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Effect of Static Magnetic Field on the Induction of Chromosome Aberrations by 4.9 MeV Protons and 23 MeV Alpha Particles

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The effect of static magnetic field applied during *in vitro* exposure to 4.9 MeV protons and 23 MeV alpha particles on the induction of chromosome aberrations in human peripheral blood lymphocytes was studied. The mean frequency of dicentrics in cells irradiated in magnetic field of a magnitude about one Tesla tended to be higher than that irradiated in the absence of magnetic field for both protons and alpha particles, and the analysis of dose-effect relationships indicated that for protons the magnetic field significantly affected the dose-effect relationship. The intercellular distribution of chromosome aberrations, one of the measures of radiation quality, was not significantly influenced by the magnetic field.

INTRODUCTION

In view of current interest in the development of fusion reactors, the effects of combined radiation and magnetic field on the biological systems in mammalian cells are particularly intriguing. Magnetic fields have been demonstrated to alter the structure of biological molecules, chemical reaction rate or metabolic state[1-4]. Cellular response to radiation is a consequence of complex biophysical and chemical processes, and thus it seems likely that such response may be modified by the magnetic field.

The magnetic field also alters the physical property of radiation. When high energy electrons are traversing the magnetic field, they experience the Lorentz force and are forced to follow spiral paths describing helices whose axes are parallel to the magnetic field. In a sufficiently strong transverse magnetic field, the radius of the helix become shorter[5,6], thus the electrons mimic high LET radiations and modify biological effects of radiations. Such a possibility has been tested by Rockwell[7] and Nath *et al.*[8] for the modification of lethal effect of X-ray on cultured

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mammalian cells. However, they reported minimal or no effects. Here, we studied the effect of a strong static magnetic field on the induction of chromosome aberrations in human peripheral blood lymphocytes applied in combination with the *in vitro* exposure to 4.9 MeV protons and 23 MeV alpha particles.

MATERIALS AND METHODS

The present experiment constitutes one of a series of experiments on the cytogenetic effects of cyclotron-produced 4.9 MeV protons and 23 MeV alpha particles, and a part of the results has been published elsewhere[9,10]. The experimental design, dosimetry and irradiation procedures were the same as described previously[9,10] except that the electromagnet was applied to the beam line and the sample holder was remodeled to adapt for the shape of the electromagnet. Briefly, peripheral blood lymphocytes obtained from a healthy adult were sandwiched in a thin layer between 5 μm thick (ϕ 20mm) polycarbonate films and placed in a 25mm plastic Petri dish, which was fixed to the sample holder. Moisture was supplied by placing a serum soaked wet prefilter underneath the polycarbonate film. The samples were positioned vertically, placed in a dipole electromagnet and irradiated with 4.9 MeV protons and 23 MeV alpha particles accelerated by a cyclotron at Kyoto University Cyclotron Laboratory. The irradiation system and beam path are shown in Fig. 1. Radiation exposure was performed under two conditions; one where the electric magnet was excited, and the other where it was not. The irradiated cells were activated

