

# An image similarity-guided correspondence correction for voxel-wise analysis applied to MR imaging of glioblastoma multiforme acquired pre- and post-chemoradiotherapy

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**Introduction:** Response assessment using a voxel by voxel comparison of longitudinal image signal may offer improved sensitivity to change compared with mean or region-based measures (i.e. RECIST) as the latter obscures heterogeneity of response within the target. However, changes in tumor morphology that may arise from treatment effects, disease progression and/or response to therapy render a voxel-wise analysis susceptible to a variety of uncertainties. Voxel-wise analysis requires that the voxels being compared according to a given spatial relationship also share a biological relationship justifying a comparison of image signal. Physiological motion, patient positioning, normal tissue deformations and mass change in the tumor can all contribute to uncertainty in localizing the image signal to a consistent biologic tissue locality. The voxel correspondence problem can be addressed by restricting analysis to a common volume, but this solution potentially rejects the most dynamic and possibly most relevant tissues from the analysis. Alternately, a fully deformable registration can be applied, but this may force voxels into alignment that do not share an underlying biological relationship.

**Objective:** A voxel-wise analysis using the functional diffusion map (fDM) method [1] was applied to co-registered T1-weighted (T1W) and diffusion-weighted (DW) MR images of patients with glioblastoma multiforme acquired pre- and post-therapy. A voxel similarity-guided template-matching algorithm was then applied to the pre- and post-therapy T1W MR image pairs to identify pseudo-correspondences between consistent anatomic image features such as the tumor periphery. The fDM analysis was then repeated. We hypothesize that the rejection of anatomically inconsistent voxel correspondences and the establishment of voxel correspondences based on local anatomic feature matching will improve the accuracy of the fDM analysis.

**Methods and Materials:** Eleven patients with histologically-confirmed glioblastoma multiforme receiving definitive radiotherapy (RT) concurrent with temozolamide chemotherapy were imaged as part of an ethics board-approved multiparametric MR imaging study. Scans were acquired at post-operative baseline (BL) prior to the commencement of RT, and at the sixth week of RT and chemotherapy (WK6). All images were acquired on a 1.5T GE Signa Excite MR scanner (GE Healthcare, Waukesha, WI, USA). The image acquisition parameters were as follows: post-contrast axial T1-weighted fast-spin echo (TE = 20 ms, TR = 416.66 ms, FA = 90°, slice thickness = 5 mm, slice spacing = 7 mm, 0.859×0.859 mm resolution). Axial diffusion-weighted imaging (TE = 67.8 ms, TR = 10,000 ms, FA = 90°, slice thickness = 3 mm, slice spacing = 3 mm, 0.9375×0.9375 mm resolution, b = 0 and 1000 s/mm<sup>2</sup>). Scalar invariant mean ADC maps were computed from the DW images. For each patient, the WK6 T1W images and BL and WK6 ADC maps were aligned to the orientation of the BL T1W volume through image registration by normalized mutual information. Examples of pre- and post-therapy T1W image pairs are shown in Figure 1. The fDM analysis was then applied to the BL and WK6 ADC maps [Figure 2]. A 95% confidence interval for detecting significant ADC change was established by measuring ADC change in normal brain contralateral to disease and outside areas of primary dose deposition, applying a linear least squares fit and computing the standardized residual [1]. The number of voxels with increased ADC (V<sub>R</sub>), decreased ADC (V<sub>B</sub>) and total fraction of significantly changing ADC voxels V<sub>T</sub>=V<sub>R</sub>+V<sub>B</sub> were computed across a 3D rectangular region bounding the tumor, and were displayed as an overlay on the T1W images. Maps of pair-wise voxel similarity were then calculated between the BL and WK6 T1W volumes using an intensity invariant multi-dimensional feature metric based on histogram moments and intensity gradients [2]. The similarity maps allowed an assessment of morphological change across the image volume. Where the similarity metric indicated that voxel-voxel correspondence was lost, the ADC voxels were masked from the fDM analysis. Where similarity was poor, but correspondence was possible, template matching was used to establish pseudo-correspondences based on local anatomic features such as the tumor periphery on the T1W images, and correct the co-registered ADC maps [Figure 3]. The fDM analysis was then repeated using the corrected ADC maps.

