Volume reduction of ENU-induced rat brain tumors by irradiation with synchrotron radiation

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Rationale and objectives

Human glioblastomas are one of the most devastating types of brain tumor. If no treated, patients die within 6 months from the moment of diagnostics. Today, there is no cure for this type of tumors, and radio- or chemotherapy are administrated as merely palliative treatments [1]. Several approaches to therapy have been developed, both in clinical and preclinical studies. The best results know to the date have been achieved in pre-clinical studies with the SSRT (synchrotron stereotactic radiation therapy) technique, specific to synchrotrons [2]. The technique combines a x-ray irradiation in a tomotherapy geometry, combined with a chemotherapy treatment with a platinated agent, administrated by intratumoral injection. The technique was applied on the F98 rat glioma model. Tumors are developed by the implantation of tumoral cells in the brain of the animals.

The success of this technique encouraged us to try a model of spontaneous tumours, closer to the clinical case than cell implantation. The model chosen was the ENU(ethyl-nitros urea)-induced tumors, which develops tumours of the CNS (central nervous system), being mainly in the brain [3]. Tumors may be either oligodendrogliomas-like or glioma-like and they grow mainly around the corpus callosum.

Methods

The SSRT technique was applied to these tumors, slightly modified to adapt to the singularities of the model. Animals were split into three study groups, or three different treatmets: radiotherapy alone, chemotherapy alone and combined radio-chemotherapy. A fourth group was kept untreated, as controls. The tumor volume was measures by means of MRI images of the animals before and at several stages after the treatment.

Results

Partial tumoral regression was observed in general in almost all the animals that were only irradiated, and in some cases a total regression of the tumour was found. The tumours treated by the combination of irradiation and a platinated drug did not follow the same general regressive trend. On the other hand, for the groups treated by chemotherapy alone, the temporal evolution of the tumoral volume was very close to those tumors of the control animals, i.e. fast growing. This model has proven to be a difficult one, due to its disparate nature: the tumors appeared in multiple locations, with different grades and of different types. Moreover, the animals would not die of their brain tumors, and some others would die from other causes (extracraneal lesions). This last difficulty made impossible to do survival curves, therefore the tumours were followed-up by MRI imaging.

Conclusion

Despite the difficulties of the model, some tumoral regression due to the treatment has been observed in these animals. This observation is new in this model and it helps to the characterisation of the model and sheds some light on the nature of chemically induced glioblastomas.

References

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