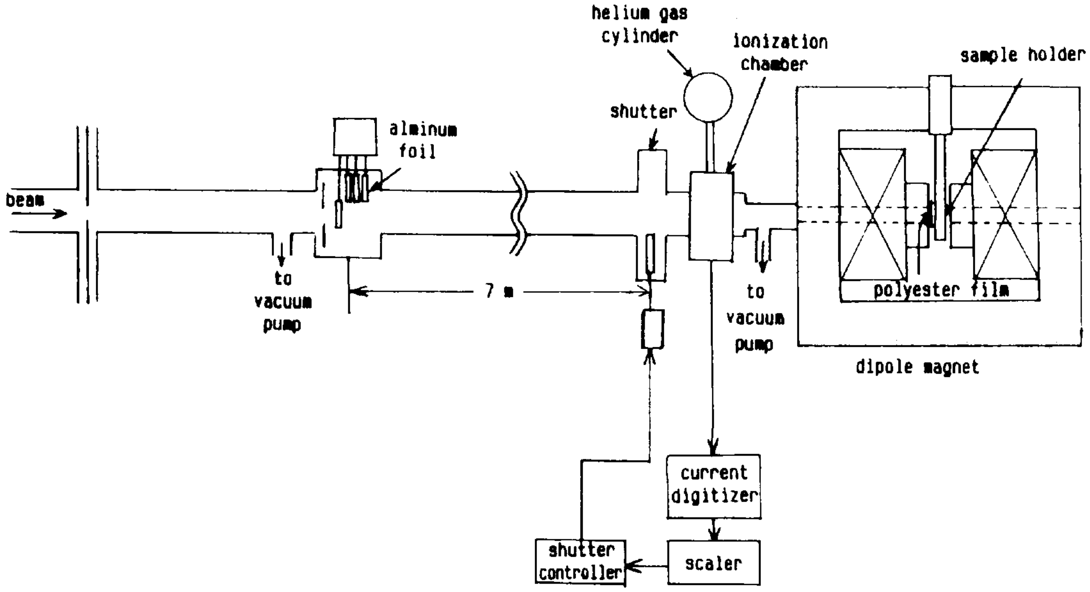

Fig. 1. Schematic diagram of irradiation system. The beam is scattered by the aluminum foils and unevenness of beam profile was not observed at the position of the sample holder. Dose of the beam is measured by the ionization chamber and controlled by the beam shutter.

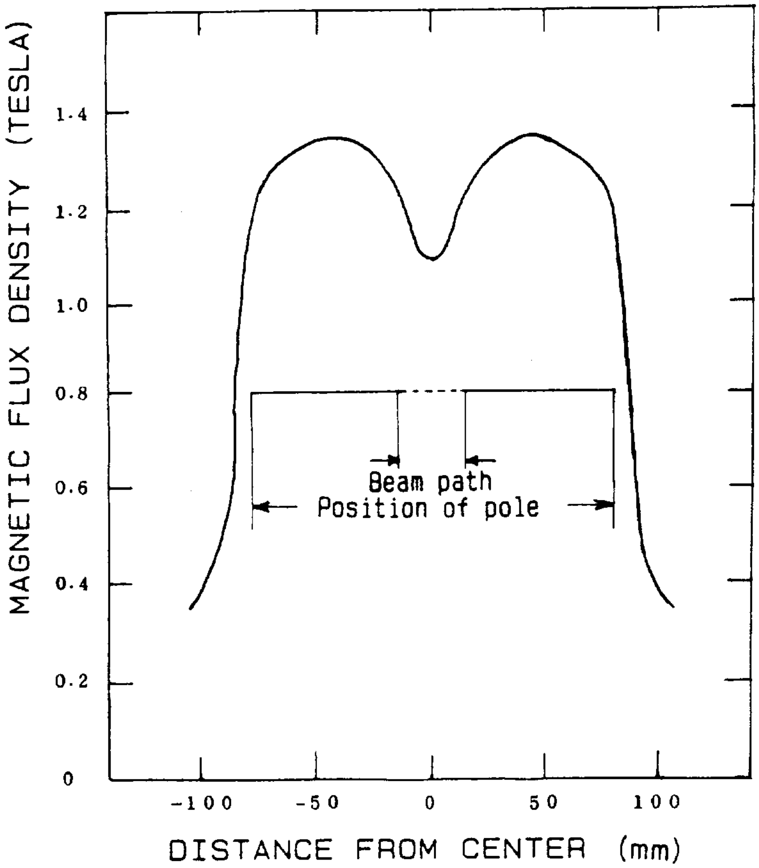

Fig. 2. Intensity distribution of magnetic field at pole gap of the electromagnet where samples were placed.

by PHA, cultured for 50 hours with colcemid for the final 20—24 hours, and processed for chromosome preparation in the same way as described previously[9,10].

