Title

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DISCLAIMER

MEASUREMENT OF OXYGEN EFFECT AND BIOLOGICAL EFFECTIVENESS OF A 910-MeV HELIUM ION BEAM USING CULTURED CELLS (T-1)

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ABSTRACT

The depth-dose distribution of a 910-MeV monoenergetic helium ion beam is modified by using a ridge filter in the beam path so that the region of maximum dose is uniform over a distance of about 6 cm of water. The biological effectiveness and oxygen enhancement ratio (OER) at different depths within a rectangular Lucite phantom are measured by using human kidney cells (T-1). The results indicate that the biological effectiveness at the broad peak region is about 1.3 to 1.4 compared with that at the beam entrance, and the OER is found to be about 1.7 to 1.9. This significant reduction in OER even when the beam is modified to cover 6 cm of tissue may be of radiotherapeutic interest in treatment of deep seated tumors containing hypoxic cells.

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Helium ion beam

Tissue culture

Ridge filter

INTRODUCTION

In radiation therapy, ideally one would like to deliver a tumorcidal dose to the tumor; however, in practice one is limited by normal-tissue injury. Radiations and techniques that help in delivering more dose to the tumor with minimum dose to the surrounding normal tissue could improve the cure rates and reduce the complications due to normal-tissue injury. Significant progress has been made by employing penetrating radiations. However, the use of heavy charged particles such as protons and helium ions is not very extensive, although such radiations are promising in improving radiotherapy results in principle and have been available at a few places for many years. This is probably because these facilities (cylotrons) are not in radiotherapy departments.

The therapeutic use of the 910-MeV helium ion beam from the 184-in.-synchrocyclotron at Berkeley has been mainly for pituitary irradiations of patients with acromegaly, diabetic retinopathy, Cushing's disease, or breast cancer (1). When the narrow Bragg peak is broadened by means of a variable absorber in the beam, it is possible to use this beam for other radiotherapeutic applications. Since, in such cases, the dose contribution due to high-LET components at the broadened Bragg-peak region is small, it was felt that such a beam may not be useful in overcoming the oxygen effect considerably (2). However, the experimental determination of the oxygen enhancement ratio of 1.6 for

14-MeV neutrons indicates that a small fraction of dose due to high-LET alpha particles produced by 14-MeV neutrons in tissue is mainly responsible for reducing the OER (3, 4).

It is of interest to find out how a small fraction of dose due to high-LET components (low-energy alpha particles) at the broadened Bragg-peak region would affect the radiobiological properties of therapeutic interest, such as biological effectiveness and oxygen enhancement ratio. Such measurements will be helpful in assessing the therapeutic capabilities of this beam.

Our preliminary measurements of oxygen effect at the broadened Bragg peak region over a depth of 3 cm indicated significant reduction in oxygen enhancement ratio (5). In this investigation the 910-MeV helium ion beam is modified so that the dose at the peak region is uniform over 6 cm of water. The biological effectiveness and OER over this broad-peak region and at the beam entrance are measured.

MATERIALS AND METHODS

Physical

The width of the Bragg peak of a monoenergetic charged particle beam is small when compared with typical tumor sizes. One technique for modifying the depth-dose distribution of monoenergetic charged particles to uniformly irradiate the treatment volume is to use a ridge filter (6, 7).

The ridge filter consists of a series of similar units, usually made of a dense metal such as copper. These units are placed side by side to form a composite filter whose cross section is larger than the beam area. Each unit is essentially a stepwise variable—thickness absorber. The width of an individual step determines the relative intensity, and the total thickness of the step determines the residual energy. The use of a ridge filter permits the simultaneous superposition of the depth-dose distributions of all the components required to produce the desired depth-dose distribution. As more components are used to approximate the desired distribution, the number of steps increases and the cross section of the individual units more closely approximates a smooth curve.

The 910 MeV helium ion beam has a range of about 32 cm in water; this energy is much higher than is necessary for radiotherapeutic applications. Such high-energy heavy charged-particle beams give a lower ratio of dose at the peak to the entrance because of multiple scattering effects and the loss of the particles before they stop. The beam is first degraded by a 3.2-cm copper absorber. The residual energy of the beam after passing through copper is 500 MeV. This residual beam is further modified by using a ridge filter so that the peak of the depth-dose distribution is broad enough to cover 6 cm of water. In a Lucite phantom this is equivalent to about 5 cm ($6 g/cm^2$ of Lucite).

