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Abstract

The oxygen enhancement ratio (OER) for stopping π^- mesons by use of *Vicia faba* is measured. The dose rate of π^- beam is ≈ 30 rads/hr and it has 30% electron and muon contamination. The OER values are respectively 1.35 and 1.5 when beans are exposed at room temperature and at 4° C. The OER is dependent on dose rate when bean roots are exposed at room temperature. The OER of 1.35 for π^- mesons is to be compared with the value of about 2 for conventional radiation such as ^{60}Co gamma rays.

The OER when bean roots are exposed at a low temperature such as 4°C is relatively independent of dose rate and hence the value of 1.5 may be applicable to acute dose rate of π^- mesons.

Thus a significant reduction in OER is observed for stopping π^- mesons in spite of the contamination in the beam.

The dose delivered to a medium by a negative π-meson beam increases very slowly with increasing depth in the beginning and gives rise to a sharp maximum near the end of the range, as do other heavy charged particles. In addition, when negative π mesons stop in a medium, they are captured by nuclei in the medium, causing the nuclei to explode into short-range and heavily ionizing fragments. Thus the dose delivered near the end of the range is higher than at the entrance. In addition, these heavily ionizing fragments may overcome some of the radioresistance of the anoxic tumour cells. Hence in principle the use of π^- mesons in therapeutic application should be very advantageous. A few workers, including one of the authors (Richman), appreciated this possibility as early as 1952. Detailed calculations by Fowler and Perkins[1] generated heightened interest in the use of π^- mesons for radiotherapy. Their calculations clearly indicate the usefulness of these particles in radiotherapy.

Biophysical experiments have been carried out in this Laboratory for the last five years. The 184-inch synchrocyclotron is the most intense source of low-energy π^- mesons available today. Accelerators that will be able to produce intense beams of π mesons (10 to 100 rads/min) are under construction at Los Alamos (New Mexico), Vancouver (British Columbia), and Zürich (Switzerland).

Negative π mesons are always associated with muon and electron contamination. It is quite possible to obtain a pure beam, but at the cost of reducing the π-meson intensity considerably. We therefore used the contaminated beam in our experiments. It has 25% electrons and 10% muons.

Physical measurements indicate that the dose at the peak is about three times as great as at the entrance with a full width at half maximum of about 5 cm.[2-4]

Biological experiments indicate that the RBE at the peak is about 4 for the proliferative capacity of ascites tumour cells,[5] 2.5 for polyploidy induction in ascites tumour cells,[6] and 2.5 for anaphase abnormalities in Vicia faba root meristems.[7]

This paper describes the measurements of oxygen enhancement ratio (OER) for stopping π^- mesons by use of Vicia faba. The OER values obtained with this system are about the same as those obtained with cultured mammalian cells. The Vicia faba system yields OER values of 2.6 and 1.5 for conventional radiations (x-rays and γ-rays) and 15-MeV neutrons respectively.[8,9]

The depth-dose distribution of the contaminated π^- meson beam used in this experiment is shown in Fig. 1. This distribution is measured by using a small tissue-equivalent ionization chamber filled with air (0.75 ml). The dose at the peak is 1.7 times that at the entrance. The width of this curve is unusually small for this dose ratio. This is probably due to the beam optics in this setup. The biological effect at the entrance is quite similar to the conventional radiation.[6] The region of interest is at the peak. The horizontal and vertical profiles at the peak position, as measured with a small tissue-equivalent ionization chamber, are shown in Fig. 2.

The beam is monitored by using an ion chamber, larger than the beam, placed before the absorber used to obtain the peak. The dose at the peak is measured by using a ^{60}Co calibrated small tissue-equivalent ionization chamber (0.75 ml). The dose at the peak is measured by this small ionization chamber for a fixed amount of charge liberated in the monitor ion chamber. The total dose at the peak is then estimated from the measured total charge of the monitor during a given exposure.

The biological technique we used is quite similar to the one used by previous workers.[8, 10] The seeds used are Sutton Longpod obtained from England. They are allowed to germinate for 3 days at a temperature of about 19° C in a water tank with a constant flow of water and air. Nearly 80% of the seeds sprout. The sprouted seeds are transferred to an enclosed box filled with moist vermiculite and are kept for a period of 3 to 4 days. The healthy bean roots are individually numbered, and their lengths are measured from a reference mark made with Indian ink on the hypocotyl. They are then transferred to a water tank kept at about 19° C with a constant flow of water and aeration. After 2 to 3 days in water the roots grow to a total length of about 10 to 13 cm. The bean roots with either subnormal or abnormal growth are discarded. The healthy-looking bean roots with more or less similar growth are about 30 to 40% of the number of seeds used for germination.

The beans are packed in a Lucite box such that most of the bean tips are in the central part of the beam and the variation in dose received by various root tips is no more than 15%. Sometimes a few tips could not be packed in the central part of the beam. Such beans are not included in the data. The box is provided with a tube in the bottom through which cold water can be circulated. Thus bean roots can be maintained at lower temperature during exposure, if necessary. The box is also provided with another tube with small holes through which either air or nitrogen is bubbled to keep the beans in either an oxygenated or anoxic state. The box is also provided with a 1- mil (0.001 in.) Mylar window, and the beans are packed very close to it. Two bean boxes with their windows facing each other are placed at the peak position obtained by interposing the necessary thickness of the Lucite absorber in front of the boxes. Figure 3 shows the experimental arrangement during exposure. The beans in both the boxes are within about 5 mm of one another. Air is bubbled through one box and nitrogen is bubbled through the other. The nitrogen-bubbled box is sealed on the top. The amount of oxygen present in the nitrogen-bubbled bean box is analysed by passing the exit gas through a Hersch cell, and it is kept lower than 25 parts per million during exposure. Our system was checked by measuring the OER for acute level of ^{60}Co gamma radiation at room temperature as well as at 3° C. Our results agree with those of Hall and Cavanagh.[10]

