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TITLE: Longitudinal Multivoxel MR Spectroscopy Study of Pediatric Diffuse Pontine Gliomas Treated by Radiotherapy

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ABSTRACT BODY:

Purpose/Objective: Diffuse intrinsic pontine gliomas (DIPG) represent 80% of brainstem glioma and account for 15% of pediatric brain tumors. The diagnosis of DIPG relies on clinical manifestations and magnetic resonance imaging (MRI) findings without biopsy. Conventional external beam radiation therapy (RT) is the mainstay of treatment and is followed in most cases by clinical improvement. However, a local recurrence occurs usually within six months and prognosis is very poor with median survival times less than one year. No longer simply a research tool, multivoxel proton magnetic resonance spectroscopic imaging (MRSI) is being used clinically for adult gliomas in monitoring tumor response, particularly in supratentorial locations. The metabolic abnormalities in high-grade tumors are an elevated Choline peak and a depressed N-Acetyl-Aspartate (NAA) peak. Typically, single voxel MRSI are performed on lesions of the posterior fossa due to technical difficulties induced by anatomical constraints. The lack of substantial multivoxel MRSI data for pediatric diffuse pontine gliomas prompted us to analyze serial multivoxel exams and correlate them with clinical and MRI findings.

Materials/Methods: Twenty-five serial examinations of MRI/MRSI (7 2D and 18 3D-MRSI) were performed in the past two years at our institution for 8 patients with DIPG who received local RT. A total of 3270 voxels were categorized as normal appearing or abnormal based on corresponding imaging findings on FLAIR and contrast-enhanced T1-weighted MRI. Changes in the Cho to NAA ratio (CNR), within each category of MRI abnormality, were evaluated before RT, at response, and at recurrence. The statistical significance of the changes in CNR was quantified using paired t-test.

Results: Median age at diagnosis was 6 years (range 4-9 years), and median follow-up was 17 months (range 12-34 months). All patients showed initial tumor response within 2 months following RT but relapsed within a median time of 4 months after RT (range 2-25 months), leading to death in five of the eight patients in a median time of 12 months after diagnosis (range 10-19 months).

In all exams in which spectral data from normal appearing regions were obtained (n= 20), the CNR values in the imaging abnormalities (6.3 +/- 5) were significantly higher than the mean CNR values in normal appearing regions (0.97 +/- 0.3) (p<0.005). Moreover, CNR values decreased from studies at diagnosis to studies at time of response to RT, 5.39 +/- 4.8 and 2.365 +/- 0.98 respectively (p=0.13) followed by increased CNR values at the time of relapse (5.84 +/- 4.25, p=0.08).

In 2 patients, spectral abnormalities preceded the radiological and clinical deterioration by 2-5 months. In one patient with suspected clinical relapse, the longitudinal stability of both CNR and symptoms confirmed the MRI findings of treatment related changes rather than tumor recurrence.

Conclusions: Multivoxel MRSI is a feasible and reproducible noninvasive tool for pediatric DIPG. It offers more coverage than single voxel technique, and provides good quality spectral data. Our study suggests that longitudinal changes in metabolic ratios, rather than at a single time point, better predict dynamic changes in tumors undergoing therapy. Longitudinal multivoxel MRSI measurements have a potential value in assessing response to radiation or other therapies. A prospective study is currently underway at our institution to further investigate the value of 3D MRSI in monitoring the changes in healthy and tumor
tissues in pediatric PIDG before and after RT.

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