The design of the ridge filter is optimized by the use of a computer program which can translate either an experimental or a theoretical narrow Bragg curve to the required curve with a broadened peak region. The output of the computer program includes the necessary information for punching a paper tape, which can be used with a paper-tape-controlled milling machine to make the required filter. The experimental measurements of the modified depth-dose distribution agree very well with the computer-predicted dose distribution (8). The computer printout of the ridge filter used in this investigation is shown in Fig. 1, and the experimental determination of the depth-dose distribution of helium ion beam is shown in Fig. 2.

Biological

Human kidney cells (T-1) were used in this investigation. The tissue culture techniques employed have already been described(9, 10). Instead of feeder cells, enriched medicum containing 15% fetal calf serum was used to improve the plating efficiency. Cells in early logarithmic growth phase were plated in 35-mm plastic dishes in appropriate numbers so that surviving colonies would be about 100 in each dish. The dishes were placed in the incubator at 37°C for 4 to 7 hours before exposure to radiation.

A sample loading wheel was used for mounting the dishes for irradiation(11). The medium was removed from the dishes before they were mounted in the wheel. Compressed air or nitrogen with 5% carbon dioxide saturated with water vapor was admitted into the wheel and circulated over the dishes during exposure. In the case of exposures in nitrogen, the cells were pregassed for at least 5 minutes before exposure to radiation. Dishes containing cells were exposed to different doses of radiation at three positions marked 1, 2, and 3 in Fig. 2. Three to four dishes were exposed for each dose point. Twelve to fifteen days after exposure the colonies were stained with methyline blue. All the visible colonies were counted and the percent survival calculated.

RESULTS AND DISCUSSION

Figure 3 shows the survival curves obtained for exposures of the three positions in a Lucite phantom. Biological effectiveness compared with that of entrance position (marked 1 in Fig. 2) and OER were calculated at 10% survival.

The biological effect at entrance is very similar to that of conventional radiation. The biological effectiveness at positions 2 and 3 compared with position 1 is 1.3 and 1.4 respectively. The OER values at positions 1, 2, and 3 are 2.5, 1.8, and 1.7 respectively. These preliminary results indicate that there is a significant reduction in OER in the broad peak region. This significant reduction in OER even when the peak is broadened to cover 6 cm of water is rather unexpected, in the same way an OER of 1.6 was for 14-MeV neutrons.

The trend of variation of RBE and OER over the peak region can be expected from variation of LET, which increases with depth. Early experiments with anoxic mammalian tumor cells studied in vivo indicate that dose response was significantly altered at the broadened Bragg peak of a 910-MeV helium ion beam, when compared with that at the entrance (12).

A high-energy helium ion beam has a radiotherapeutic application similar to that of high-energy protons because of its excellent depth-dose distribution characteristics in the treatment of deep-seated tumors located near sensitive and vital structures. Further, the significant reduction in OER indicates an additional advantage of high-energy helium ion beams in treating tumors containing hypoxic cells. The anoxic gain factor (damage to anoxic cells when compared with oxygenated cells) for helium ion beam is greater than conventional radiation, but slightly less than that for fast neutrons. Unlike with neutrons, this gain factor is in the region of interest only and the type of damage to surrounding normal tissue is similar to that of conventional radiation. The anoxic gain factor for neutrons when compared with conventional radiation gets reduced appreciably for small fractions of doses (13). This may possibly be true for helium ion beams. However, with the excellent depth-dose distribution and beam shaping that can be obtained for helium ion beam, it is possible to deliver large single doses to the tumor region and spare the normal surrounding tissue. Thus, helium ion beam may be very effective in radiotherapy where large doses of conventional radiation have been found to be useful.