Five pairs of irradiation boxes with 30 beans in each are exposed at the peak to different doses in the range 50 to 150 rads at room temperature. The longest exposure took about 6 hr. We also have a few groups of control beans that are treated in the same way as the others but without radiation exposure. There is no detectable difference in the 10-day growth for the control beans in oxygen and in nitrogen for 6-hour period. The length of the roots is measured and they are transferred to a water tank after the radiation exposure. The water tank is aerated and maintained at 19 ± 0.5° C. The length of the bean roots is measured once every 24 hr for a period of 10 days. There was fungus infection on the cotyledons of some of the beans during the latter part of the 10-day period. However, such infection did not significantly affect the growth of the beans. At the end of the 10-day period about 27 roots appeared to be normal morphologically in each group, and these were used for growth measurements.

The average 10-day growth for each group of bean roots is expressed as percent fraction of the control group. The percent 10-day growth for the groups of bean roots exposed in air and in nitrogen is plotted as a function of dose and is shown in Fig. 4. Regression lines are drawn through the experimental points by the method of least squares. The 95% confidence limits were calculated for both N_2 and air regression lines. The highest OER value was obtained by taking the ratio of doses of the maximum value for nitrogen to the minimum value for air at a given percent growth. The minimum value was obtained by taking the ratio of doses from the lowest nitrogen value to the highest for air. The OER may be calculated to be 1.35, with 95% confidence limits of 1.1 and 1.8.

The daily growth rate, expressed as percent of normal growth rate, for different groups of bean roots exposed to different doses in oxygen and nitrogen atmospheres, plotted as a function of days after exposure, is shown in Fig. 5. As can be seen from the figure, the growth rate is reduced after the radiation exposure, reaching a minimum about the 6th day, and then increases again. One can also calculate the OER by constructing a plot of minimum growth rate versus dose. Such a plot is shown in Fig. 6. The OER calculated in this fashion yields the same value of 1.35 as obtained from 10-day growth. The 95% confidence limits are 1.2 and 1.6. It may be noted from the figures that the minimum growth rate is about the same for 120 rads in air and 150 rads in nitrogen, and hence the OER is about 1.3.

Our preliminary results on OER using ^{60}Co gamma rays for acute and chronic exposures agree with those of Hall and Cavanagh.[10] The RBE for π^- beam at this dose rate of ≈0.5 rad/min, when compared with our preliminary results of ^{60}Co gamma rays at a dose rate of 1 rad/min is 3.

A plot of variation of OER with dose rate for ^{60}Co, made from the results of Hall and his collaborators,[10-12] is shown in Fig. 7. The OER for ^{60}Co at a dose rate that is used in the π^- experiment is about 1.8. It may be more meaningful to compare the OER of a π^- beam with ^{60}Co at a higher dose rate, such as ≈90 r/hr, taking the RBE value into consideration. The OER for ≈ 90-r/hr ^{60}Co gamma radiations is 2.2. The OER of 1.35 for the π beam has to be compared with either 1.8 or 2.2 for ^{60}Co instead of the value of 2.7 for acute irradiation.

It is of interest to extrapolate the OER measured at this available dose rate of ≈0.5 r/min to the OER at acute exposure of negative π-mesons. The aerated dose response curve varies with dose rate, whereas the hypoxic dose response curve is virtually independent of dose rate at room temperature. Consequently the OER is reduced for low-dose-rate exposures at room temperature. However, the results of Hall and Cavanagh[10] indicate that when the beans are exposed to a dose rate of 46 r/hr of ^{60}Co radiation at 3° C, the dose-rate effect is small in aerated conditions, probably due to slower repair of sublethal damage at this temperature. Hence the OER measured at 3° C at a dose rate of 46 r/hr is found to be about the same as for acute γ-irradiation at room temperature. The dose rate of 20 to 30 r/hr of π^- mesons is equivalent to about 50 r/hr of

^{60}Co radiation if the RBE of π mesons is taken into consideration. Then the OER measured at 3°C for π^- mesons with the presently available dose rate of 20 to 30 r/hr may be about the same as OER for acute π irradiation. With this in mind, we also repeated the experiment at lower temperature.

Because of some problems encountered with the cooling units, the temperature could be maintained at about 4°C instead of 3°C. The procedure adopted is quite similar to that of Hall and Cavanagh.[10] Figure 8 shows the results of the experiment at 4°C for 10-day growth. Regression lines were fitted for the experimental points. The calculated OER is 1.5, with 95% confidence limits of 1.4 and 1.6. Figure 9 shows the results for minimum growth rate. The calculated OER is 1.51, with 95% confidence limits of 1.3 and 1.7. This measured OER value of 1.5 at this dose rate of 20 to 30 r/hr may be applicable to the acute π^- irradiation.

Experiments on ^{60}Co gamma radiation at chronic level, similar to Hall and Cavanagh, are in progress.

We also exposed groups of bean roots to the π^- meson beam at different doses in aerated and hypoxic conditions. Permanent slides were made at different fixation times to study chromatid aberrations. The scoring of the slides is in progress and the results will be reported later.

In conclusion, our findings show a significant reduction in OER for stopping π^- mesons in spite of contamination in the beam. The OER should be lower for a pure beam.

