Location of Brain Tumor Intersecting White Matter Tracts Predicts Survival Prior to Therapy

Nikolai J Mickevicius[1], Alexander Carle[2], Stephanie Santarriaga[3], Trevor Bluemel[4], and Peter S LaViolette[4]

[1]Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States, [2]Biomedical Engineering, Purdue University, Indiana, United States, [3]Neuroscience, Medical College of Wisconsin, Wisconsin, United States, [4]Radiology, Medical College of Wisconsin, Wisconsin, United States

Intended Audience: Clinicians and scientists interested in diffusion imaging and brain tumors.

Purpose: The purpose of this study was to determine if the location of brain tumor intersecting white matter tracts predicted patient survival. Brain tumor migration and infiltration occurs preferentially down white matter tracts[1]. We therefore hypothesized that patients with tumors intersecting the cortico-spinal tract and corpus callosum would have decreased survival compared to those with tumors elsewhere because these tracts .

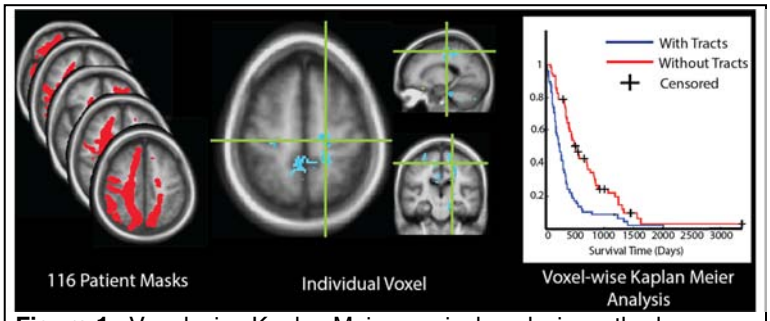

Figure 1. Voxel-wise Kaplan Meier survival analysis method.

Methods: 116 patients with glioblastoma multiforme (GBM) brain tumors with T1-post-contrast weighted (T1+C) imaging acquired prior to tumor resection were analyzed retrospectively for this analysis. A tumor region of interest (ROI) was drawn on the T1+C volume for each patient. The T1+C images were co-registered to the Montreal Neurological Institute (MNI) brain template. We then generated a template space library of white matter tracts using DTIQuery software (http://graphics.stanford.edu/projects/dti/software) and a DTI atlas from the University of Illinois. Custom MATLAB (Natick, MA) software was developed in-house to extract the template space tracts intersecting each patient's enhancing tumor. Tract maps were then partially blurred and binarized to generate a tumor-intersecting WM tract ROI for each patient (Figure 1, Left). Voxel based analytic methods[2] were used to calculate a Kaplan Meier survival test and subsequent Log-rank statistical test for each voxel, where survival was compared between patients with tumor intersecting WM tracts to those without (Figure 1). A whole brain map of z-scores corresponding to the Log-rank comparison was then thresholded at a significance level of $p<0.05$ with 10 contiguous voxels. Voxels without at least 10 patients in each category (intersecting and non-intersecting tumor ROIs) were excluded from the analysis.

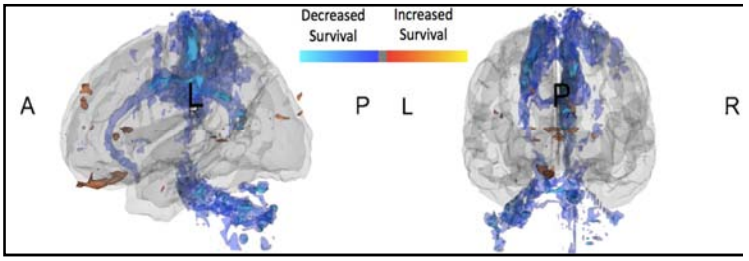

Figure 2. Three-dimensional survival map. Note the corpus callosum and cortical spinal tracts are associated with decreased survival.

Results: Patients with tumors intersecting the cortico-spinal tracts, corpus callosum, and cerebellar WM were found to have a decreased survival compared to patients with tumors intersecting other WM tracts. Figure 2 shows the map-level analysis in 3-D for ease of WM tract localization while thresholded axial images are shown in Figure 3.

Conclusions: We find that brain tumors intersecting major WM tracts such as the cortico-spinal tract and the corpus callosum are associated with decreased survival, even prior to any therapy. This is likely due to brain tumors having direct migrational routes to the brain stem and other structures imperative for physiological function such as breathing, swallowing, and maintaining blood pressure. This information may be beneficial to oncologists and surgeons planning for tumor resection; it will give insight as to how aggressive to be during the surgery. Treatment regimen and extent of resection was not controlled for and provides interesting routes for future research. It also remains to be seen whether gross-total versus partial resection plays a role in survival as well age and gender will affect GBM patient survival.

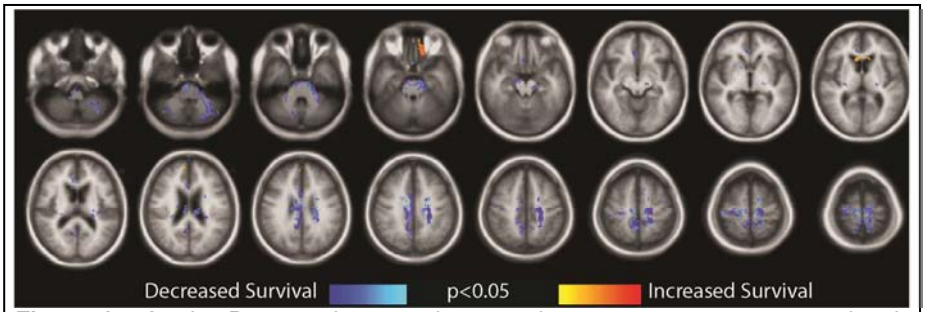

Figure 1. Axial 2-D survival map indicating white matter tracts associated with decreased survival.

References:

1. Price SJ, Burnet NG, Donovan T, et al. *Clin Radiol.* Jun 2003;58(6):455-462. **2.** Bates E, Wilson SM, Saygin AP, et al. *Nat Neurosci.* May 2003;6(5):448-450.