

THE IMPACT OF TARGET VOLUMES OF EHRlich ASCITES CARCINOMA IRRADIATED WITH A PENCIL SCANNING BEAM OF PROTONS AT A TOTAL DOSE OF 60 GY ON THE TUMOR GROWTH AND REMOTE EFFECTS IN MICE

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INTRODUCTION

The most promising type of proton therapy: pencil beam scanning or PBS technology, has recently been used. It increases the beam-efficiency factor, provides the homogeneity of the dose in a target, and lowers the input of secondary particles to the dose and skin radiation exposure. The application of scanning proton beams allows a decrease in the efficient dose on a patient's body by an order of magnitude; this is directly connected with a decrease in the risk of secondary tumors. Consequently, it is clear that further proton beam therapy improvement requires the assessment of hypofractionation or even oligofractionation (one to three fractions) of irradiation, which allows one to reduce the treatment time and increase its efficiency due to decrease the number of factions and increase the single dose.

MATERIALS AND METHODS

Animals

The experiments were performed on 8-9-week-old male of white outbred SHK mice with a weight of 24–28 g. Each group consisted of 10–30 animals. A solid form of Ehrlich ascites carcinoma (EAC) was used as a model of tumor growth, which is a rapidly growing, aggressive, radioresistant, non-steadying tumor with 100% death of animals within a month after inoculation of 1-2 million cells.