Acknowledgments

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Figure Captions

Fig. 1. Depth dose of π^- beam.

Fig. 2. Beam profiles at the peak of depth-dose distribution.

Fig. 3. Experimental setup during exposure.

Fig. 4. The 10-day growth plotted as a function of dose at the peak of π^- beam.

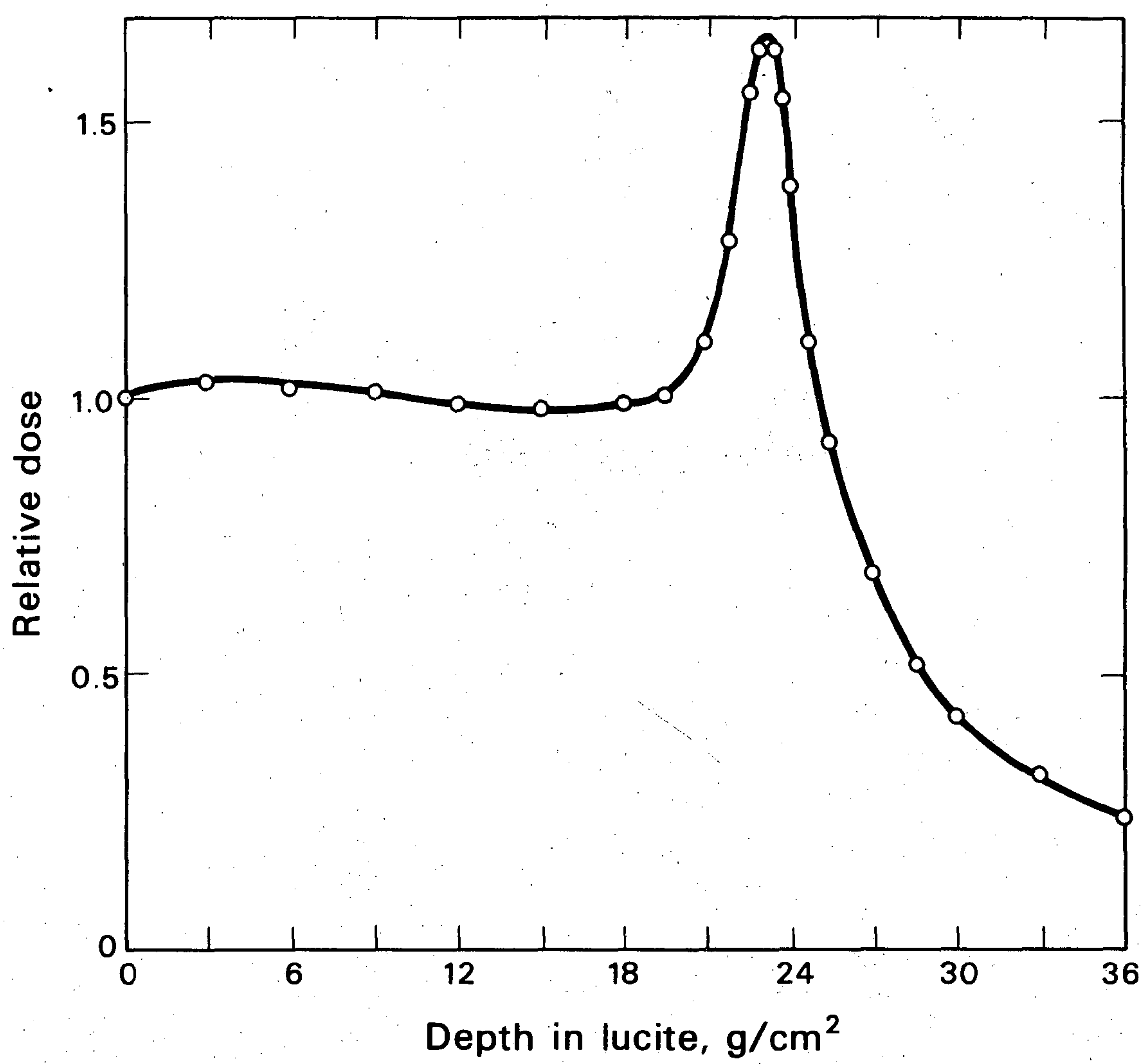
Fig. 5. Daily growth rate plotted as a function of days after exposure.

Fig. 6. Minimum growth rate plotted as a function of dose at the peak of π^- beam.

Fig. 7. Variation of OER as a function of dose rate for ^{60}Co (γ rays).

Fig. 8. The 10-day growth plotted as a function of dose at the peak of π^- beam.

Fig. 9. Minimum growth rate plotted as a function of dose at the peak of π^- beam.



