

# Use of fractional anisotropy for determination of the cut-off value in $^{11}\text{C}$ -methionine positron emission tomography for glioma.

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## Abstract

Multimodal imaging is one of the necessary steps in the treatment of malignant brain tumors, and use of magnetic resonance imaging (MRI) and positron emission tomography (PET) are the current gold standard technique for the morphological and biological assessment of malignant brain tumors. In addition, fractional anisotropy (FA) obtained from diffusion tensor imaging (DTI) and  $^{11}\text{C}$ -methionine PET are useful to determine the tumor border at the tumor and white matter interface. Although there is no question of their value, a universally accepted cut-off value to discriminate normal and abnormal tissue has not been established. In this study we attempted to calculate and determine the cut-off values in FA and  $^{11}\text{C}$ -methionine PET that will allow delineation of the tumor border at the tumor and white matter interface by combining these two modalities.

## Methods

**Patients:** We collected data from 11 patients harboring gliomas who underwent both DTI and  $^{11}\text{C}$ -methionine PET studies as presurgical examination. DTI was performed using 3.0- or 1.5-T magnetic resonance imaging (MRI). Post-surgical histological examination revealed 1 grade II, 3 grade III and 7 grade IV glioma patients.

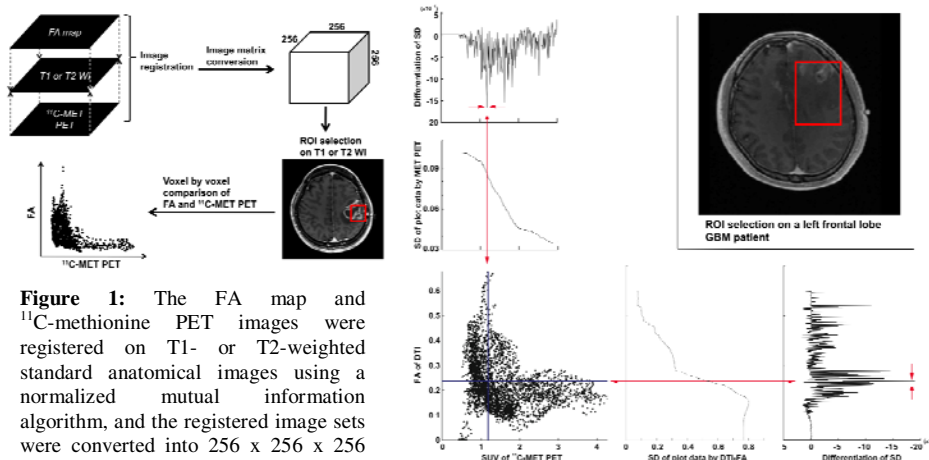
**Image analysis:** After the FA maps and PET data was obtained, these images were registered on to contrast enhanced T1- or plain T2- weighted standard anatomical images using normalized mutual information (NMI) with the Vinci image analyzing software from Max-Planck Institute for Neurological Research Cologne (<http://www.nf.mpg.de/vinci/>). Registrations of the images were visually confirmed. After image registration was completed, all of the image sets, which included the standard anatomical MR images, and the DTI and PET data, were converted into  $256 \times 256 \times 256$  isotropic  $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$  images enabling further voxel by voxel comparison of the images (**Figure 1**).

**Determination of the cut-off values of  $^{11}\text{C}$ -methionine PET and FA of DTI:** We mathematically evaluated the

data plots in order to establish the cut-off values that would allow each of high FA and low MET-PET group, low FA and low MET-PET group, and finally low FA and high MET-PET group, to be determined in an objective manner. First, as shown in **Figure 2**, the standard deviation of the data plot was calculated as a function of both FA and SUV of  $^{11}\text{C}$ -methionine PET. Next, the point where the largest change in the standard deviation occurred was considered the point at which the pattern of the scattered data plots changed. In order to calculate this point, the differentiation of the standard deviation was calculated as a function of both FA and SUV of  $^{11}\text{C}$ -methionine PET, and the point with the maximum absolute value of the differentiation was set as the cut off value (**Figure 2**). All calculations were done by MATLAB 7.6 software (MathWorks, Natick, MA).

