NEUTRON-INDUCED DNA DAMAGE AND CELLULAR LETHALITY IN CULTURED MAMMALIAN CELLS

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The induction and repair of DNA lesions induced by fast neutrons as well as their killing effect were compared to those by low LET radiations in mouse leukemic L5178Y cells.

Fast neutrons (1.43 Gy/min) were obtained from a cyclotron at the Institute of Medical Sience (IMS), University of Tokyo by bombarding a Be target with 15 MeV deuterons. Gamma-rays (0.9 Gy/min) were from ^{60}Co source in IMS. X-rays were obtained from a deep therapy machine operated at 230 kV, 22 mA. Dose rate was 3.5 Gy/min. Irradiation of the cells with fast neutrons, gamma-rays, or X-rays was carried out at 0°C.

After exposure to fast neutrons or gamma-rays, surviving fractions of the cells were estimated as colony forming ability in soft agar medium. As is shown in Fig.1, killing effect of fast neutrons was greater than that of gamma-rays.

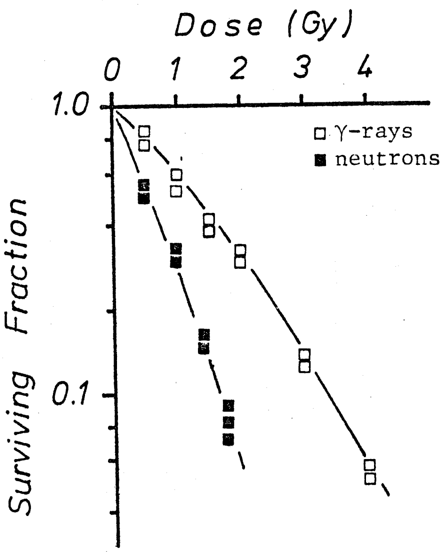

Fig. 1: Dose-survival curve of L5178Y cells exposed to gamma-rays or fast neutrons

Initial number of DNA lesions were determined immediately after irradiation using alkaline separation technique[1]. Fig. 2 shows that the fast neutrons induced smaller extent of DNA breaks in spite of their higher efficiency in cell killing than gamma-rays.

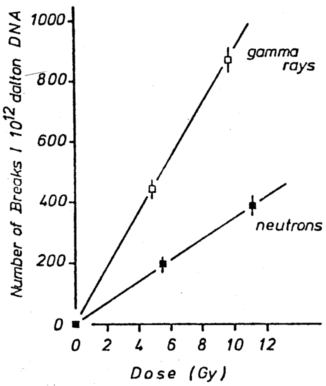

Fig. 2: Dose-response curve of initial breaks induced by gamma-rays or fast neutrons

In order to study repair profile of DNA damage, L5178Y cells were irradiated with 18 Gy of gamma-rays or 58 Gy of neutrons, which induced similar amount of DNA breaks. After irradiation the cells were incubated at 37°C, and the number of DNA lesions was measured after various periods of incubation (Fig. 3). The breaks induced by gamma-rays were repaired quickly, while those induced by neutrons showed long-lived fraction even after 8 hours of post-irradiation incubation time.

Previous study[1] indicated that DNA breaks induced by low LET radiation (230 kV X-rays) were grouped into three: fast-reparable, slow-reparable, and non-reparable. This was also the case for fast-neutron-induced damage. The three types of lesions were compared in the Table.

It should be noted that the rejoining rates of fast-reparable and slow-reparable breaks were the same whether they were induced by X-rays or fast neutrons, and that neutrons induced smaller extents of fast- and slow-reparable damage but greater amount of non-reparable damage.

It is also obvious from Fig. 4 that non-reparable damage is induced more efficiently by fast neutrons than by gamma-rays, paralleling the efficiency in cell killing.

These results indicate that greater cell killing caused by fast neutrons would be explained not by the fast-reparable, nor the slow-reparable damage but by the non-reparable lesions on DNA molecules.

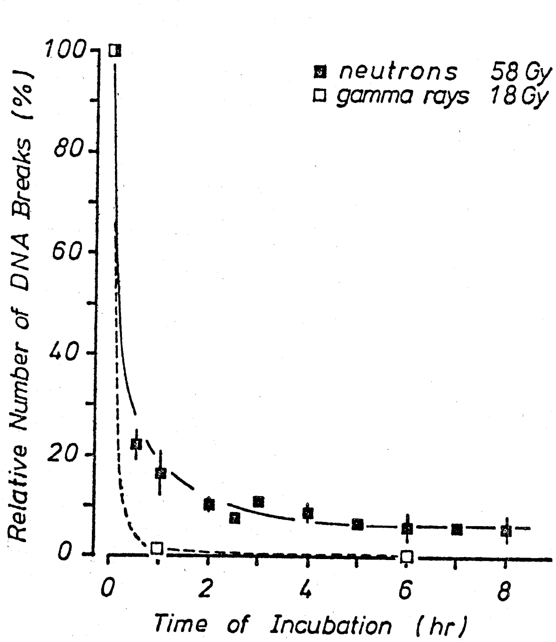

Fig. 3: Rejoining profile of DNA breaks induced by 58 Gy of neutrons or 18 Gy of gamma-rays

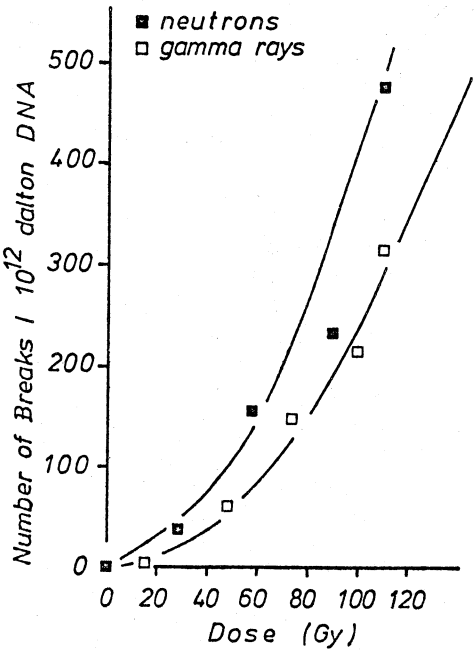

Fig. 4: Dose-response curve of non-reparable DNA damage induced by neutrons or gamma-rays

		fast-reparable damage	slow-reparable damage	non-reparable damage
X-Rays	half time of rejoining	5 min	70 min	---
	breaks/10^{12}dalton DNA	4700	480	90
Neutrons	half time of rejoining	5 min	70 min	---
	breaks/10^{12}dalton DNA	1500	430	160

Table: Comparison of the three types of DNA damage in L5178Y cells exposed to 58 Gy of X-rays or fast neutrons

Reference 1) Sakai, K. and Okada, S.: An Alkaline Separation Method for Detection of Small Amount of DNA Damage. J. Radiat. Res. 22, 415-424 (1981)