Segmentation of tumor infiltrative and vasogenic edema in brain tumors using voxel-wise analysis of 11C-methinonine and FDG PET and its comparison with diffusion tensor imaging

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Abstract

Precise imaging of glioma cell invasion into the white matter has been challenging. Exact identification of the areas with tumor cell invasion is necessary for achieving maximum tumor resection and radiation therapy planning. In order to meet these demands, use of diffusion tensor imaging (DTI) has been proposed for the detection of tumor cell invasion. It has been suggested that fractional anisotropy (FA) is reduced in areas where the tumor cells invades the white matter, disrupting the neural fiber bundles (Ref. 1). However, other reports have suggested that reduction of FA can also be influenced by vasogenic edema, and that solely relying on the reduction of FA is insufficient to accurately detect tumor cell invasion (Ref. 2). In this report, we have been able to segment the possible area with and without tumor cell invasion in the T2-WI high intensity area in malignant glioma patients using a voxel-wise analysis of both ^{11}C-methionine and FDG positron emission tomography (PET). We clearly showed that decoupling versus coupling of ^{11}C-methionine and FDG uptake can clearly discriminate between tumor cell infiltration and vasogenic edema in malignant gliomas. Furthermore, we also showed that the profile of FA and apparent diffusion coefficient (ADC) calculated from DTI does not differ between these two. Our results suggest the possibility of using voxel-wise analysis of ^{11}C-methionine and FDG PET for tumor cell invasion in the T2-WI high intensity area in glioma patients. It also questioned the use of DTI for discriminating infiltrative from vasogenic edema in glioma patients.

Methods

Patients: We collected data from 10 patients harboring gliomas and 8 patients harboring meningioma who underwent both ^{11}C-methionine and FDG PET studies and DTI as presurgical examination.

Image analysis: After the FA and ADC maps and PET data were obtained, these images were registered on to contrast enhanced T1- or plain T2-weighted standard anatomical images using normalized mutual information. All of the image sets were converted into 256 x 256 x 256 isotropic 1 mm x 1 mm x 1 mm images enabling further voxel by voxel comparison of the images.

^{11}C-methionine and FDG uptake coupling analysis: We mathematically evaluated the data plots in order to establish estimated correlation profile of ^{11}C-methionine and FDG in normal white matter. We next, examined the profile of these two tracers in the T2-WI high intensity area in both glioma and meningioma patients (**Fig. 1**). The decoupling score of each plot was defined as the standard deviation from the calculated linear regression line of the correlation between ^{11}C-methionine and FDG uptake. Images of the decoupling score were also reconstructed as shown in **Fig. 2**. All calculations were done by an in-house made software using MATLAB 7.6 (MathWorks, Natick, MA).

Comparison of FA and ADC in the T2-WI high intensity area in glioblastoma: T2-WI high intensity area was segmented into ^{11}C-methionine and FDG decoupling (tumor infiltrative edema) and coupling (vasogenic edema) and the FA versus ADC profile was compared (**Fig. 4**).

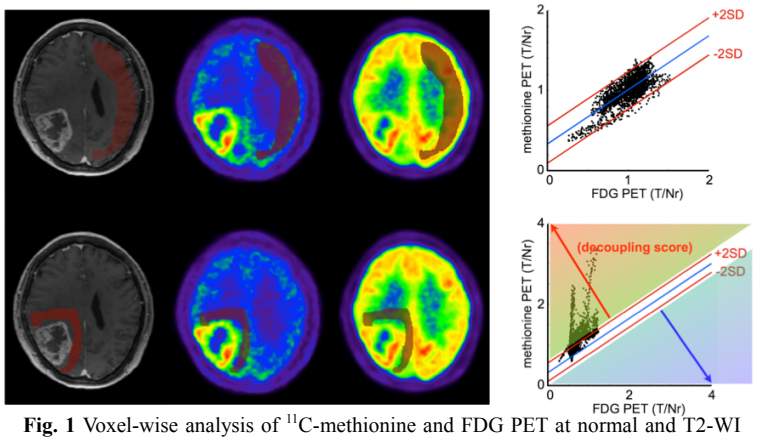

Fig. 1 Voxel-wise analysis of ^{11}C-methionine and FDG PET at normal and T2-WI high intensity white matter in a glioblastoma patient.