The electromagnet was set up so that the magnetic field direction was parallel to the beam of protons or alpha particles. The beam passed through a hole penetrating the pole of the electromagnet along the axis. The intensity of magnetic flux density (when the electromagnet was on) was measured by a gauss meter (Maezumi MG-330DS). The distribution of the intensity at the pole gap where sample was placed is shown in Fig. 2. The intensity at the beam path where the sample was located was about 1.1 Tesla (T). The coil of the electromagnet was cooled by water flow so that there was no rise in temperature by electric current near the sample holder. In the experiment with the magnetic field, the electromagnet was excited after samples were set up and switched off before samples were removed. Time of exposure to the magnetic field was less than 30 minutes.

RESULTS

Dicentric chromosomes were scored. With the culture method applied in this study, the mitotic cells recorded at 50 hours were virtually all in their first post-irradiation mitosis. The results of experiments with no magnetic field have been published elsewhere[9,10]. Table 1 shows the results of the experiments with the magnetic field. The frequencies of dicentrics plotted against proton or alpha dose in the magnetic field were compared with those obtained in the experiments in which no magnetic field was applied but otherwise processed in the same way (Fig. 3). As seen therein, the data in the presence and absence of magnetic field, were quite comparable, but aberration frequencies in experiments with magnetic field generally showed somewhat higher values. To compare the efficiencies of dicentric formation per unit dose (D in Gy), the dicentric data were fitted to a linear-quadratic model, $Y = \alpha D + \beta D^2$. The calculated regression coefficients, α and β, are presented in Table 2. It is evident that the higher yield of chromosome aberrations in the presence of magnetic field is mainly due to the increase in the one-track component (α term), suggesting an increase in LET. Therefore, the difference between two conditions is more pronounced in the low-dose range. Fig. 4 shows the joint confidence regions of the coefficients. The frequency of dicentric formation in cells irradiated in the magnetic field was larger than in its absence for both protons and alpha particles. The regression coefficients for protons were significantly different between the two conditions at 5% significance level. However, for irradiation with alpha particles, the difference was not significant.

Distribution of dicentrics among cells irradiated in the magnetic field is also presented in

Table 1. Results of experiments using irradiation in the magnetic field of 1.1 Tesla.

Radiation	Dose (Gy)	Fluence (μm^2)	No. of cells scored	No. of cells with indicated number of dicentrics										Mean (per cell) ±SE	Relative variance ±SE
				0	1	2	3	4	5	6	7	8	11		
	0.33	0.26	200	171	23	5	1							0.180±0.034	1.271±0.149
4.9	0.41	0.32	200	147	44	9								0.310±0.039	0.985±0.072
	1.01	0.80	197	102	65	26	4							0.655±0.056	0.939±0.074
MeV	1.48	1.17	209	95	70	27	9	8						0.876±0.072	1.245±0.108
	2.00	1.58	117	46	37	16	12	4	2					1.120±0.113	1.358±0.148
proton	2.50	1.99	111	21	31	27	15	13	3	1				1.829±0.135	1.102±0.122
	3.00	2.30	44	7	10	6	6	6	6	2	1			2.568±0.295	1.492±0.235
	0.256	0.0527	200	153	39	7	1							0.280±0.039	1.083±0.106
23	0.50	0.105	250	155	68	16	10	1						0.540±0.077	1.101±0.145
	1.00	0.211	200	92	65	22	14	4	2	1				0.915±0.081	1.436±0.155
MeV	1.50	0.316	200	61	58	44	24	6	6	0	1			1.395±0.095	1.282±0.132
	2.00	0.422	200	53	47	43	21	15	7	2	1	1		1.740±0.112	1.422±0.142
alpha	2.56	0.527	200	44	54	33	34	20	9	3	2	1		1.935±0.118	1.450±0.134
	2.99	0.633	150	17	27	39	25	18	6	10	4	3	1	2.700±0.167	1.545±0.189

Table 1. No systematic difference was seen for the distribution of aberrations in the presence of magnetic field as compared with that in its absence.

