

Intracerebral Delivery of 5-Iodo-2'-Deoxyuridine in Combination with Synchrotron Stereotactic Radiation for the Therapy of the F98 Glioma.

Julia Rousseau^{1, 2, 3}, Jean-François Adam^{1, 2, 3}, Pierre Deman^{1, 2, 3}, Ting-Din Wu^{4, 5}, Jean-Luc Guerquin-Kern^{4, 5}, Barbara Gouget⁶, Rolf. F Barth⁷, François Estève^{1, 2, 3, 8} and Hélène Elleaume^{1, 2, 3, 8, *}

¹ INSERM U836, Equipe 6, Grenoble Institute of Neurosciences, Grenoble, France;

² Université Joseph Fourier, Grenoble, France;

³ European Synchrotron Radiation Facility, Medical Beamline ID17, 38043 Grenoble, France;

⁴ Institut Curie, Laboratoire de Microscopie Ionique, Orsay, 91405, France;

⁵ INSERM U759, Orsay, 91405, France;

⁶ Laboratoire Pierre Süe, Groupe Toxicologie Humaine et Environnementale, CEA-CNRS UMR 9956, Gif-sur-Yvette, F91191, France;

⁷ Department of Pathology, The Ohio State University, Columbus, Ohio 43210;

⁸ Centre Hospitalier Universitaire, Grenoble, France.

ABSTRACT

Purpose: Iodine-enhanced synchrotron stereotactic radiotherapy (SSR) takes advantage of the radiation dose-enhancement produced by high Z elements when irradiated with monoenergetic beams of synchrotron X-rays. In this study, we have investigated whether therapeutic efficacy could be improved using a thymidine analogue: 5-iodo-2'-deoxyuridine (IUdR), as a radiosensitizing agent.

Materials and Methods: IUdR was administered intracerebrally (i.c.) over 6 days to F98 glioma-bearing rats using Alzet[®] osmotic pumps, beginning 7 days after tumor implantation. On the 14th day, a single 15 Gy dose of 50 keV synchrotron X-rays was delivered to the brain. Animals were followed until the time of death and the primary endpoints of this study were mean and median survival times.

Results: The median survival time for irradiation alone, chemotherapy alone or the combination were 44, 32 and 46 days, respectively, compared to 24 days for untreated

controls.

Conclusions: The chemotherapeutic effect of the prolonged infusion of IUdR was significant, but its combination with a single, 15 Gy dose of X-rays did not significantly improve survival compared to that of X-irradiation alone. Further studies are required to understand why the combination of chemo-radiotherapy was no more effective than X-irradiation alone.