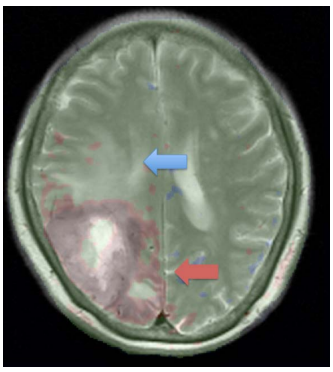

Fig. 2 Image reconstruction of the decoupling map. Two types of edema, namely edemas with (red arrwow) or without (blue arrow) ^{11}C-methionine and FDG uptake decoupling can be appreciated.

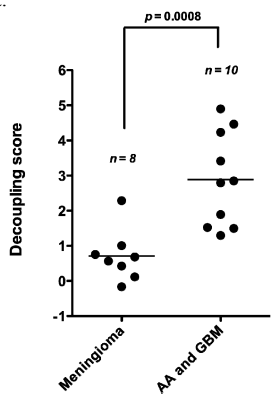

Fig. 3 Average decoupling score in the T2-WI high intensity area of both meninigoma and malignant glioma

Results and Discussion

As in **Fig. 3**, we clearly showed that ^{11}C-methionine and FDG uptake couples in in T2-WI high intensity areas of meningiomas, whereas they decouple in those of malignant gliomas. These results suggest that both ^{11}C-methionine and FDG uptake decreases in vasogenic edemas, while in tumor infiltrative edema, ^{11}C-methionine uptake is much higher than predicted by FDG uptake, possibly because tumor cells have higher ^{11}C-methionine uptake capability by amino acid transporter overexpression on their cell membranes. As a result, it is considered that the decoupling score reflects the magnitude of tumor cell invasion into the white matter. When we reconstructed the decoupling map, two types of edemas (T2-WI high intensity areas) were observed in malignant glioma patients (**Fig. 2, 4**). Areas with high (2<) decoupling score can be considered as tumor infiltrative edema, and low (2>) score as vasogenic edema. Segmentation of these two types of edema in malignant glioma patients was possible (**Fig. 4**), and the FA was plotted as a function of ADC in these two types of edema. The results, however, showed that the correlation of FA and ADC did not differ between these two types of edema (**Fig. 4**). Our results showed that tumor infiltrative and vasogenic edema can be discriminated by voxel-wise analysis of both ^{11}C-methionine and FDG PET. Use of DTT for this purpose, however, should be considered limited.

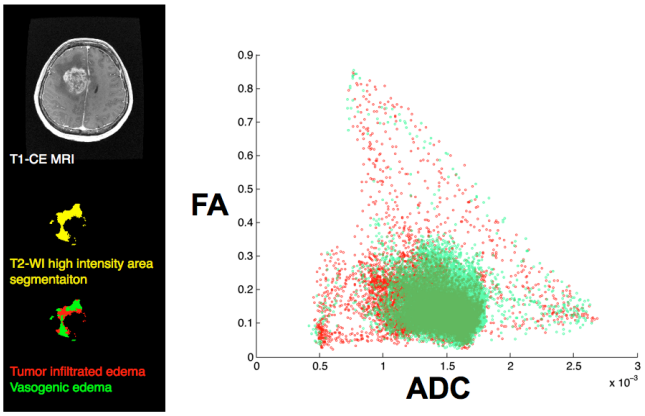

Fig. 4 The T2-WI high intensity area of malignant gliomas was segmented into high (2<) and low (2>) decoupling score areas, and assigned as tumor infiltrative and vasogenic edema. The FA was plotted as a function of ADC, and the plot patterns between these two areas were compared.

References

1. Lu S et al. Diffusion-tensor MR imaging of intracranial neoplasia and associated peritumoral edema: introduction of the tumor infiltration index. ***Radiology***. 2004 Jul;232(1):221-8
2. Kinoshita M et al. Diffusion tensor-based tumor infiltration index cannot discriminate vasogenic edema from tumor-infiltrated edema. ***J Neurooncol***. 2010 Feb;96(3):409-15.