Correlating DTI-based cancer cell migration model predictions with the location of secondary tumors

A. Krishnan[1], D. Davis[2], P. Okunieff[3], and W. G. O'Dell[3]
[1]Biomedical Engineering, University of Rochester, Rochester, NY, United States, [2]Imaging Sciences, University of Rochester, Rochester, NY, United States, [3]Radiation Oncology, University of Rochester, Rochester, NY, United States

Purpose: We have shown that the direction of tumor recurrence is correlated with the location of major fiber bundles passing near the primary brain tumor [1]. We have recently developed a random walk model of tumor cell migration constrained by the local diffusion environment determined using Diffusion Tensor Imaging (DTI) to better predict the microscopic spread of gliomas [2]. In the current study we implement a method for applying a statistical test to evaluate the strength of the correlation between the model predictions and the location of secondary tumors.

Materials and Methods: The DTI data for this analysis were obtained as part of a retrospective study. The DTI data of ten glioma patients obtained at the earliest time point prior to the observation of any secondary tumor was used. The random walk model was run using only data obtained at the time of treatment, with 250 cells in each tumor surface voxel and each walk had 2500 steps. The post-contrast T1-weighed anatomical image showing recurrence was registered to the pre-treatment DTI B0 image through the anatomical image obtained at the same time point. The concentration of cells in each voxel was normalized by the maximum voxel concentration for that patient and the result was interpreted as being the probability that a cancer cell would migrate to that voxel location in the brain. To account for the decrease in the predicted cell concentration with the distance from the primary tumor, the normalized cell concentration on an equidistant surface from the primary tumor was used as the control (Figure 1). The normalized cell concentration was averaged over the entire secondary tumor and also averaged over all voxels on the equidistant surface. In pure isotropic diffusion these averages would be identical. A Mann-Whitney test was performed to compare the average normalized cell concentration (ANCC) in the secondary tumor with the equidistant surface, with the criteria that a p-value < 0.01 would indicate a significant difference between the two populations.

Results and Conclusions: The histogram of normalized cell concentration for voxels on the equidistant surface for one representative patient is shown in Figure 2. The average normalized cell concentration in the secondary tumor was higher than that of 78% of control voxels (Table 1). The magnitude of the U metric of the Mann-Whitney test for the ten patients was > 200 for each subject, each corresponding to a p-value < 0.0001. This result establishes that the predicted cell probability at the site of tumor recurrence was statistically different (higher) than regions outside the site of tumor recurrence.

Patient ID	1	2	3	4	5	6	7	8	9	10
ANCC	0.0039	0.042123	0.006167	0.004215	0.002801	0.018579	0.151647	0.025852	0.090341	0.016253
% < voxels	79.03	93.21	76.74	66.01	89.67	81.27	82.53	76.56	60.79	75.23
U metric	-741	-1002	-869	-999	-1776	-255	-562	-898	-230	-547

Table1. Evaluation of the average normalized cell concentration (ANCC) at the site of recurrence versus equidistant control voxels for each of ten subjects. Shown is the ANCC for the recurrence site and the corresponding percentage of voxels in the control group having a lower normalized cell concentration. The bottom row gives the computed Mann-Whitney U-metric, all of which correspond to p-values < 0.0001.

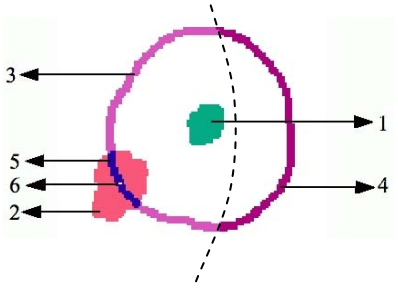

Figure 1. Prescription for identifying equidistant surface voxels for the patient shown in Fig. 2. The voxels in light green [arrow 1] denote the primary tumor; pink [2] the secondary tumor; purple [3] the equidistant surface inside the brain; magenta [4] the equidistant voxels outside the brain; blue [5] the equidistant voxels inside the secondary tumor; and the single white voxel [6] the centroid of the secondary tumor. The dotted line marks the outer surface of the brain.

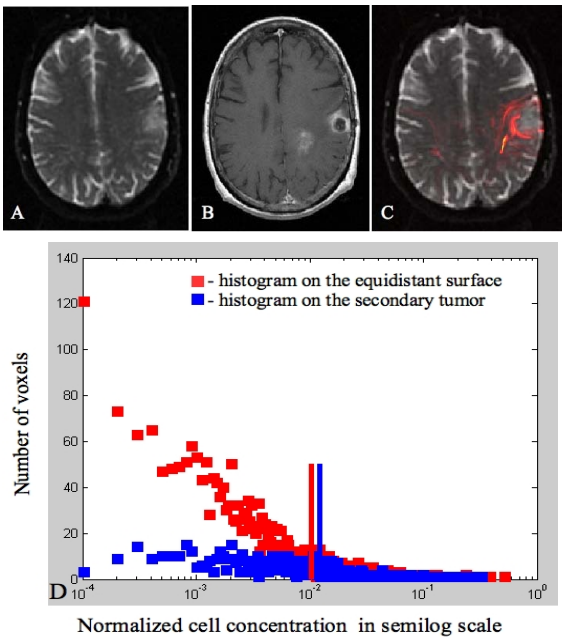

Figure 2. Predicted cell concentration map and histogram of a representative patient – patient 6 in table 1.
[A] DTI B0 image showing the primary tumor at time of treatment.
[B] T1W post-contrast image showing the secondary tumor 3-months post-treatment.
[C] Cell probability map run at time of treatment with voxels in yellow(red) having a high(moderate) cell concentration.
[D] Histogram of normalized cell concentration for voxels inside the secondary tumor [blue] compared with those on the equidistant surface [red]. The X-axis gives the normalized cell concentration values ranging from 0.0 to 1.0 presented on a log scale. The average normalized cell concentration (ANCC) for the secondary tumor voxels is represented by the vertical blue line while that for the control voxels is given by the vertical red line. This difference appears small on a log scale but is statistically significant (p < 0.0001).