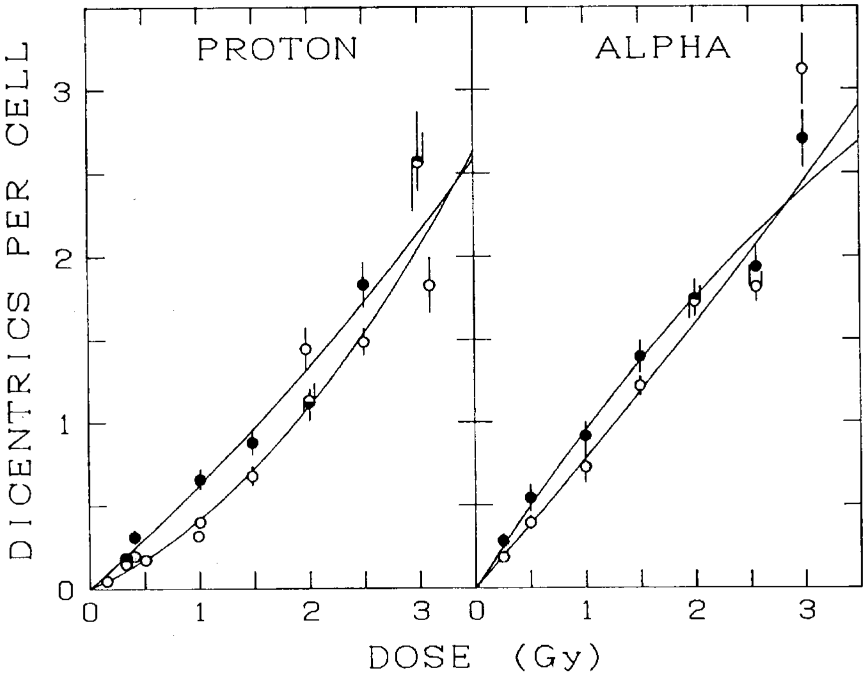

Fig. 3. Frequency of dicentrics plotted against dose. Bar indicates the standard error of the mean. Closed circles: irradiation in the magnetic field. Open circles: irradiation in the absence of magnetic field.

Table 2. Regression coefficients, α and β of a linear quadratic model, $Y = \alpha D + \beta D^2$.

Radiation	Coefficient	No magnetic field	Magnetic field (1.1 T)
4.9 meV	α	$(2.76 \pm 0.46) \times 10^{-1}$	$(5.70 \pm 0.86) \times 10^{-1}$
proton	β	$(1.36 \pm 0.28) \times 10^{-1}$	$(4.8 \pm 4.7) \times 10^{-2}$
23 MeV	α	$(7.55 \pm 0.96) \times 10^{-1}$	1.020 ± 0.089
alpha	β	$(2.1 \pm 4.8) \times 10^{-2}$	$(-7.2 \pm 4.0) \times 10^{-2}$