DBL 687-5324

Fig. 1

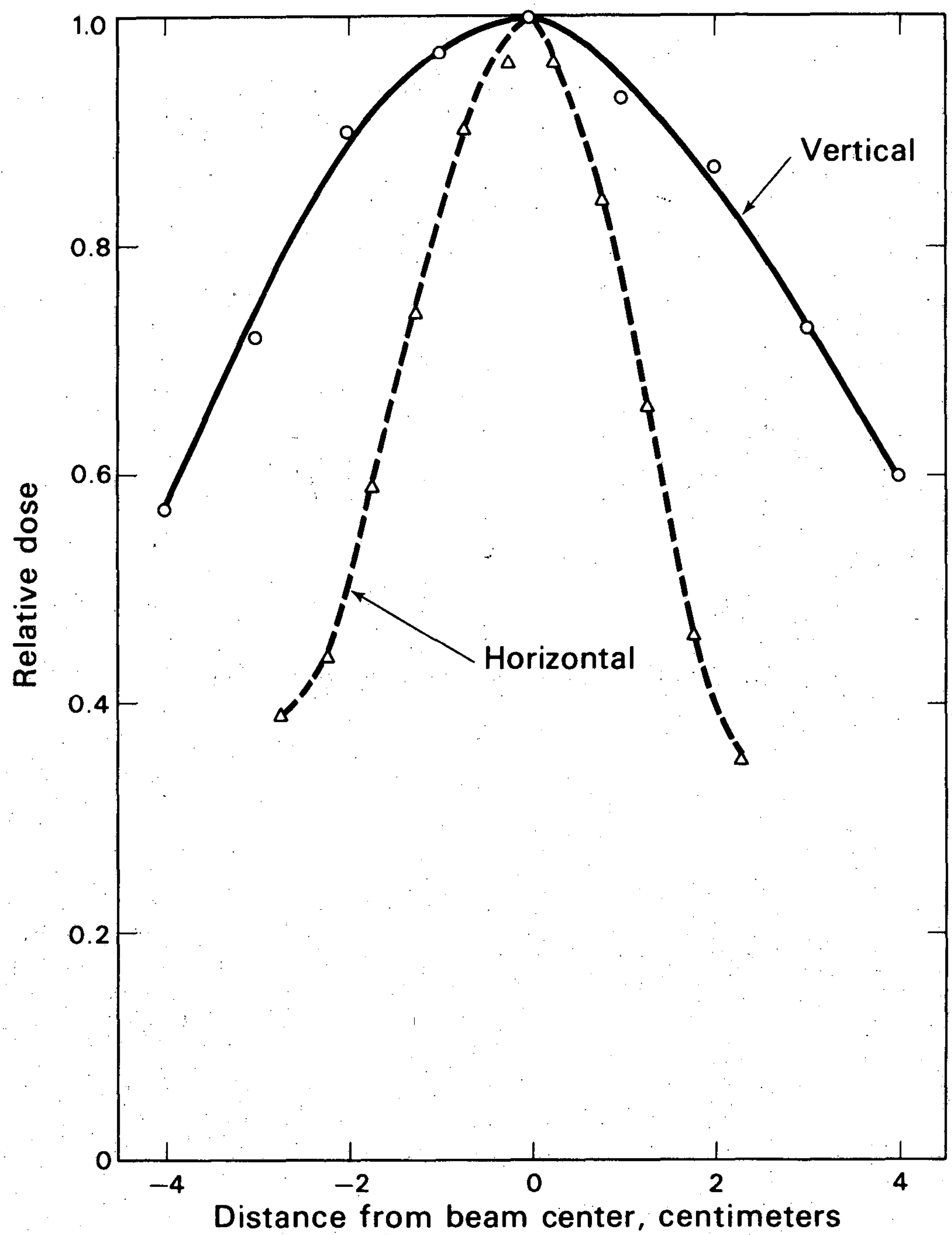


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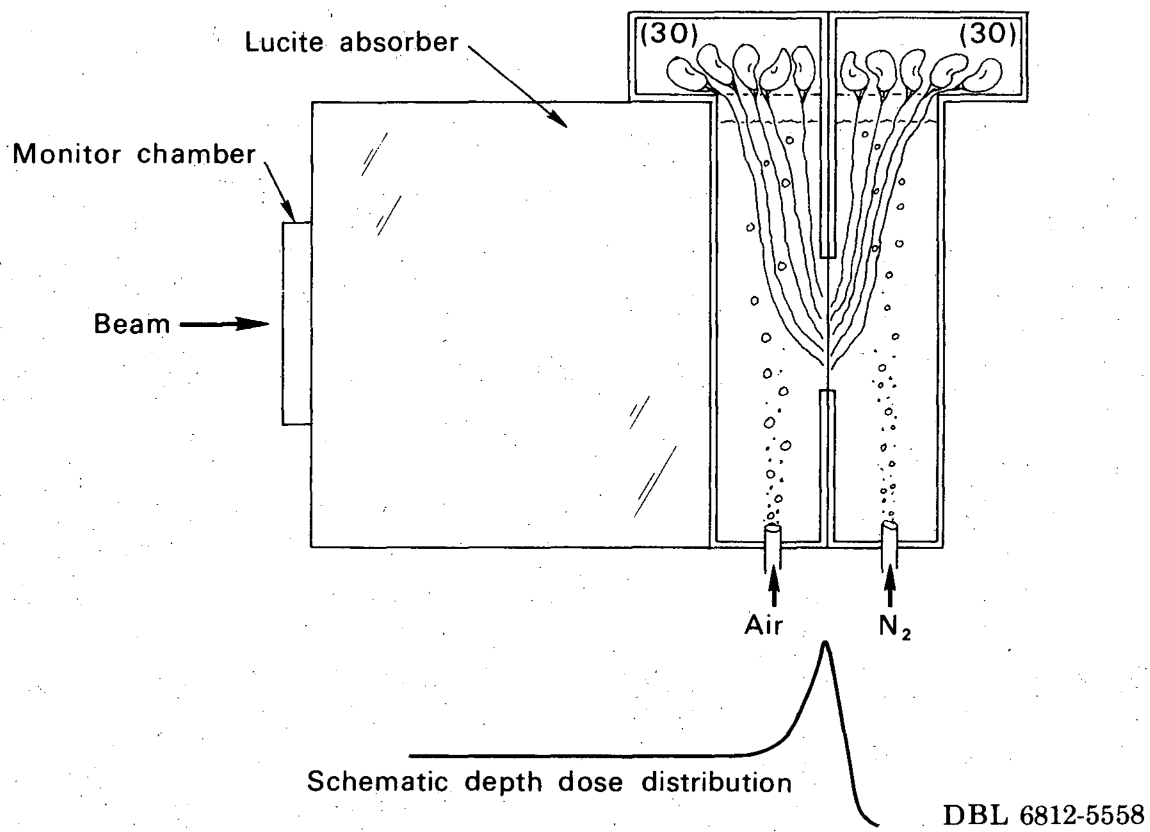
Fig. 2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(30)
(30)
Monitor chamber
Beam
Air
N_2
Schematic depth dose distribution
DBL 6812-5558

