Hybrid functional diffusion and perfusion maps for evaluation of gliomas

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Introduction

In vivo identification of tumor cell density and vascularity are critical parameters in the assessment and treatment of human gliomas. Diffusion and perfusion MRI are non-invasive imaging tools that can be applied in vivo to elicit insight into the cellular and vascular microenvironments. Functional diffusion maps (fDMs) and functional perfusion maps (fPMs) were developed to examine voxel-wise changes in apparent diffusion coefficient (ADC) and relative cerebral blood volume (rCBV) during serial MRI comparisons, thus providing spatial localization of changes in cellularity and vascularity within brain tumors. In the current study we have merged these two techniques into a Hybrid Functional Diffusion and Perfusion Map in order to localize and quantify regions with both increasing cellularity and increasing vascularity during treatment with the anti-angiogenic agent bevacizumab.

Methods

Eight patients with recurrent intracranial tumors were enrolled in the current study. Baseline MRI sessions were performed prior to treatment with bevacizumab (10mg/kg) and irinotecan (125mg/m²), and multiple MRI sessions were performed during treatment. MRI sessions consisted of clinical MRI (SPGR, FLAIR, and pre/post-contrast T1-weighted images), perfusion MRI (dynamic susceptibility contrast, or DSC-MRI), and diffusion MRI (DWI). DSC-MRI estimates of rCBV were corrected for any confounding leakage effects and standardized as previously described. Estimates of ADC were calculated from the DWI obtained at b = 0 and b = 1000 s/mm². Registered sequential diffusion weighted images were used to calculate fDMs, within the FLAIR abnormalities, using ADC thresholds of 0.55 x 10⁻³ mm²/s, as per the fDM protocol. Volumes were classified as decreasing (hypercellular, blue), increasing (hypocellular, red), or not changing (green) according to this threshold. Similarly, fPMs were calculated from registered sequential rCBV maps. With the FLAIR abnormality, the fPM voxels were classified as decreasing (hypovascular, blue), increasing (hypervascular, red), or no change (green) using a threshold of change of 100%. Hybrid fDM+fPMs were created by spatially determining regions of hypercellularity (blue regions from fDMs), hypervascularity (red regions from fPMs), and regions containing both hypercellularity and hypervascularity (yellow). The volume of hypercellularity (physical volume of blue voxels in fDMs, in mL), hypervascularity (red voxels in fPMs, in mL), and volume of both hypercellularity and hypervascularity (yellow voxels in hybrid fDM+fPMs, in mL) were calculated after each MRI scan session.

Results

Hybrid fDM+fPMs were useful in spatially localizing high-risk lesions in all patients observed in this study. Fig. 1 illustrates one example of clinical MRI (FLAIR), fDM, fPM, and hybrid fDM+fPM localization. The average spatial separation between hypercellular and hypervascular clusters was 2.02 ± 0.33 cm. Surprisingly, the volume of hypercellularity and hypervascularity resulted in distinctively different temporal profiles easily categorized into either vascular-independent (Pearson’s Correlation Coefficient of \( R < 0.5 \)) or vascular-coupled tumor growth (\( R > 0.5 \); Fig. 2).

Discussion

Hybrid fDM+fPMs represent a new method of combining multimodal MRI datasets to both spatially localize and temporally monitor high-risk regions of recurrent brain tumors. This technique may be useful in pre-surgical planning and/or image-guided biopsy of lesions having a high probability of recurrence. Trends in the volumes of hypercellularity, hypervascularity, and hypercellularity-hypervascularity from hybrid maps suggest different tumor types may be prevalent in recurrence during treatment with the anti-angiogenic agent bevacizumab: vascular-independent and vascular-coupled tumor growth. These two tumor types likely represent two distinct tumor cell populations or phenotypes of tumor cells: infiltrative tumor cells that thrive in ischemic/hypoxic conditions (such as “stem-like” tumor cells) and tumor cells that proliferate largely in the presence of high blood volume.

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References