A Preliminary Study Evaluating the Functional Diffusion Map for Early Detection of TACE Treatment Response in Patients with Liver Carcinoma

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Introduction：Liver carcinoma is fairly common in China , but most patients lost the opportunity to surgery for the difficulty of early detection. TACE is an effective treatment for those people, however, the therapeutic response is typically evaluated by traditional imaging methods by measuring tumor size (e.g. RECIST Criteria) several months later[1]. Therefore, an early biomarker of tumor response favorable for making early decisions for clinic protocols is being investigated, e.g. DWI,MRS,PWI,BOLD imaging and PET-CT. Recently, Bradford, Benjamin et al have proved that Functional Diffusion Map (FDM) is valuable and powerful for early assessment in glioma[2,3] but there is no FDM result reported on liver. This study is a preliminary trial of evaluating treatment response of liver carcinoma based on FDM.

Method： 20 patients with liver carcinoma were enrolled in our research, and treated with TACE. T1-weight and DWI(b=800) were performed before treatment and 4 weeks later(GE Signa Twin Speed 1.5T). All images for each patient were registered to their own pre-treatment T1-weighted images using a mutual information algorithm and a 12-degree of freedom transformation using FSL (FMRIB, Oxford, UK). After registration, voxel wise subtraction was performed between ADC maps. Then the three-color FDM was overlaid on the T1-weighted images: red voxels($\mathbf{V_R}$) for which the ADC increased significantly, blue voxels ($\mathbf{V_B}$) for which the ADC decreased significantly, and green voxels($\mathbf{V_G}$) for which the ADC did not change significantly, where total voxels($\mathbf{V_T}$= $\mathbf{V_R}$+$\mathbf{V_B}$) for which the ADC changed significantly. We use $39\times10^{-5}mm^2/s$ as the significance threshold which represented the 95% CI(Confidence Intervals) for changes of ADC in normal liver tissue of 30 patients. Each patient was examined by dynamic contrast-enhanced CT or MRI every 3 months during the follow-up.

Result: All the patients were classified into three groups: partial response (PR), stable disease (SD) and progressive disease (PD) by traditional imaging evaluation (RECIST Criteria) 3 months later. Table 1 is the percentages of V_R, V_B, V_T and V_G of three typical patients with PR, SD and PD, respectively. Figure 1 shows the FDMs of the treatment response of these three patients after TACE. A, C, and E are the regional spatial distribution of ADC changes (FDMs) of a single slice through each tumor as color overlays for the PR, SD, and PD patients, respectively. The red pixels indicate areas of ADC increased significantly, whereas the green and blue pixels indicate regions of ADC unchanged and decreased significantly, respectively. The scatter plots (B, D, and F) show quantitatively the distribution of ADC changes for each corresponding patient (A, C, and E), respectively.

Status	V_R	V_B	$V_T(V_R+V_B)$	V_G
PR	86.0%	0.6%	86.6%	13.4%
SD	36.3%	0.2%	36.5%	63.5%
PD	7.3%	5.2%	12.5%	87.5%

Table. 1

Conclusion: For those three kinds of patients, the percentage of V_R, V_B, V_T and V_G varied significantly, especially the increased ADC region (V_R) and changed ADC region (V_T). As a preliminary result, FDM probably is a robust imaging biomarker for detection of treatment response in patients with liver carcinoma. However, we have not gotten a statistic correlation between them because more patients' data are needed. In addition, we can also analyze the overall survival and time-to-progression. For the successful application in glioma, we hope we could prove that FDM is also feasible in early evaluation of efficacy of TACE for liver carcinoma after further work.

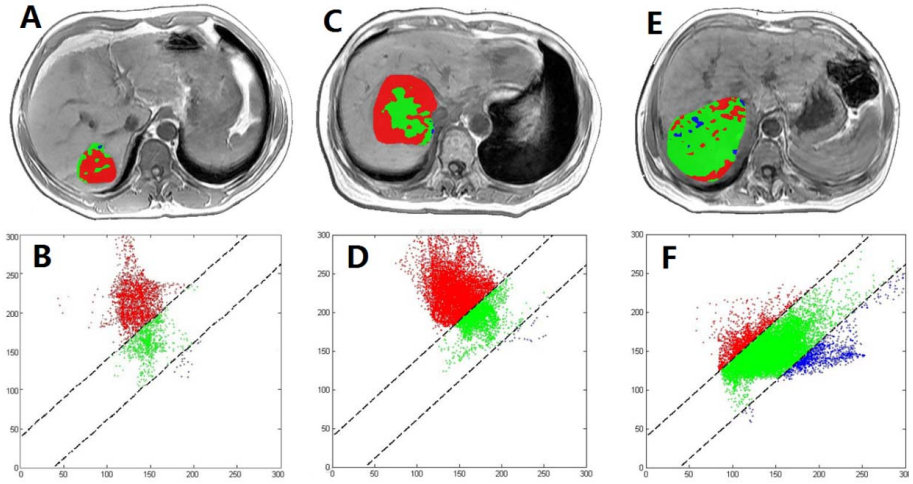

Figure. 1

Reference: 1. Bonekamp S, et al. Radiology. 2011;260(3):752-61. 2. Bradford AM, et al. PNAS. 2005; 102:5524-5529. 3. Benjamin ME, et al. J Neurooncol. 2010; 97(3): 419-423.