Fig. 3

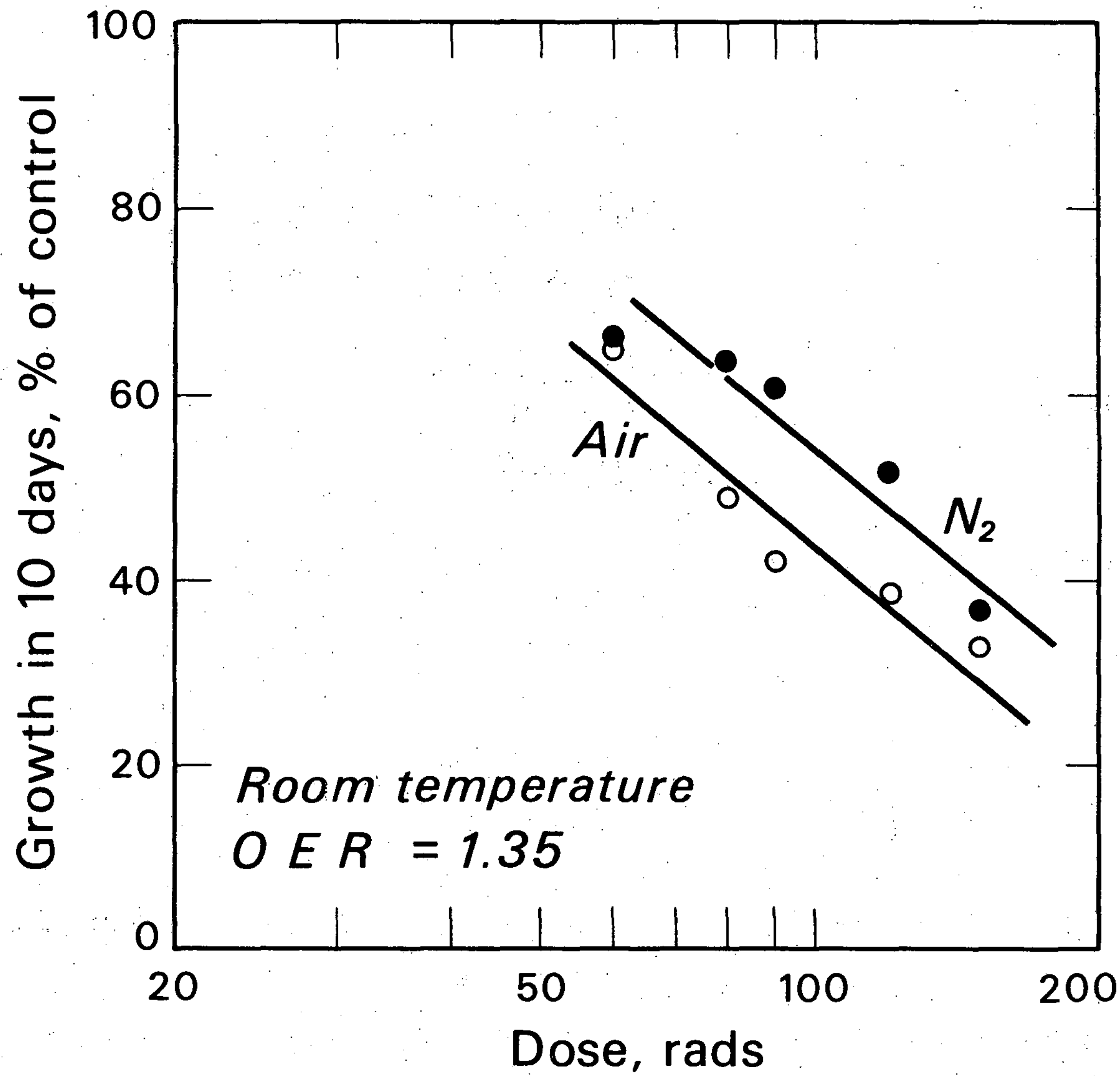

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Fig. 4

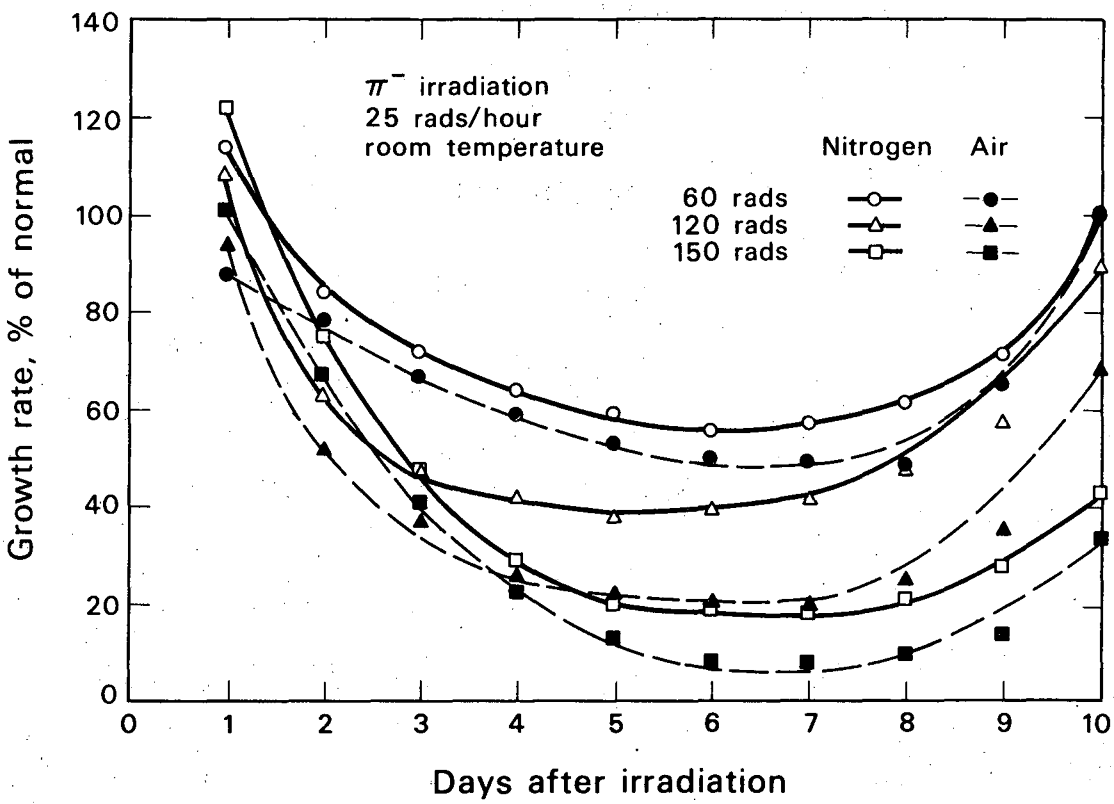

