Adaptive Clustering of MR Diffusion Parameter Space for Brain Tumor Tissue Characterization

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BACKGROUND

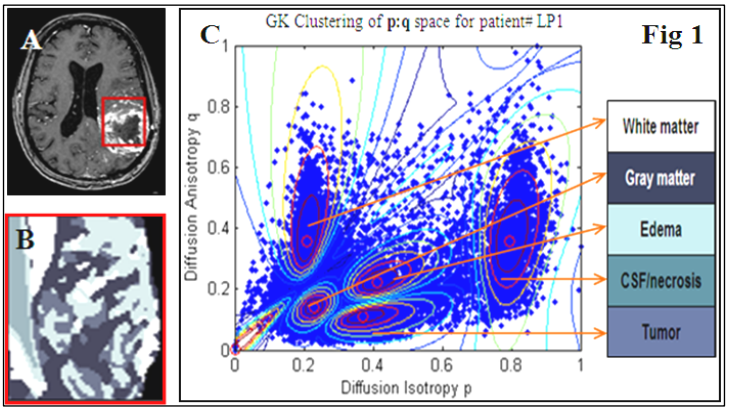
Objective determination of brain tumor extent is of significant interest in assessing therapy response, radiation treatment, and surgical resection planning. Planning effective treatments for highly heterogeneous and infiltrative high grade tumors requires non-invasive methods to evaluate their rapidly changing morphology. Though several MR contrast mechanisms are in use radiologically, it is still a challenge to manually delineate regions of necrosis, infiltrating tumor, edema, surrounding healthy gray matter (GM), and white matter (WM). We present a method to classify brain tumor imaging data into various tissue-compartments of interest using a two-dimensional semi-automated adaptive clustering technique that we apply to MR Diffusion Tensor Imaging (MR-DTI) data. Two DTI-derived scalar parameters namely diffusion isotropy "**p**", i.e. a scaled measure of Mean Diffusivity, and anisotropy "**q**", a measure of the deviation of diffusion tensor from pure isotropy, are plotted on a 2D feature space (1). Earlier work illustrates the utility of the **p:q** space in spatio-temporal visualization of the changing morphology of glioma and surrounding tissue for quantitative assessment of therapy response (2). A fuzzy clustering approach is presented to overcome the inherent heterogeneity in DTI datasets. Our method employs the Gustafson-Kessel (GK) clustering algorithm (3) to compute the fuzzy connectedness between a pair of pixel elements based on their spatial proximity and contrast similarity in the **p:q** feature space. The algorithm adapts the cluster shape to group similar tissue in a non-rigid manner. The iterative computation results in partitioning of the dataset, which is then used to create individual tissue maps. Follow up scans are similarly partitioned, allowing longitudinal interrogation of changing tumor and surrounding tissue constituents.

MATERIALS AND METHODS

A total of six patients were imaged for development of our clustering methodology. Three patients (LP1-3), undergoing therapy with G207, a genetically engineered oncolytic virus, and three patients (GP1-3) undergoing conventional chemo/radiation therapy, were evaluated. MR-DTI was performed on a 3T MRI scanner (Intera, Philips Medical Systems, Cleveland, OH) using a SENSE head coil. A diffusion single-shot EPI sequence was run with diffusion gradients applied in 15 directions (TR/TE = 3250/88ms, FOV 230 mm^2, slice thickness/gap = 4/1mm, 24 slices to cover the tumor and representative surrounding regions, b-value = 1000s/mm^2, matrix size = 256^2). Pre-contrast FLAIR and post-contrast T1 weighted images were also acquired for anatomic reference and visual compartmentalization of the tumor pathology. The G207 patients were imaged prior to G207 inoculation (baseline), at 4, and 8 weeks, post-inoculation. The patients receiving chemo/radiation therapy were imaged at baseline, at 8, and 16 weeks during course of therapy. Diffusion tensor post-processing included eddy current correction, skull-stripping, and intra-subject longitudinal registration performed using FSL (Analysis Group, FMRIB, Oxford, UK). Parametric isotropy (**p**) and anisotropy (**q**) data were computed using custom-written MATLAB (The MathWorks Inc, Natick, MA) code. The normalized **p:q** data for each slice of interest were plotted to yield a 2D feature space (1) and were compartmentalized using the Gustafson-Kessel (GK) algorithm with the aid of the Fuzzy Clustering and Data Analysis toolbox (4). The adaptive distance norm measure was employed in mapping the membership function. The resulting partitioned data were then classified into tissues constituents based on a priori knowledge of their diffusion characteristics (2). The following tissue maps were generated: healthy WM, healthy GM, tumor, vasogenic edema, and necrosis. The follow up scans were partitioned with respect to the cluster centers generated from the baseline scan, and the tissue fractions were calculated for chosen regions of interest (ROI). All studies were approved by the University of Alabama at Birmingham Institutional Review Board (Protocol # X080311002).

