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THE EARLY RELATIVE BIOLOGICAL EFFECTIVENESS OF SINGLE DOSE OF FAST NEUTRONS (35 $MeV_{p\rightarrow Be}$) FOR BONE MARROW IN MICE

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The early RBE of the bone marrow in mice after single irradiation with fast neutrons (35 $MeV_{p\rightarrow Be}$) was studied. ^{60}Co-γ ray was used for referent beams. Using the dose making 50% loss of the nucleated cells of bone marrow in mice relative to control group mice to calculated the RBE value which was 2.13± 0.18. Meanwhile, the relationship of the RBE values and the dose of neutrons was noted. On log-log plot, the RBE values decrease with increasing dose of fast neutrons and it is consistent with a slope of -0.39± 0.10. The α/β ratios were estimated from linear-quadratic model of cell survival, they are 14.4±1.30 Gy for fast neutrons and 0.83± 0.10 Gy for γ-ray, respectively.

Key words: Fast neutrons, Relative biological effectiveness, Bone marrow, Early reaction.

The fast neutron therapy has specific advantage comparing with photon therapy for some tumors. These tumors that possess the strong capacity of sublethal and potentially lethal damage repair and gave a poor level of reoxygenation and contain a high proportion of hypoxic cells are all resistant to photon radiation. They could be received a good therapeutic gain factor by neutron therapy. Fast neutrons providea high RBE (Relative Biological Effectiveness) value because they are densely ionizing and are referred to as high LET (Linear Energy Transfer) radiation. The influence of different tissues on RBE values is different. There is a higher RBE value for late effects than for early effects.[1] RBE values are under various influences such as the number of fractionation,[2] the dose per fraction,[3] neutron energy,[4] microdosmetric distribution of neutrons[5] and so on. It is necessary to explore what is appropriate RBE values for fast neutrons in radiotherapy. In this paper the early RBE of single dose of fast neutrons (35 $MeV_{p\rightarrow Be}$) for bone marrow in mice has been studied.

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MATERIALS AND METHODS

Animals

The 140 mice of Kunming strain were used in our experiments and male and female mice were all equal numbers. They were six to eight weeks of age and 20 to 22 gram of weighg. There were 10 mice per group.

They were fed in animal house under specific-pathogen-free conditions.

Experimental Beams

The experimental beams were fast neutrons produced by bombardment of beryllium target with 35 MeV protons which come from proton linear accelerator in Institute of High Energy Physics, Academia Sinica. The distance from the target to skinsurface is 143 cm. The dose rate is 0.12 to 0.14 Gy/min. The neutron beams are horizontal. There were 30 mm thick paraffin in both side of irradiated mice as compensation. Irradiation were given from front and behind side with equal doses. Seven dose levels were used in our experiment from 0.24 to 3.38 Gy. In neutron beams the γ-ray dose contribution was incorporated into the total dose and not considered in calculating the relative biological effectiveness.

Reference Beams

^{60}Co-γ ray were used as reference beams provided by Beijing Institute for Cancer Research. The dose rate was 0.60 Gy/min. Irradiation have been finished in range of 1.50 to 8.0 Gy. Six dose points have been studied. The same experimental set-up was used as neutron beam irradiation. Animals were laid within 80% dimension of irradiation field in order to obtain uniform dose distribution. The ion chamber with balance tissue was placed among mice to monitor dose received by mice.

Method

All animals without anaesthesia were irradiated whole body with single doses in the case of fast neutrons and γ-ray respectively. One group of mice was regarded as control group without irradiation.

On 8 days after irradiation all animals were sacrificed by encephalospinal amputation and left femurs were taken. The cells in bone marrow cavity were washed out with 0.9% NaCl. The cell suspensions have been prepared in which the total cells were counted then centrifuged. So that, the cells were settled down the slide for staining and doing differential count.

The doses of 50% number reduction of nucleated cells after irradiation of fast neutrons and photons comparing with control group were used to calculated the RBE values.

RESULTS

The dose-related changes in the percentage of nucleated cells of bone marrow in mice (relative to the unirradiated bone marrow which was used as normal control group animals) after irradiation with single doses of fast neutrons and γ-ray are shown in Figure 1. In our experiment, the number of nucleated cells of bone marrow in control group mice are $242.49\times10^3\pm37.6\times10^3$ /mm^3 which animals were not irradiated with any ray and this value as common origin point was used for the two survival curves.

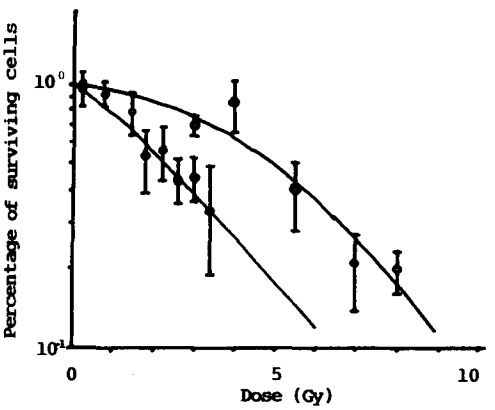

Fig. 1. The survival curves for early effects of the nucleated cells of bone marrow in mice after irradiation with with single doses of fast neutrons (35 $MeV_{p\rightarrow Be}$) and ^{60}Co-γ ray.

