Contribution ID: **205** Type: **Poster Presentation**

Validating a mathematical model of brain tumour growth with the apparent diffusion coefficient

Monday, 9 July 2018 19:45 (15 minutes)

The Proliferation-Invasion (PI) mathematical model of patient specific glioblastoma (GBM) growth utilizes T1 and T2-weighted/fluid attenuated inversion recovery (FLAIR) magnetic resonance (MR) images to estimate net proliferation (ρ) and net invasion (D) rates. We have previously developed methods to parametrize this model from these routine MRIs such that higher D/ρ tumours are considered more invasive than lower D/ρ tumours. More advanced MR imaging methods such as diffusion-weighted imaging (DWI) allow for the calculation of quantitative measurements. The apparent diffusion coefficient (ADC), which is calculated from DWI, is believed to be predictive of tumour cellularity and microstructure. Our objective is to validate that the PI model's measure of invasiveness D/ρ derived from routine MRIs is consistent with quantitative MRI measurements. We hypothesize that D/ρ will be correlated with the distributions of ADC values within the tumour. Further, we expect that the proportion of high ADC values values (low cellularity) will predominate for low D/ρ (highly invasive) tumours. T1Gd and FLAIR images were segmented and regions of interest (ROIs) created for patients with contrast-enhancing GBMs. A FLAIR penumbra ROI was created by excluding the T1Gd ROI from the corresponding FLAIR ROI. ROI's were then used to mask the co-registered ADC maps and the ADC values from within the ROI were plotted as a histogram. The ADC histogram from the FLAIR ROI was fit using a bimodal Gaussian model. ADC histogram peak boundaries were calculated as being +/- one averaged standard deviation from the averaged peak location (FLAIR ROI histograms). The averaged boundaries were then applied to each histogram. We calculated the percent of ADC voxels classified as being below each peak, within the lower or upper peak, within both peaks, or above the peaks. The percentage of voxels within each region were then plotted against D/ρ. Understanding the relationship between D/ρ and ADC allows us to connect observations on multiparametric imaging and elucidate the tumour biology. These results support the practical applicability of the PI mathematical model in quantifying patient-specific invasion characteristics by cross-correlating those findings with that seen on other imaging techniques and parameters, in this case ADC.

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Session Classification: Poster Session

Track Classification: Disease - non-infectious