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Prospective serial proton MR spectroscopic assessment of response to tamoxifen for recurrent malignant glioma

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Tejas Sankar¹, Zografos Caramanos², Rachid Assina¹, Jean-Guy Villemure^{3, 4}, Richard Leblanc³, Adrian Langleben⁵, Douglas L. Arnold^{2, 3} and Mark C. Preul^{1, 2} 

- (1) Neurosurgery Research Laboratory, Division of Neurological Surgery, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, 350 W. Thomas Road, Phoenix, AZ 85013, USA
- (2) MR Spectroscopy Unit, Montreal Neurological Institute, McGill University, Montreal, QC, Canada
- (3) Department of Neurology and Neurosurgery, McGill University, Montreal, QC, Canada
- (4) Division de neurochirurgie, Departement de chirurgie, Universite de Montreal, Montreal, QC, Canada
- (5) Department of Oncology, McGill University, Montreal, QC, Canada

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Abstract *Objective* Early prediction of imminent failure during chemotherapy for malignant glioma has the potential to guide proactive alterations in treatment before frank tumor progression. We prospectively followed patients with recurrent malignant glioma receiving tamoxifen chemotherapy using proton magnetic resonance spectroscopic imaging (¹H-MRSI) to identify intratumoral metabolic changes preceding clinical and radiological failure. *Methods* We performed serial ¹H-MRSI examinations to assess intratumoral metabolite intensities in 16 patients receiving high-dose oral tamoxifen monotherapy for recurrent malignant glioma (WHO grade III or IV) as part of a phase II clinical trial. Patients were followed until treatment failure, death, or trial termination. *Results* Patients were officially classified as responders (7 patients) or non-responders (9 patients) 8 weeks into treatment. At 8 weeks, responders and non-responders had different intratumoral intensities across all measured metabolites except choline. Beyond 8 weeks, metabolite intensities remained stable in all responders, but changed again with approaching disease progression. Choline, lipid, choline/NAA, and lactate/NAA were significantly elevated ($P < 0.02$), while creatine ($P < 0.04$) was significantly reduced, compared to stabilized levels on average 4 weeks prior to failure. Lactate was significantly elevated ($P = 0.036$) fully 8 weeks prior to failure. In one patient who was still responding to tamoxifen at the conclusion of the trial, metabolite intensities never deviated from 8-week levels for the duration of follow-up. *Conclusions* Characteristic global intratumoral metabolic changes, detectable on serial ¹H-MRSI studies, occur in response to chemotherapy for malignant glioma

and may predict imminent treatment failure before actual clinical and radiological disease progression.

Keywords Brain neoplasm - Chemotherapy - Glioma - Magnetic resonance imaging - Magnetic resonance spectroscopy - Tamoxifen

✉ **Mark C. Preul**

Email: mpreul@chw.edu

Email: neuropub@chw.edu

References secured to subscribers.

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