1 day after inoculation

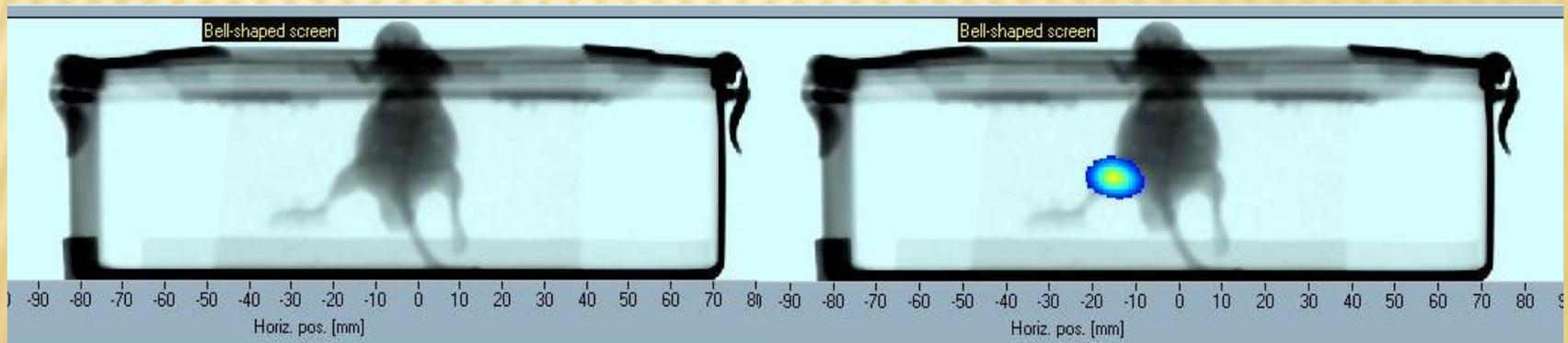
14 days after inoculation

30 days after inoculation

MATERIALS AND METHODS

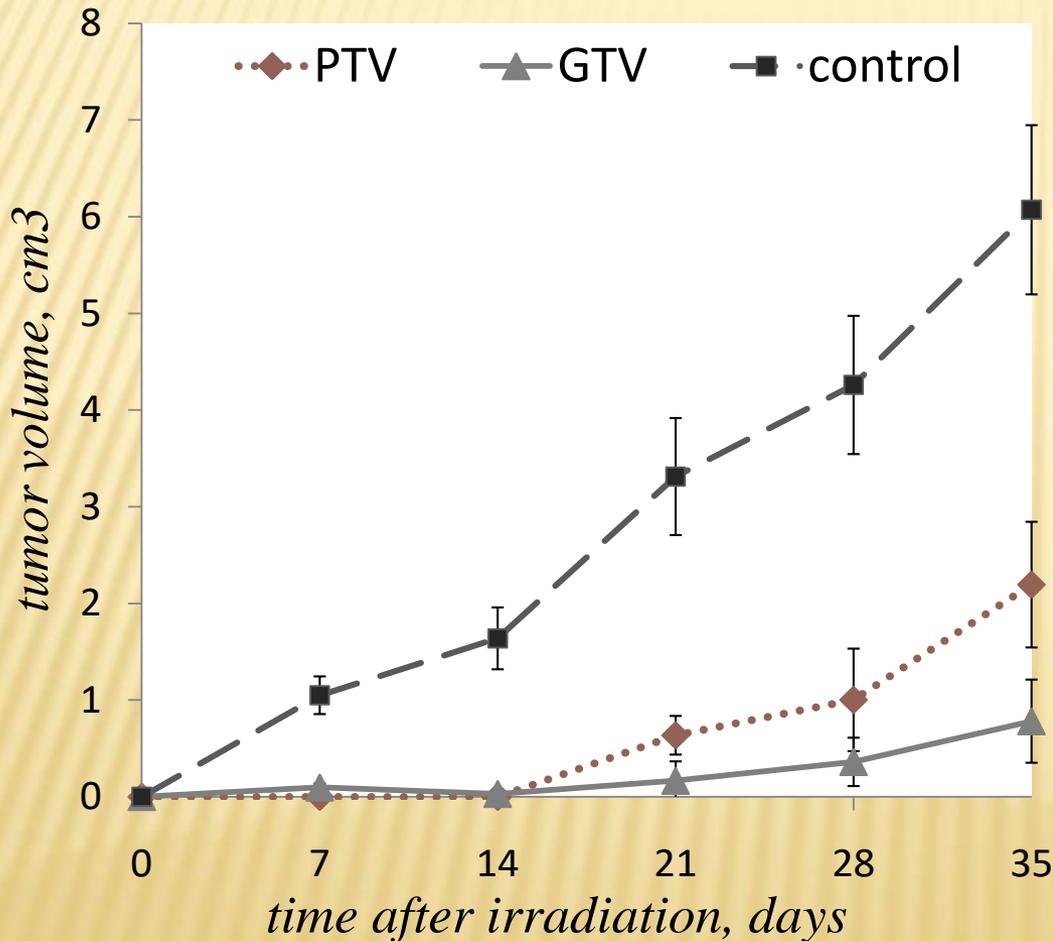
Irradiation

Mice were irradiated two fractions of 30 Gy each with interval 24 h. Irradiation was carried out in a proton synchrotron accelerator “Prometeus” (Russia, Protvino) with a PBS from two opposite fields. In order to determine the volume of irradiated tissue, a tomogram of a mouse in the water phantom was obtained and a gross tumor volume (GTV) that is equal to the average size of 0.47 cm^3 was specified using a specially developed 3D planning system. In another group of animals the irradiated tissue region was increased to the planning target volume (PTV) which was equal to 1.5 cm^3 .



RESULTS

The dynamics of EAC growth within a month

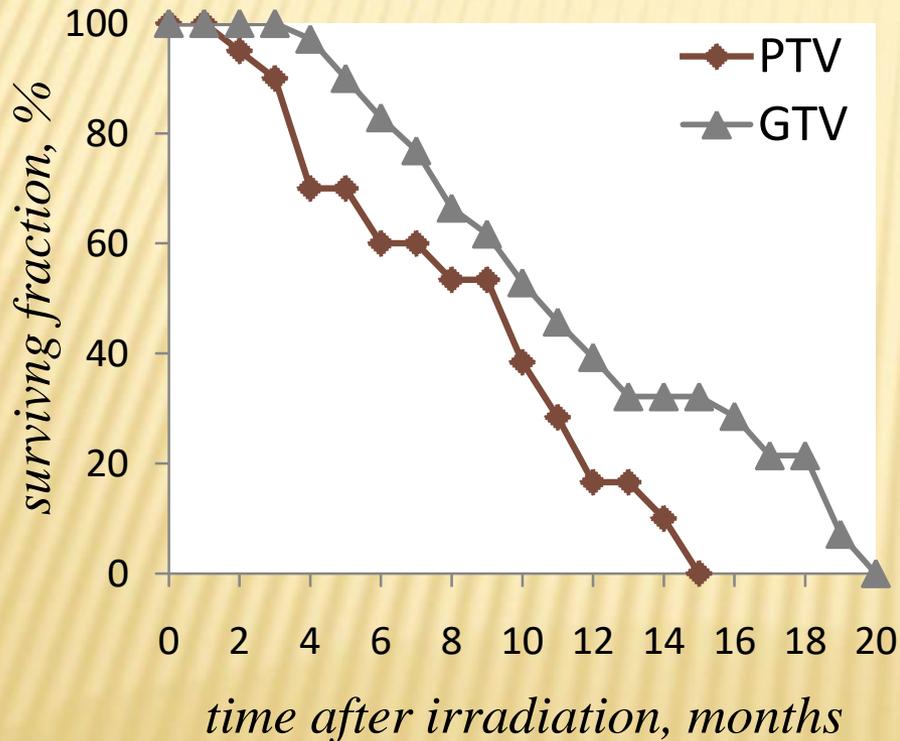


The rate of tumor growth was significantly lower in the irradiated groups than in control mice. The antitumor efficiency was higher in case GTV irradiation than PTV irradiation. The tumors were absent in 81% of the animals following irradiation by GTV and 45% following irradiation by PTV.