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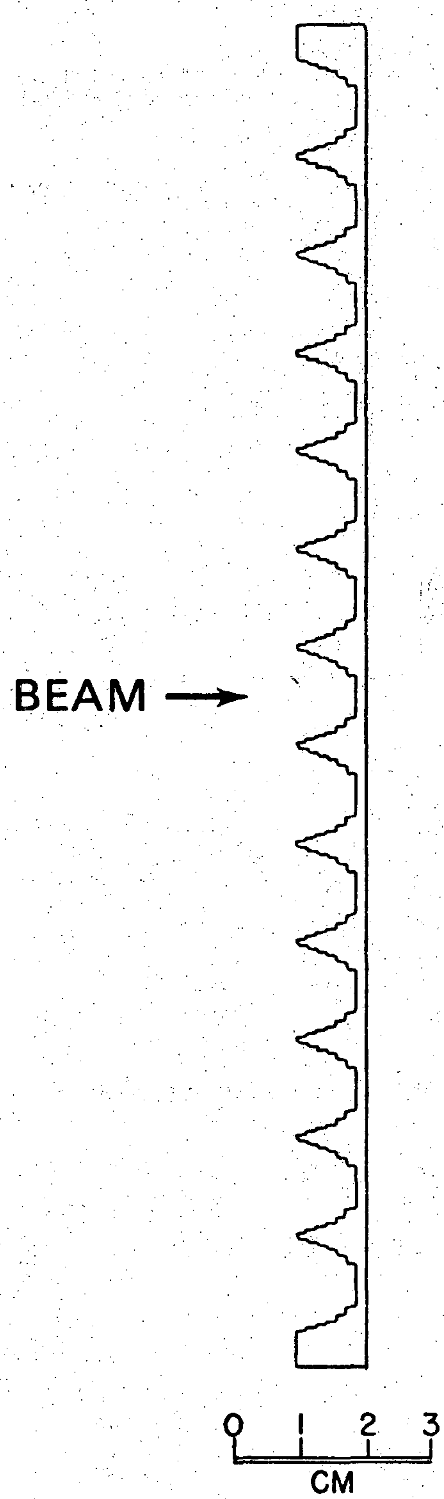
FIGURE LEGENDS

Fig. 1. Ridge filter.

Fig. 2. Modified depth-dose distribution of a 910-MeV helium ion beam, showing the three exposure positions.

Fig. 3. Survival curves for T-1 cells exposed under aerobic and anoxic conditions at the three positions marked 1, 2, and 3 in Fig. 2.



XBL 7011-7024

Fig. 1.