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Fig. 5

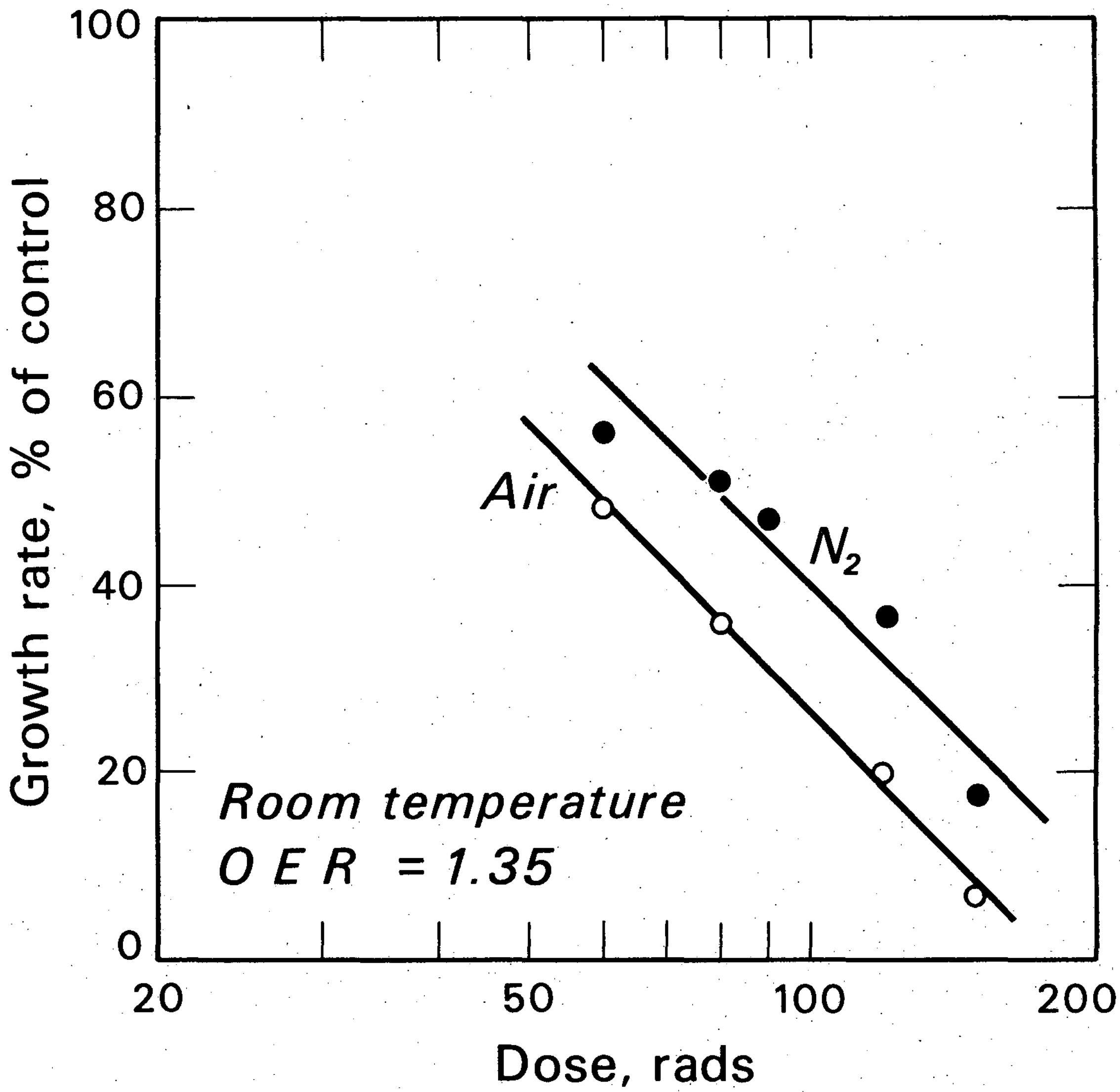

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Fig. 6

