An efficient interpretation of DCE-MRI data for Cancer treatment assessment

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Introduction:
Dynamic Contrast Enhanced magnetic resonance imaging (DCE-MRI) has been shown to be a powerful tool to study properties of tissue microvasculature. Its ability to measure vascular permeability that could be associated with tumor angiogenesis makes it a potential technique for characterizing tumor response to antiangiogenic treatment. DCE-MRI data can be evaluated by a variety of quantitative methods. The kinetic parameters derived from such measurement might be analyzed on the basis of mean changes within a defined region of interest; or by using pixel-by-pixel mapping throughout the tumor. Here we proposed a k-means (KM) clustering approach to segment the area of enhancing tumor into several intrinsic regions based on its signal dynamic behavior. This method reduces the data complexity and increases the efficiency of interpretation. It avoids the oversimplification caused by ROI analysis and at the same time, still allows us to explore the heterogeneity of the tumors.

Methods:
A. Image acquisition
DCE-MRI data were acquired from a glioblastoma patient (recruited by an IRB approved phase 2 AZD2171 investigational study at the Dana-Farber/Harvard Cancer Center[1]) using a 3 Tesla MRI system (TimTrio, Siemens Medical Solutions, Malvern, Pennsylvania). The DCE imaging parameters include TR = 5.7 sec, TE = 2.7 sec and flip angle = 10. 0.1 mMol/kg of Gd-DTPA was injected 52 seconds after the beginning of the acquisition at 5 cc/second. Data to allow computation of a T1 map of the tissue of interest is created using five different flip angles (2, 5, 10, 15, 30 degrees). Later, the T1 map is used to convert DCE-MRI dynamic signal intensity into Gd-DTPA concentration. The patient underwent DCE-MRI on days -5, -1, +1 (at least 24 hours after the first administration of the antiangiogenic agent AZD2171 and before the second dose), +28, 4 visits before and after AZD2171 treatment.
B. Tumor characterization
KM algorithm[2], a method of clustering, was used to identify the characteristic kinetic curves within a glioblastoma tumor region. The tumor region is outlined by an experienced radiologist on a Post-Contrast T1-weighted image and then registered them to DCE images. The signal intensity at all time points within each voxel of the outlined ROI regions were used as our data set. It is reasonable to postulate that inside each tumor there exist several (say K) "intrinsic" regions in which the physiological parameters are similar. In order to find those K intrinsic regions, the data set was processed by KM clustering and AUC (area under the curve), a model-free parameter is extracted from each characteristic regions. We repeated the process by increasing the number of clusters (from two) until we can not improve or even worsen the average silhouette value[2] where the silhouette value is a measure of the KM clustering performance. In other words, we repeated the process until the "optimum" K intrinsic regions in the tumor were found. We also tested this approach on nine other patients enrolled in the same study.

Results and Discussions:
Figure 1 is the contrast agent concentration curves and the characteristic curves derived from KM clustering respectively within the tumor region for each visit. The original data (one line for each voxel showing enhancement on T1-weighted images) shows substantial complexity and is visually difficult to interpret. On the other hand, KM method provides an intuitive way to observe the data. Figure 2 compares the AUC maps derived respectively from voxel-by voxel based analysis and KM clustering. From Fig. 2, we could see the AUC values increase abruptly from visit 1 to visit2. In this particular patient, once the AZD2171 was administered to the patient, in 24 hours, the AUC values of visit 3 quickly drop back to the level of visit1 and they continues to decrease at visit 4. Our approach preserves the information present in the traditional voxel-based approach, e.g., in this patient the immediate and significant biological effect of AZD2171. Both our simplification and the standard approach demonstrate a sustained reduction in AUC which suggests the decrease in blood permeability inside the tumor[3]. However, the decrease in K over time suggests differing populations of tissue types, and suggests the possibility of different classes of tumor vessel behavior, each corresponding to a K term. Similar findings were present in the other patients analyzed.

Conclusions:
A KM clustering approach is used to simplify the analysis of DCE-MRI data for glioblastoma patients. The characteristic curves and corresponding segments inside the tumor are identified based on the signal dynamic behavior for each visit. This approach provides an intuitive and efficient way to follow the signal dynamic behavior and its corresponding regions' evolution within the tumor over the course of the treatment. This approach may have aid DCE-MRI as a tool to evaluate tumor microvasculature response to antiangiogenic treatment.

Reference:
1. Batchelor TT, Sorensen AG, et al. Cancer Cell (submitted); 2. J. B. MacQueen, Proceedings of 5-th Berkeley Symposium on Mathematical Statistics and Probability (1967): 3. Jesberger JA et al. JMRI. 24:586-594, 2006

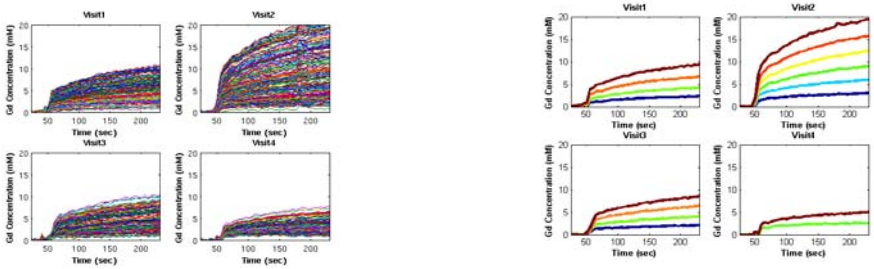

Fig. 1 shows all the signal dynamic (left) and characteristic curves (right) derived by KM clustering inside the tumor region for each visit. KM clustering significantly simplifies the complexity of the original data and increases the efficiency of the interpretation. It also provides an intuitive way to observe the data.

Fig.2 shows AUC maps calculated from voxel-by-voxel analysis (left) and KM clustering (right) respectively. Even though we only use few characteristic parameters in KM clustering to map the tumor; nonetheless, it has already captured all the important details provided by voxel-based analysis.