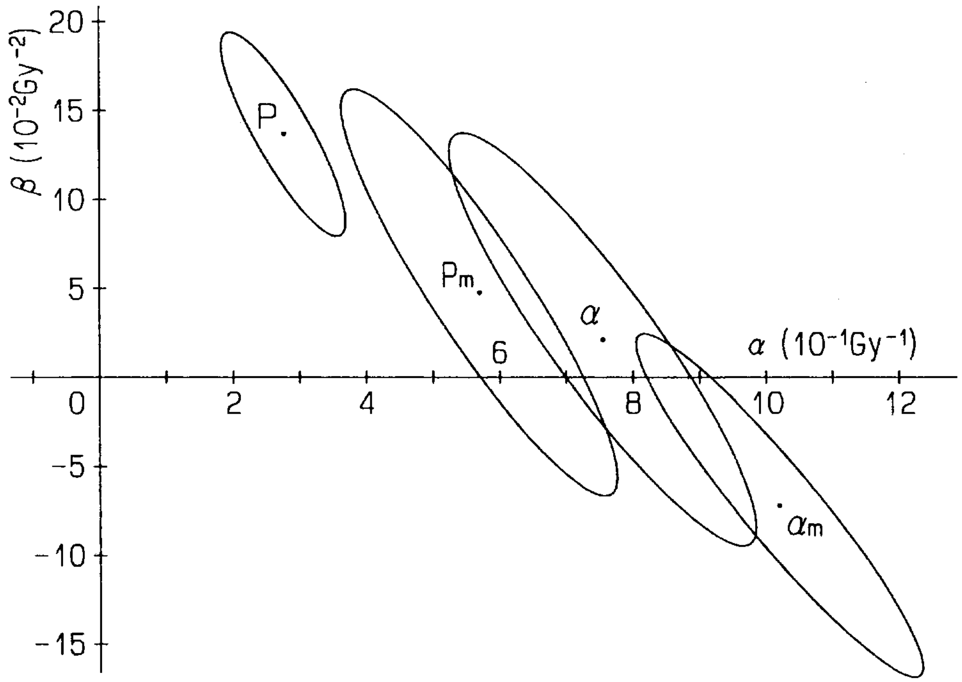

Fig. 4. Ninety-five percent joint confidence ellipses of regression coefficients α and β for the linear-quadratic model, $Y = \alpha D + \beta D^2$. P and α denote 4.9 MeV protons and 23 MeV alpha particles, respectively. The subscript m indicates irradiation in the magnetic field.

DISCUSSION

A charged particle moving in a magnetic field experiences Lorentz force, $\boldsymbol{F}$, as expressed by,

$$\boldsymbol{F} = q\boldsymbol{v}\times\boldsymbol{B}$$

where q is electric charge of the particle, v is velocity of the particle, and $\boldsymbol{B}$ is the magnetic flux density. $\boldsymbol{F}$, $\boldsymbol{v}$ and $\boldsymbol{B}$ are vectors, and × indicates vector product. In a vacuum, the charged particle moves on a helical path whose axis is parallel to the magnetic field. The cord length of one rotation along the helix can be expressed as follows.

$$L = 2\pi \frac{mv}{qB\sqrt{1-\frac{v^2}{c^2}}},$$

where m is the mass of the particle and c is the speed of light.

Motion of electrons in matter scattered by a proton or an alpha particle is deflected by collisions in matter and such an electron does not keep to describe a helix even in the magnetic field. However, if L is equal to or smaller than mean path length, the motion of electrons perpendicular to the direction of magnetic field may be reduced.

A charged particle at kinetic energy of 5 MeV per nucleon is estimated to deposit energy in 1 μm from its track[11)] in no magnetic field, and the energy distribution may be more localized in a very strong magnetic field parallel to the track by Lorentz force.

In Fig. 5, 5% transmitted electron projected range (it is almost equivalent to conventional extrapolated range which is specified only above 500 eV) and the *L* are plotted against kinetic energy of electron. The range is referred to empirical formula[12)] based on data of ranges in collodion foils. For the electron of energy larger than about 55 keV, *L* is smaller than the projected range at magnetic field of 1 T and therefore the motion of the electron must be modified. The largest kinetic energy of an electron which is first at rest and then scattered elastically by a 4.9 MeV proton is 10.68 keV, and most of the scattered electrons have much less kinetic energy. To get *L* comparable to the projected range, a magnetic field of the order of at least 10 T is necessary. However, it should be noted that the mean path length is not equal to the projected range. The values of the projected ranges closely coincide with the values of the mean path length calculated with continuously slowing down approximation (CSDA) from the theory of collision stopping powers of Bethe[13)] and the theory of stopping due to photon radiation (Bremsstrahlung) of Bethe and Heitler[14)] over the applicable range of the theories (>10 keV). Therefore, the

