

Differentiating pseudoprogression from true progression using DTI and DSC-MRI

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Introduction

The current standard of care for newly diagnosed glioblastomas is surgical resection followed by radiation therapy and concomitant and adjuvant temozolomide (TMZ) chemotherapy. Treatment outcome is typically monitored by standard clinical MRI using the McDonald or updated RANO criteria¹. However, these criteria often fail to accurately identify pseudoprogression (PsP), which is characterized by an appearance of progressive and enhancing lesions on MRI within the first 6-months after treatment. These lesions are caused by treatment effect rather than true tumor progression (TP). Accurate identification of PsP is critical for patient management as unnecessary repeat surgery/biopsy can be avoided in these patients and they can continue on effective TMZ regimen. On the other hand, accurate diagnosis of TP will allow termination of ineffective TMZ and initiation of repeat surgery or placement in alternative therapeutic trials. It has been reported that diffusion weighted imaging (DWI)¹ and dynamic susceptibility contrast (DSC) enhanced imaging²⁻⁵ can be helpful in differentiating PsP from TP. But there is no report about diffusion tensor imaging (DTI) in the diagnosis of PsP. Our previous studies reported that DTI is useful in characterizing glioblastomas^{6,7}. The purpose of this study is to determine whether DTI and DSC metrics can help in differentiating PsP from TP.

Materials and Methods

Thirteen glioblastoma patients with enhancing lesions who had undergone radiation therapy with or without TMZ chemotherapy after surgical resection were retrieved from our institutional databases. The final pathologic diagnosis included six PsP (2M/4F, age 24-63) and seven TP (5M/2F, age 32-67). All patients underwent MR studies on a 3T Siemens Tim Trio scanner with a 12-channel phased-array head coil. DTI data was acquired using a single shot spin echo EPI sequence with parallel imaging using GRAPPA (acceleration factor = 2). Sequence parameters were as follows: TR/TE = 5000/86, NEX = 3, FOV = 22 x 22 cm², b = 1000 s/mm², number of diffusion weighting directions = 30, slice thickness 3 mm. DSC T2* weighted gradient-echo echo planar images were obtained during the first pass of the standard dose of bolus injection using the following parameters: TR/TE = 2000/45, FOV = 22 x 22 cm², in-plane resolution = 1.72 x 1.72 x 3 mm³, and 20 slices covering the brain. MD and FA maps were computed using in house software. Leakage corrected CBV maps were generated using Nordic ICE (Nordic Imaging Lab). K^{trans} was estimated using first-pass pharmacokinetic modeling (FPPM)⁸. Contrast-enhanced T1 weighted images, FLAIR, MD, FA, CBV and K^{trans} maps were co-registered and all the parameters were measured from the enhancing region. A pair-wise comparison was performed for each parameter using a Mann-Whitney U test in terms of median values.

Results

Representative DTI and perfusion images are shown in Fig.1. Box plot of imaging parameters are shown in Fig.2. Significantly elevated MD was observed from the enhancing region in patients with PsP compared with those in TP (p=0.05). The median rCBV from PsP was significantly lower than that of TP (p=0.05). FA and K^{trans} in PsP tend to be lower but didn't reach any significant difference.

Discussion

Pseudoprogression is a subacute treatment-related reaction. Pathologically, it is found to correspond to gliosis and reactive radiation-induced changes including disruption of the BBB, inflammation, increased permeability and edema. These changes causes increased enhancement on MR and thus mimic TP¹. Increased MD in PsP compared to TP may be due to the early radiation necrosis. rCBV is higher in TP because of the angiogenesis of the viable tumor. Our preliminary data was consistent with previous reports²⁻⁵. DTI and DSC may be helpful in differentiating PsP from TP. More patients will be needed to validate our result.

Reference

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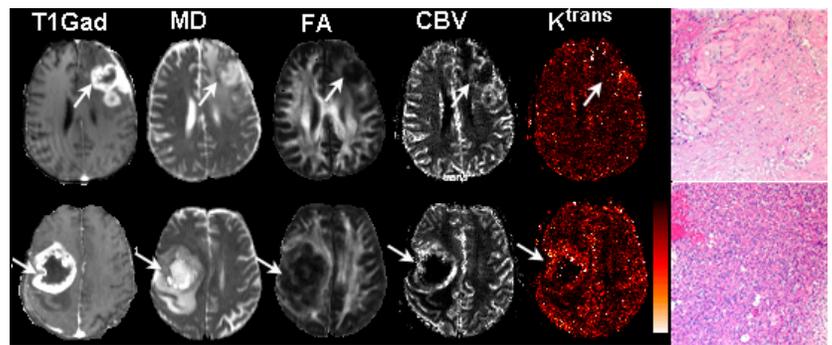


Fig 1. Representative images from pseudoprogression (PsP, upper row) and true progression (TP, lower row). FA, rCBV and K^{trans} values from the enhancing part (arrows) in TP appears to be higher than that of PsP. Histopathologic (H&E, 100x magnification) features from PsP shows necrosis with abundant macrophages and vascular hyalinization, whereas TP demonstrates increased cellularity with nuclear atypia and mitoses.

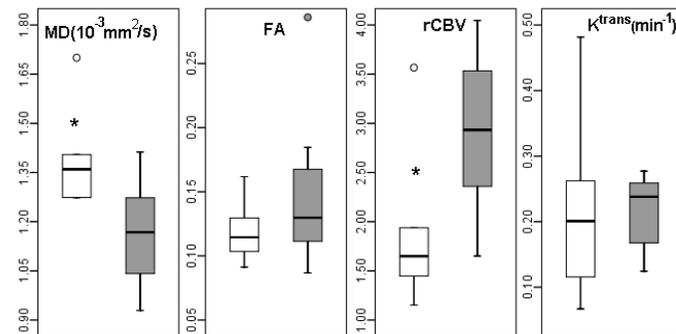


Fig.2. Box plot of diffusion and perfusion characteristics in pseudoprogression (PsP, white) and true progression (TP, grey). The solid line inside the box represents the median value, while the edges represent the 25th and 75th percentiles. Straight line (bars) on each box indicates the range of data distribution. The outliers are represented by circles. * indicates significant difference (p<0.05).