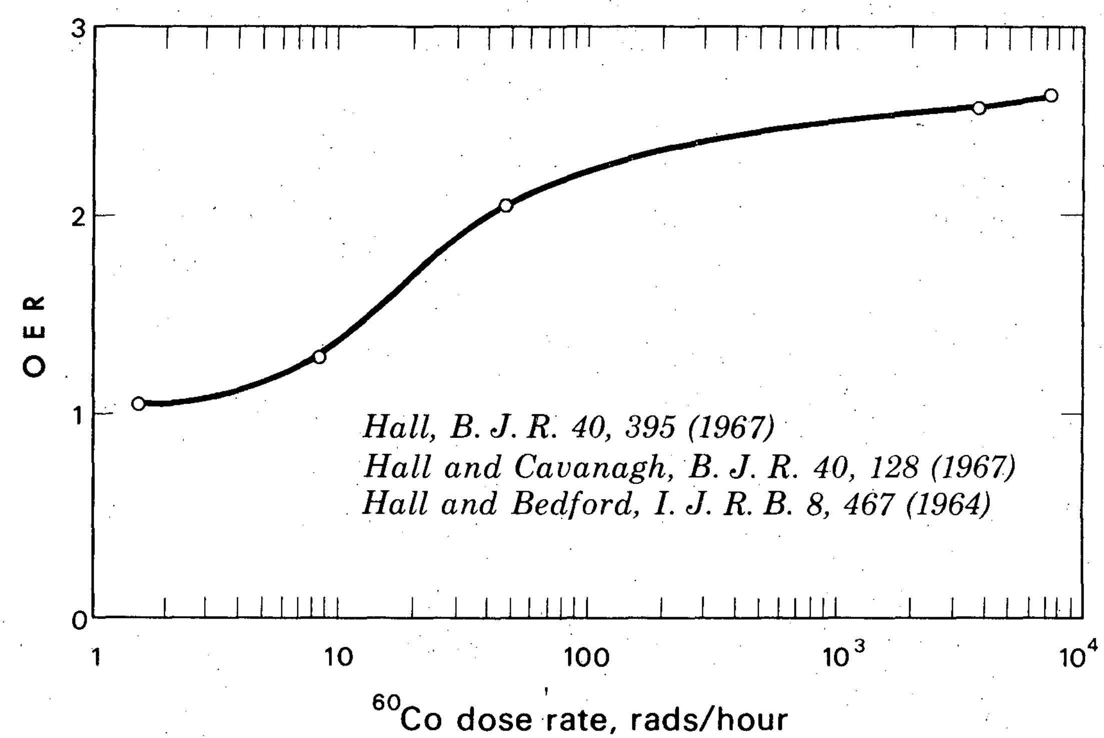

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Fig. 7

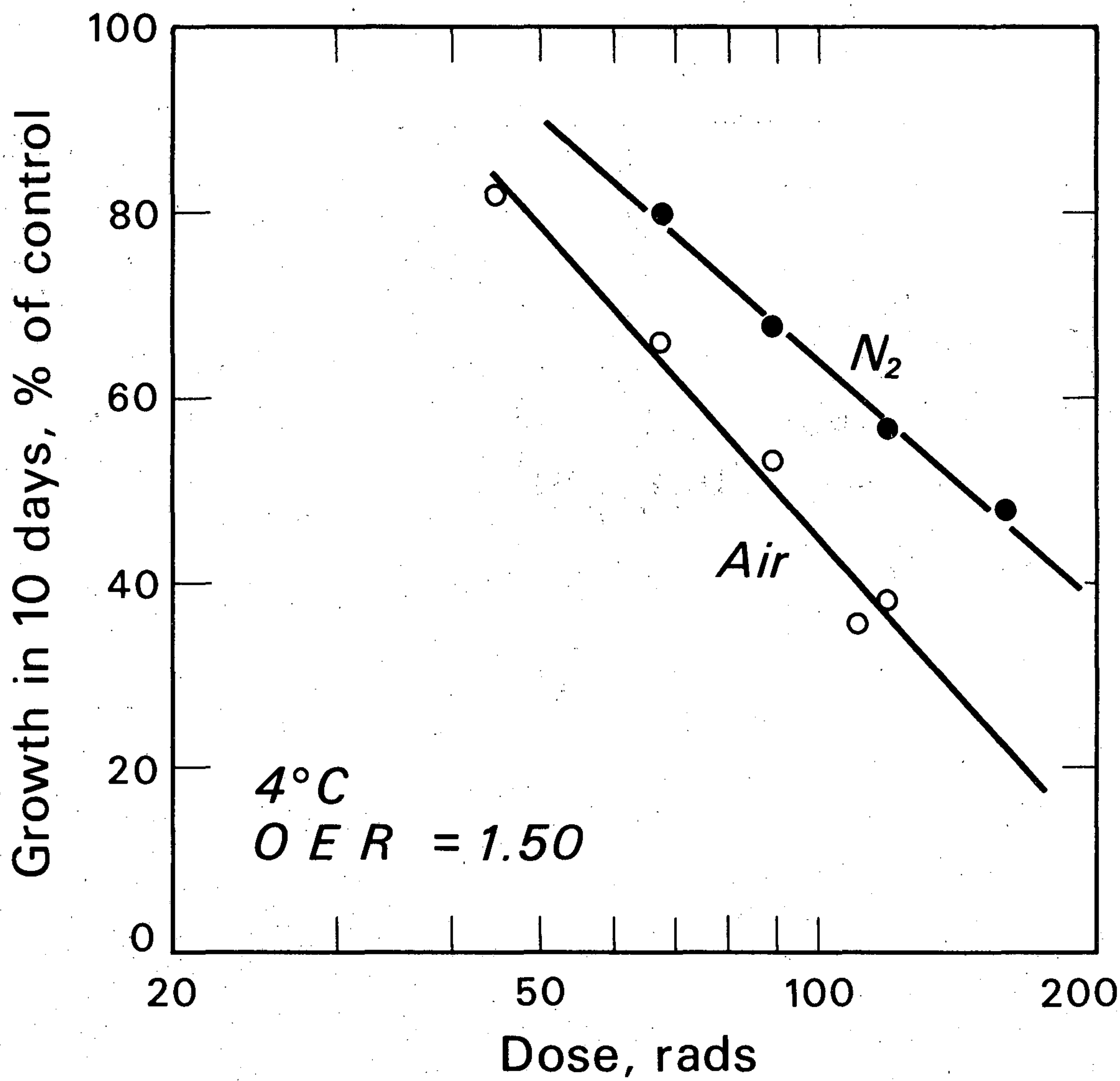