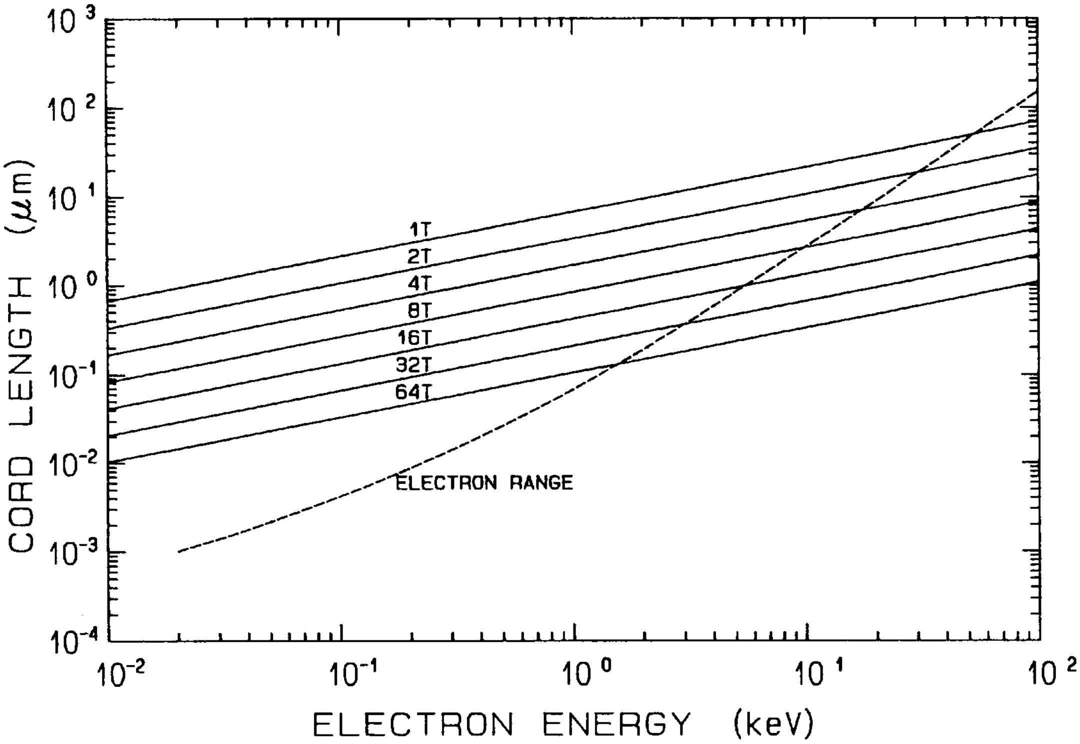

Fig. 5. Cord length and projected range in a function of kinetic energy of electrons. Solid lines are cord length of one rotation along the helices that electrons will describe (*L* in discussion) in the magnetic field of indicated intensity of magnetic flux density. Broken line is 5% transmitted electron projected range by Cole (1969).

electron must describe a rather straight path while its kinetic energy is larger than 10 keV. But the real mean path length must be larger than the projected range because of the very tortuous path of the low energy electron[12]. The real mean path length of an electron of kinetic energy larger than 10 keV must be approximated by the sum of projected range while the electron is slowing down to 10 keV and the real mean path length of the 10 keV electron, and larger than the CSDA value. Actually, the mean path length of 19.6 keV electrons in oxygen gas is 1.2 times as long as the extrapolated projected range (which is almost equal to 5% transmitted projected range) and 10 times as long as the mean projected range[15], and the mean path length is expected to be very much larger than the 5% transmitted projected range for lower energy electrons. Therefore, the electron motion may be modified even by a magnetic field of 1 T and the modification may influence track structure, such as radial distribution of energy deposition, and local distribution of energy deposition by modification of electron trajectory near the end point. With a fixed strength of magnetic field, the modification of track structure may be more pronounced for sparsely ionizing particles than densely ionizing particles. The experimental data presented here are in line with this idea: as indicated by the increase in one-track component, the charged particles behaved like higher LET radiation in the presence of magnetic field than in its absence, and the effect was more pronounced for the 4.9 MeV proton ($\mathrm{LET} = 7.9$ keV/ μm) than for 23 MeV alpha particles ($\mathrm{LET} = 29.6$ keV/ μm). The rather decreased yield of two track component may be a reflection of selective killing of cells by particle traverse, which is also sensitive to the quality of radiation[10].