We can see that the percentage of nucleated cells of bone marrow decrease rapidly with increasing irradiation dose. In the fast neutron survival curves shown in Figure 1 there is a slight detectable curvature,

but it appears linear at low doses without obvious shoulder. In the meanwhile, there is apparent an initial shoulder region for γ-ray survival curve.

By means of linear quadratic model of cell survival the α/β ratios were obtained for early reaction of the bone marrow in mice after fast neutron and γ-ray irradiation. They are 14.4±1.3 Gy and 0.83± 0.1 Gy, respectively. The values of α and β for fast neutrons are 0.253 Gy^{-1} and 0.0176 Gy^{-2} respectively. For γ-ray the values of α and β are 0.0208 Gy^{-1} and 0.0249 Gy^{-2}, respectively. The data reveals that the α coefficient for fast neutrons is much greater than the γ-ray, and the β coefficients are very near for the two ray.

The RBE value for early reaction on the bone marrow in mice irradiated with single doses of fast neutrons (35 $MeV_{p\text{-}Be}$) was investigated in this experiment. According to the instance of the doses for making 50% loss of the nucleated cells of bone marrow in mice irradiated with fast neutron and γ-ray, RBE value has been calculated. It is found that the RBE value is 2.13± 0.18.

Moreover, a characteristic of RBE obtained from the fast neutrons and ^{60}Co-γ ray survival curves was noted. The RBE values were not constant with changing the dose of neutrons irradiation. The RBE value decrease with increasing the dose of fast neutrons. The variation in RBE with fast neutrons doses is illustrated in Figure 2. On a log-log plot, the relationship was adequately described by a straight line with a slope of -0.39±0.10. There was significant difdifferent from zero (P<0.01).

DISCUSSION

In our experiment, it is seen that the fast neutron survival curve appears a slight curvature and consistent with α/β ratios of 14.4±1.30 Gy. The survival curve is not strictly logarithmic line, but the initial shoulder region is not found. This neutron survival curve indicates that repairable injury of the bone marrow in mice after irradiation with fast neutrons is very small and it can be neglected in conventional fractionated fast neutrons radiotherapy. For ^{60}Co-γ ray survival curve a large initial shoulder region exists obviously. It points out the damage repair of bone marrow after irradiation with γ-ray is important and can not be ignored.

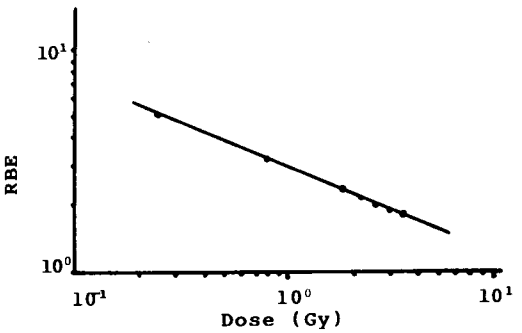

Fig. 2. Log-log plot to show he variation in the RB values for early effects of bone marrow in mice with of fast neutrons (35 $MeV_{p\rightarrow Be}$).

Hall et al.[6] reported that there was an initial small shoulder in neutrons survival curves *in vitro* data. In our experiment the initial shoulder of neutrons survival curve is not been found as the initial shoulder for γ-ray. It is relate to that the initial shoulder region would be less detectable easily in usual experiments. It is also implied that the injury repair of cells for bone marrow in mice after fast neutrons irradiation is too small and the survival curve can be regarded as a linear logarithmic.

The relationship of the RBE values and the doses of fast neutrons has been studied in this paper. The RBE values decrease with increasing doses of fast neutrons as shown in Figure 2. There is statistical significant difference between the slope of -0.39±0.10 and zero (P<0.01). When the doses of neutrons are higher the over-kill phenomenon would appear and this is one of causes of the decreasing of the RBE.

Analyzing the data by mean of linear quadratic model of cell survival the α/β ratios have been obtained. The α coefficient for fast neutrons is much greater than that for γ-ray and the β coefficients do not change obviously for neutrons and γ-ray. It is consistent with the theory of dual radiation action for a survival curve described by $\exp(-aD-bD^2)$. The α values obtained from our experiments are lower than expected. It is

maybe because of the initial slope of the survival curves to be influence due to the lower dose points is less.

REFERENCES

1. Withers HR, Thames HR, Peters LJ, et al. Biological basis for high RBE values for late effects of neutron irradiation. Int J Radiat Oncol Biol Phys 1982; 8:2071.
2. Rezvani M, Barnes DWH, Hopewell JW, et al. The relative biological effectiveness of fractionated doses of fast neutrons ($42MeV_{p\rightarrow Be}$) for normal tissues. III. Effects on lung function. Br J Radiol 1990; 63:875.
3. Gregoire V, Beauduin M, Gueulette J, et al. Radiobiological intercomparison of p(45)+Be and p(65)+Be neutron beams for lung tolerance in mice after single and fractionated irradiation. Radiation Research 1993; 133:27.
4. Hall EJ, Kellerer JK, Rossi AM, et al. RBE as a function of neutron energy. I. Experimental observations. Radiation Research 1975; 64:245.
5. Menzel HG, Pihet P, Wambersie A, et al. Microdosimetric specification of radiation quality in neutron radiation therapy. Int J Radiat Biol 1990; 57(4):865.
6. Hall EJ, Withers HR, Geraci J, et al. Radiobiological intercomparisons of fast neutron beams used for therapy in Japan and the United States. Int J Radiat Oncol Biol Phys 1979; 5:227.