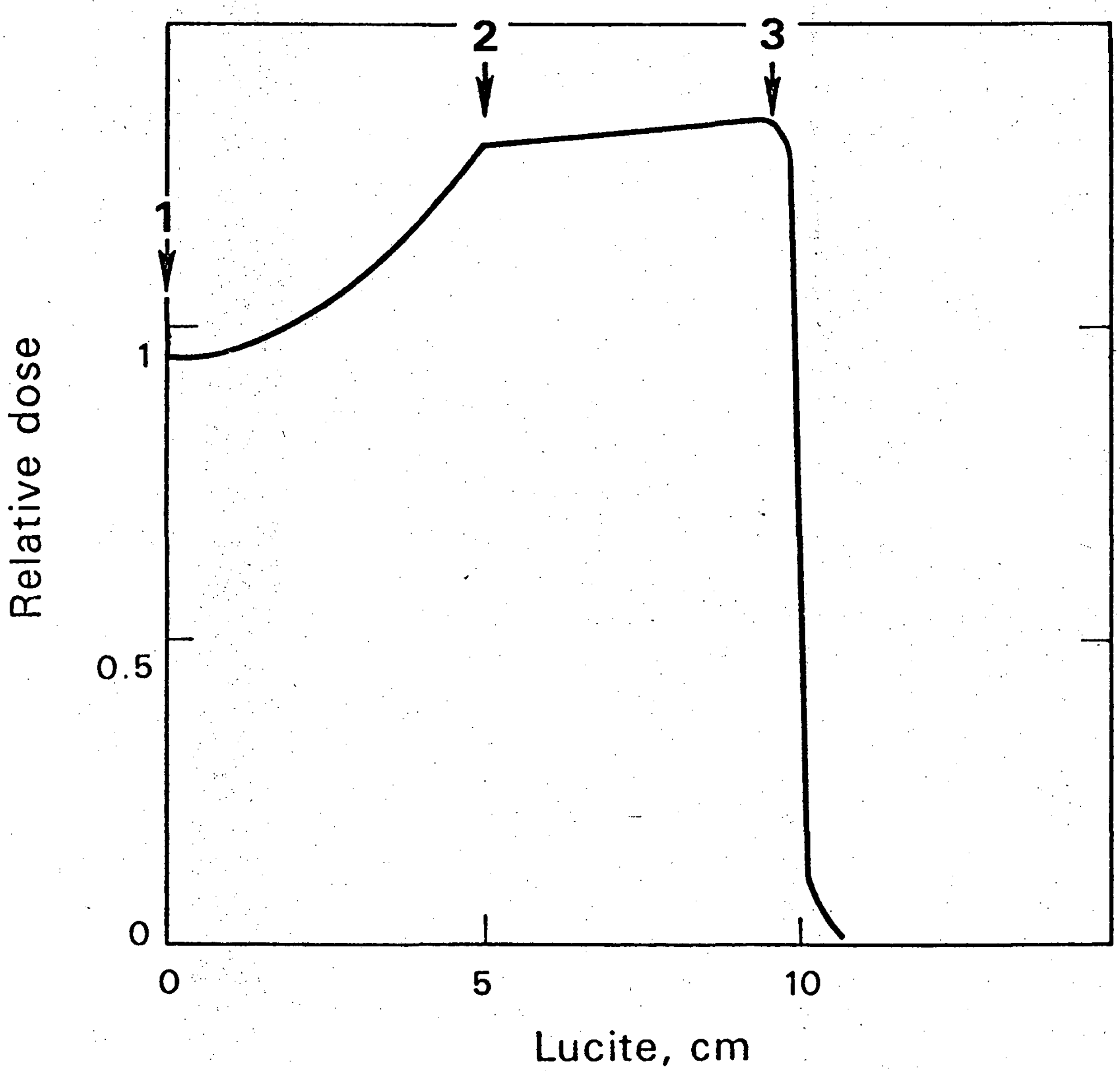


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Fig. 2

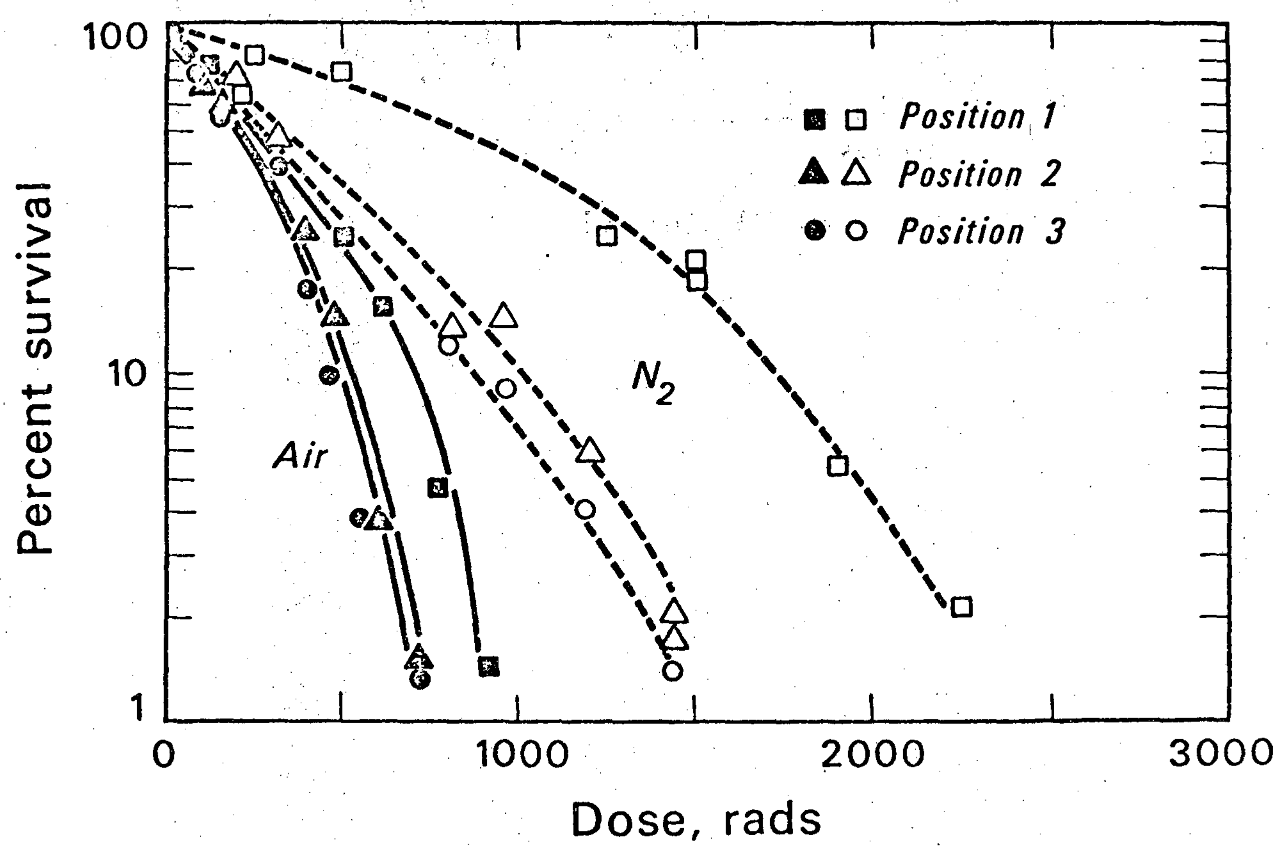

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Fig. 3

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