Radiation damage to chromosomal DNA and its repair involved in the formation of chromosome aberrations are also influenced by the changes in the biophysical and chemical conditions. Therefore, other effects of magnetic field on the modification of radiation-induced chromosome aberrations may be possible, such as 1) energy level variation of excited states of molecules by the Zeeman effect, 2) polarization of magnetic dipoles in molecules, and 3) induction of current in moving life materials. The tendency of magnetic field of the magnitude adopted in the experiment to enhance the induction of chromosome aberrations by protons and alpha-particles may be a reflection of such physico-chemical alteration as well as modification of radiation track structure.

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REFERENCES

1. Barnothy, M.F. (1964) Biological Effects of Magnetic Fields. (New York: Plenum Press).
2. Silver, I.L. and Tobias, C.A. (1974) Space Radiation Biology and Related Topics. Ed. C.A. Tobias and

P. Todd, pp. 258, Academic Press, New York.

3. Liboff, A.R., Williams, T. Jr., Strong, D.M. and Wistar, R. Jr. (1984) Time-varying magnetic fields: effect on DNA synthesis. Science **223:** 818-819.
4. Chisey, C.E.D., Takiff, L., Goldstein, R.A. and Boxer, S.G. (1985) Effect of magnetic fields on the triplet state lifetime in photosynthetic reaction centers: Evidence for thermal repopulation of initial radical pair. Proc. Natl. Acad. Sci. USA **82:** 6850-6854.
5. Shih, C.C. (1975) High energy electron radiotherapy in a magnetic field. Med. Phys. **2:** 9-13.
6. Nath, R. and Schulz, R.J. (1978) Modification of electron-beam dose distributions by transverse magnetic fields. Med. Phys. **5:** 226-230.
7. Rockwell, S. (1977) Influence of a 1400-gauss magnetic field on the radiosensitivity and recovery of EMT6 cells *in vitro*. Int. J. Radiat. Biol. **31:** 153-160.
8. Nath, R., Schulz, R.J. and Bongiorni, P. (1980) Response of mammalian cells irradiated with 30 MV X-rays in the presence of a uniform 20-kilogauss magnetic field. Int. J. Radiat. Biol. **38:** 285-292.
9. Takatsuji, T., Takekoshi, H. and Sasaki, M.S. (1983) Induction of chromosome aberrations by 4.9 MeV protons in human lymphocytes. Int. J. Radiat. Biol. **44:** 553-562.
10. Takatsuji, T. and Sasaki, M.S. (1984) Dose-effect relationship of chromosome aberrations induced by 23 MeV alpha particles in human lymphocytes. Int. J. Radiat. Biol. **45:** 237-243.
11. Kellerer, A.M. (1971) An Assessment of Wall Effects in Microdosimetric Measurements. Radiat. Res. **47:** 377-386.
12. Cole, A. (1969) Absorption of 20-eV to 50,000-eV Electron Beams in Air and Plastic. Radiat. Res. **38:** 7-33.
13. Bethe, H.A. (1933) Quantenmechanik der Ein- und Zwei-elektronen Problem. In: Handbuch der Physik **24**(i), pp.273-560, Springer Berlin.
14. Bethe, H.A. and Heitler, W. (1934) On the stopping of fast particles and on the creation of positive electrons. Proc. Roy. Soc. **A146:** 83-112.
15. ICRU (1970) Linear Energy Transfer, ICRU Report 16, p.24.