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Fig. 8

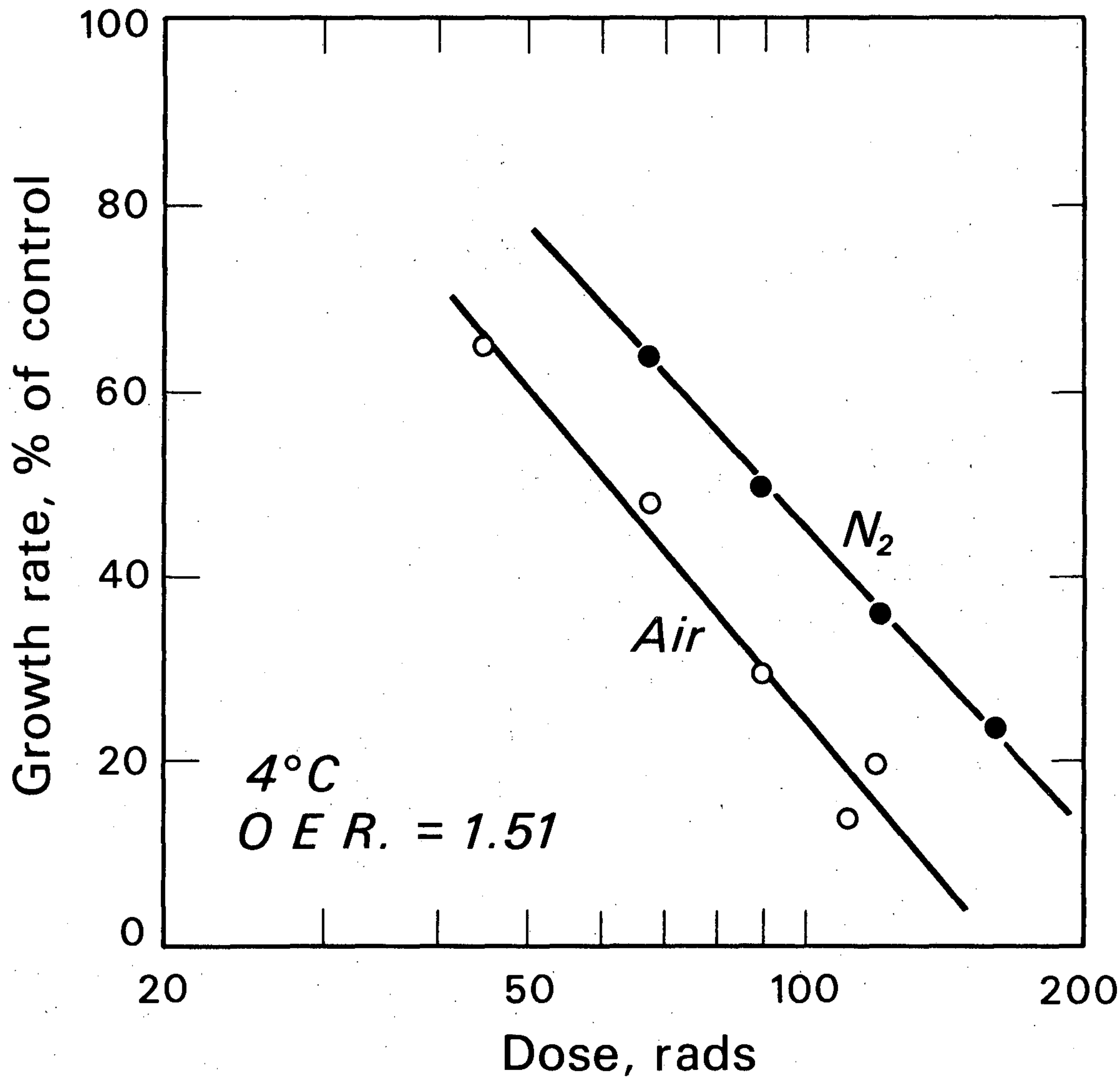

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Fig. 9