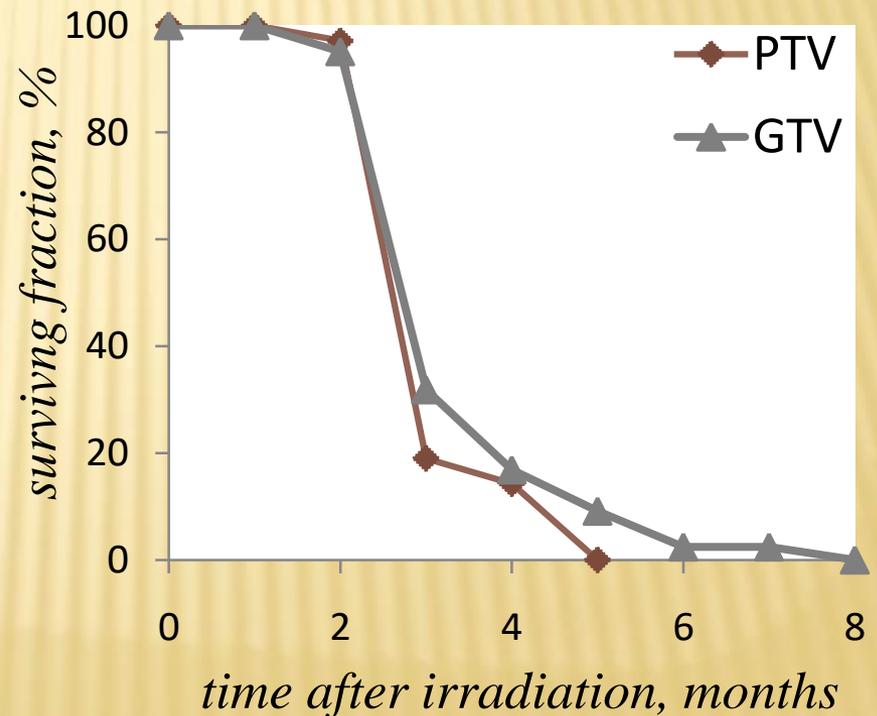
RESULTS

The dynamics of the death of tumor-bearing mice (a) without relapses and (b) with relapses upon proton irradiation of different tissue volumes

(a)



(b)



RESULTS

Then we observed remote radiation effects in mice with a complete regression of tumor nodes in one month after hypofractionation (30+30 Gy) proton therapy: relapses rate and average lifespan. The occurrence of EAC relapses in the same place was observed within a month after the complete disappearance of the primary tumor in all groups. The relapses rates following irradiation using GTV and PTV did not differ. In the group with GTV irradiation, survival was higher: the maximum life expectancy in mice without relapse was 5 months longer, and in mice with relapse it was 3 months longer. The average lifespan of mice with EAC relapses in the group with GTV irradiation was higher compared to the group with PTV irradiation (96 and 77 days after irradiation or 58 and 31 days after the occurrence of a relapse, respectively; $p \leq 0.01$). The average lifespan of mice without tumors was also notably longer in the GTV group: 283 days compared to 228 days after PTV irradiation ($p \leq 0.01$).

DISCUSSION

The results of these experiments show that the model of solid Ehrlich ascites carcinoma in mice can be used not only for the study of tumor growth upon various proton hypofractionated irradiation regimes but also for the observation of tumor relapses and other remote radiotherapy consequences. Our studies demonstrate higher antitumor efficiency and a remarkable increase in the average lifespan after hypofractionated irradiation with a proton pencil scanning beam at a total dose of 60 Gy via GTV as compared to PTV and contribute to an estimation of immediate risks to surrounding normal tissue and potential late effects. The tested system of positioning and three-dimensional planning of irradiation of the mice and the suggested schemes for hypofractionated irradiation demonstrate the possibilities of a proton facility and can be used for further development of proton beam therapy.

CONCLUSIONS

Irradiation with a PTV proton pencil scanning beam including not only the actual size of the tumor but also the surrounding tissues and GTV did not affect the EAC relapses rate and remission time. However, at equal relapses rates in both groups in variants with GTV irradiation the average lifespan of mice without tumors substantially increased. These results show that irradiation of a smaller tissue volume is favorable for the average lifespan prognosis of “cured” mice. These data demonstrate that upon for this location and size of solid EAC an increase in the volume of irradiated tissue is not necessary in order to enhance treatment efficiency.

THANK YOU
FOR YOUR ATTENTION!

