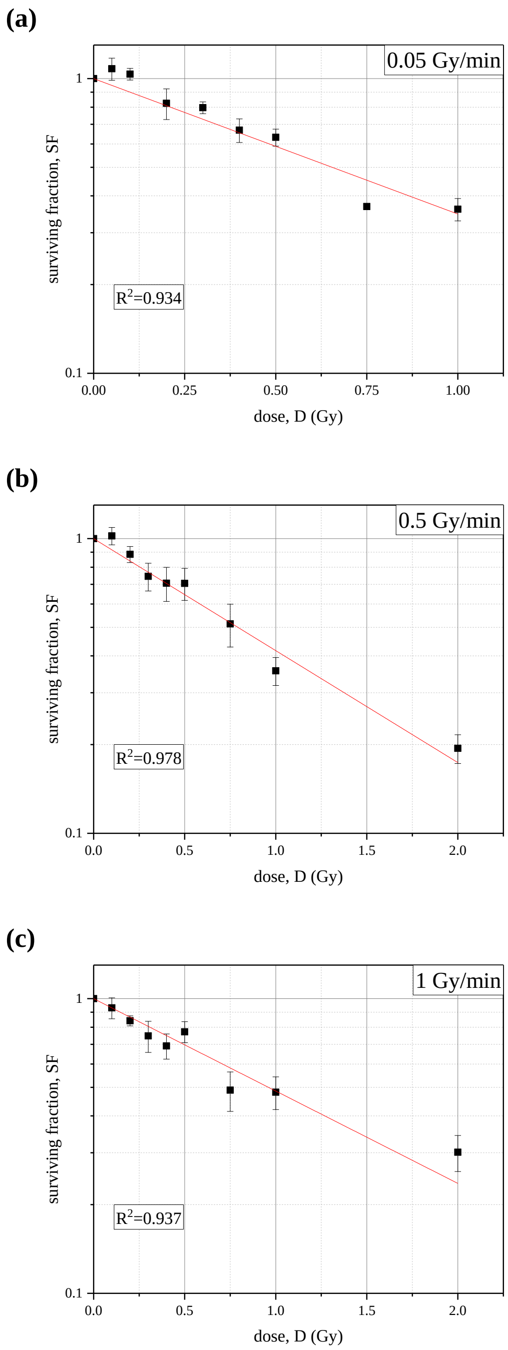

Fig 1. Clonogenic surviving fractions of rat diencephalon cells after exposure to alpha particles at dose rates of (a) 0.05, (b) 0.5, and (c) 1 Gy/min.

Data from Fig. 1 were converted to new parametric values according to Eq. (2) to locate the occurrence of HRS response.

$$-[\ln(SF_i)]/D_i = \kappa_i \qquad (2)$$

If data were fitted to the standard curve SF=exp(-αD), κ would approach α at low doses. With cells carrying HRS, κ should be greater than α at low doses (0.05-0.2 Gy). From exposures at 0.05 and 0.5 Gy/min (Fig.2 (a) and (b)), κ starts at smaller, even negative, values and increases up to a plateau level at α. The value κ has already reached the plateau from exposure at 1 Gy/min (Fig.2 (c)). The values κ in Fig. 2(c) were not significantly different from the value α ($p > 0.05$ with 95% confidence interval), which means that the response to alpha particles at 1 Gy/min complies with the high-LET linear-quadratic model.

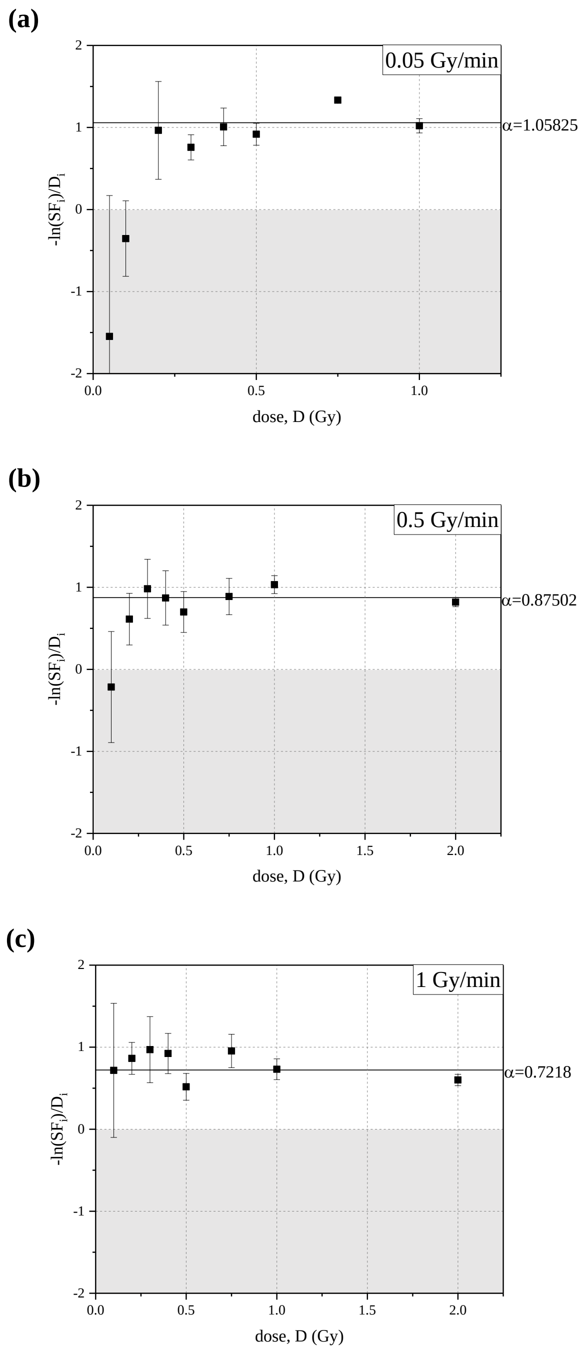

Fig 2. The $-[\ln(SF_i)]/D_i$ value varying with the dose delivered at (a) 0.05, (b) 0.5, and (c) 1 Gy/min. The values of the horizontal lines represent the α values from Eq. (1).

4. Conclusion

The response of rat diencephalon cells to alpha particles at a high dose rate of 1 Gy/min complied with the high-LET linear-quadratic hypothesis. At dose rate 0.05 and 0.5 Gy/min exposures, rat diencephalon cells expressed hormesis instead of HRS.

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