RESULTS

Fig 1A shows baseline post-contrast T1w image for a representative slice of patient LP1. Fig 1B shows the automated GK clustering of the **p**:**q** data for this slice. The tissue maps generated by our approach concur with WM fiber tract alteration patterns proposed in literature (5). Fig 1C shows on the results of DTI-segmentation for the red ROI in Fig 1A. We also noted significant disruption in the integrity of WM fibers in follow up studies (red arrow) for patient GP1 receiving chemo-radiation therapy. This is evidenced by reduced anisotropy (Fig 2B), perhaps due to tumor infiltration and increased isotropy (Fig 2C). This WM abnormality could not be observed on post contrast T1 images (Fig 2A). We report WM disruption in 5 out of 6 patients and 2 out of 3 patients receiving G207 therapy had an increase in edema fraction, suggesting inflammatory response to therapy. Our segmentation approach permits longitudinal ROI analyses and assessment of changes arising from therapy response.



CONCLUSION

A simultaneous diffusion isotropy and anisotropy based analyses by means of fuzzy clustering provides valuable insight into the neuronal tissue microstructure. This is not feasible with fiber tractography, Fractional Anisotropy (FA), or Apparent Diffusion Coefficient (ADC) maps alone. The local differentiation of necrosis, edema, tumor, and healthy WM compartments was demonstrated in this study. Subtle changes in the integrity of WM fibers were detected, and these are not possible with other anatomic imaging techniques. The quantitative methodology reported here will find utility in glioma therapy assessment, a critical step for advancing novel treatments for brain cancer.

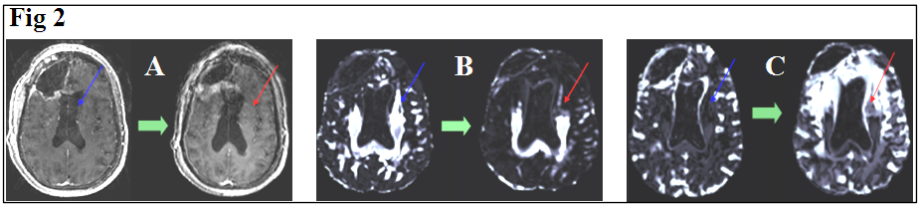


Figure 1 - **A:** Baseline post-contrast T1w with tumor ROI for patient LP1. **B:** GK clustering of the **p:q** space for image in Fig A. The contours around centers indicate the degree of membership of a pixel being a certain tissue. **C:** **p:q** clustering based tissue segmentation for ROI shown in Fig A. **Figure 2** - **A:** Post-gad T1w for patient GP1 at baseline followed by 16 weeks post therapy. **B:** Healthy WM tissue map generated from **p:q** clustering of images in Fig A. **C:** Edema & infiltrative tumor tissue map generated from **p:q** clustering of images in Fig A.

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