**Results and Discussion:** For each patient data set, the fraction of significantly changing voxels V<sub>T</sub>, calculated using the pseudo-correspondence corrected fDM was compared with the uncorrected V<sub>T</sub> [Figure 4]. When the fDM analysis was performed using the template-matching correction, there was a significant change in V<sub>T</sub> in 7 of 11 patients (p<0.005). In these patients, the % change in V<sub>T</sub> ranged from 3.4%-47.6%. By establishing pseudo-correspondences based on local anatomic feature matching, real ADC change was isolated from apparent ADC change arising from the dynamic morphology of normal and diseased tissues. In 4 patients, there was no significant change in V<sub>T</sub> (p<0.005). For these patients, the tumor and surrounding tissues exhibited stable morphology between the BL and WK6 T1W MR scans.

**Conclusion:** Accounting for anatomically inconsistent voxel pairs can aid in the differentiation of apparent from real ADC change quantified using the fDM approach. The impact on and any improvements to the predictive value of the fDM analysis for therapy response assessment must be determined.

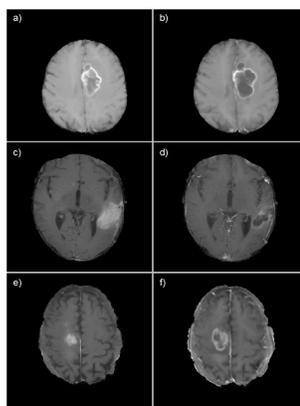


Fig. 1: Three examples of patients with tumor change between the BL and WK6 T1W MR acquisitions.

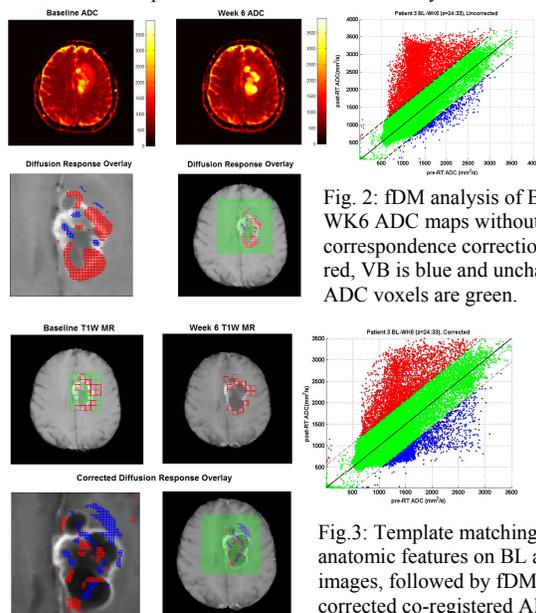


Fig. 2: fDM analysis of BL and WK6 ADC maps without correspondence correction. V<sub>R</sub> is red, V<sub>B</sub> is blue and unchanged ADC voxels are green.

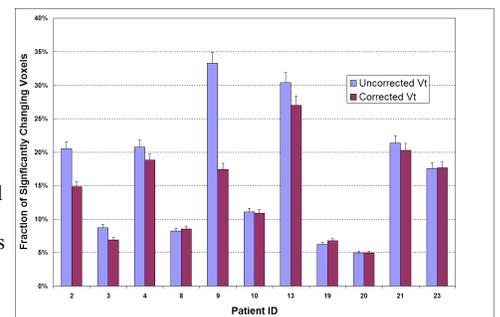


Fig. 4: Comparison of uncorrected and corrected total fraction (V<sub>T</sub>) of significantly changing ADC voxels. Error bars represent the 95% confidence interval.

## References

- [1] Moffat, B.A., et al., *Functional diffusion map: a noninvasive MRI biomarker for early stratification of clinical brain tumor response*. Proceedings of the National Academy of Sciences, 2005. **102**(15): p. 5524-5529.
- [2] Shen, D., *Image registration by geometric moment invariant matching*. Pattern Recognition, 2007. **40**: p. 1161-1172.