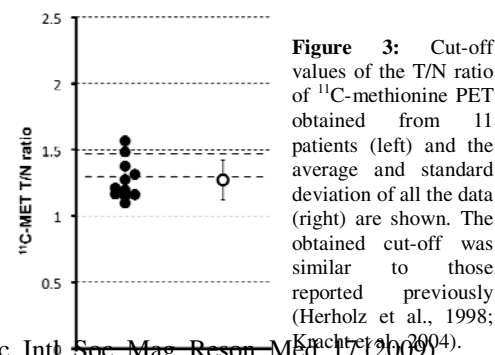
## Results and Discussion

The  $^{11}\text{C}$ -methionine PET cut-off values varied from 1.01 to 2.36 (mean 1.61, standard deviation 0.53) in SUV and from 1.10 to 1.57 (mean 1.27, standard deviation 0.15) in T/N ratio (**Figure 3**). These values are comparable to those reported previously (**Figure 3**). On the other hand, the FA cut-off values were from 0.166 to 0.35 (mean 0.26, standard deviation 0.06). The mean FA cut-off value was similar to that reported to have a 10% probability of tumor cell invasion by histological study. Since the cut off-values for FA and  $^{11}\text{C}$ -methionine PET (MET-PET) had been obtained for each patient as described above, we attempted anatomical visualization of the 3 scattered data groups, i.e., the high FA and low MET-PET group (normal white matter), the low FA and low MET-PET group (tumor border) and the low FA and high MET-PET group (tumorous tissue). As shown in **Figure 4**, three segments of the scattered data can visually be appreciated on the standard anatomical MR images. Previous studies have found that a cut-off value of 1.47 or 1.3 in  $^{11}\text{C}$ -methionine T/N ratio is suitable for tumor and non-tumor tissue discrimination, respectively. These studies were done by comparing PET images and surgically obtained histological specimens. In addition, they reported that a cut-off value of 1.47 in T/N ratio had a sensitivity of 76% with a specificity of 87% and that a cut-off value of 1.3 had a sensitivity of 87% with a specificity of 89%. As these values are averages of multiple patients, minor differences between patients are neglected. Although the T/N ratio cut-off value was 1.27 in average in our study, which is fairly close to the previously reported 1.3, it also varied from 1.10 to 1.57. Similarly, the average of FA cut-off value was 0.26, similar to a previously reported 0.25 that had a 10% chance of tumor cell invasion, but at the same time the value ranged from 0.166 to 0.35. By combining two different modalities, in the present case DTI and  $^{11}\text{C}$ -methionine PET, we

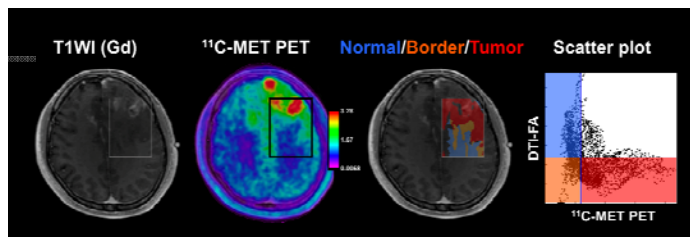


**Figure 1:** The FA map and  $^{11}\text{C}$ -methionine PET images were registered on T1- or T2-weighted standard anatomical images using a normalized mutual information algorithm, and the registered image sets were converted into  $256 \times 256 \times 256$  isotropic  $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$  images. A region of interest was chosen. DTI data obtained from every single voxel was plotted as a function of the SUV of  $^{11}\text{C}$ -methionine PET.

**Figure 2:** The standard deviation (SD) of the scatter data was plotted both as a function of the SUV of  $^{11}\text{C}$ -methionine PET (upper panel of the scatter plot) and as the FA of DTI (left panel to the scatter plot). Next the differentiation of the SD change was calculated (top panel at the left upper corner and right lower end panel). The largest absolute value was selected as the cut-off value.



**Figure 3:** Cut-off values of the T/N ratio of  $^{11}\text{C}$ -methionine PET obtained from 11 patients (left) and the average and standard deviation of all the data (right) are shown. The obtained cut-off was similar to those reported previously (Herholz et al., 1998; Knauth et al., 2004).



**Figure 4:** Areas recognized as tumor, border and normal white matter are colored in red, orange and blue respectively.