## NODDI analyses can demonstrate differences of tissue microstructure between brain metastasis and meningioma

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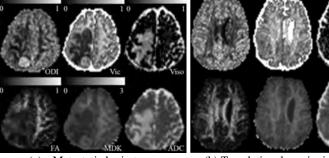
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Target audience: neurologist, neurosurgeon, and those interested in q-space imaging

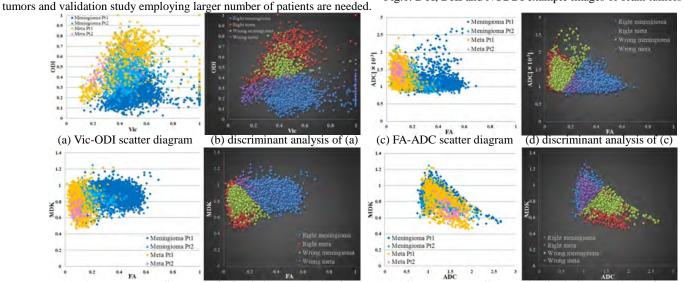
**Introduction:** Diffusion MRI (dMRI), including the conventional DTI and non-Gaussian dMRI techniques<sup>1</sup>, can evaluate tissue microstructural alterations in a quantitative manner and has been applied to various kinds of CNS disorders. Neurite Orientation Dispersion and Density Imaging (NODDI) is a recently introduced non-Gaussian dMRI method that can provide unique measures representing axon density and dispersion of fiber directions<sup>2</sup>. The NODDI model has three compartments; neurites (sticks with zero radius with an orientation distribution model by Watson distribution); extra-neurite (simple Gaussian anisotropic diffusion) and isotropic Gaussian diffusion such as CSF. The method produces maps of orientation dispersion index (ODI), intracellular volume fraction (Vic) and isotropic volume fraction (Viso). In this preliminary research, we applied NODDI analyses to brain tumors and compared its ability to represent tissue microstructural information with those of DTI and DKI.

Materials and Methods: Data Acquisition: Multi-b dMRI data were acquired in 4 patients (2 with metastatic brain tumor [breast cancer and renal cell carcinoma], 2 with transitional meningioma); age,  $53.50\pm9.26$  years)} with the SIEMENS MAGNETOM Avanto 1.5T using the following parameters: Twice Refocused Spin Echo EPI sequence; b-value = 0, 1000, 2000[s/mm2]; 30 MPGs;  $\delta\Delta$  32.7/37.4 [ms]; TR/TE = 5000/88.0 [ms]; FOV =  $25.6\times25.6$  [cm²]; acquisition matrix =  $86\times86$ ; section thickness = 3.0 [mm]; 50 axial sections; GRAPPA factor = 2; acquisition time = 320 [sec]. Image analyses: We used only b=0, 1000 images for calculating the conventional DTI parameters, FA and ADC. DKI and NODDI analyses used the entire data sets (b = 0, 1000, 2000). For DKI, Mean Diffusional Kurtosis (MDK) was calculated using DKE software. ODI, Vic and Viso were calculated from the same data by using NODDI Matlab Toolbox. The contrast enhanced 3D T1-weighted images were registered to b = 0 images. ROIs were placed manually on the registered images to contain the entire enhanced solid part of the tumor. The diffusion metrics from every voxel within the ROI were plotted on scatter diagram, to compare between meningioma and metastatic tumor. In this study, Viso was excluded from subject of the scatter diagram because of index for isotropic Gaussian diffusion such as CSF. Discriminant analysis with Mahalanobis' generalized distance was performed to examine the ability of the diffusion metrics to distinguish between metastatic brain tumor and meningioma.

Results and Discussion: The scatter plots of the diffusion metrics showed generally good discrimination between the voxels from metastasis and meningioma. In the discriminant analyses, combination of Vic-ODI showed the highest accuracy. The accuracy was 0.829, 0.799, 0.804, and 0.785, for Vic-ODI, FA-ADC, FA-MDK, and ADC-MDK, respectively. The present results suggest that NODDI can provide additional information to DTI and DKI in analyzing brain tumor, and may possibly give information relevant to histologic findings. We guess increased ODI in brain tumor reflects randomness of tissue architecture, while increase in Vic demonstrates cellularity. We acknowledge that application of NODDI to tumors raises much concern, as the NODDI three compartment models is not designed to represent compartments of tumors. Optimization of the compartment model to fit in brain



(a) Metastatic brain tumor (b) Translational meningioma Fig.1. DTI, DKI and NODDI example images of brain tumors



(e) FA-MDK scatter diagram (f) discriminant analysis of (e) (g) ADC-MDK scatter diagram (h) discriminant analysis of (g) Fig.2. Result of scatter diagrams and discriminant analyses

References: 1 Jensen JH. Magn Reson Med 2005; 53: 1432-1440. 2 Zhang H. Neuroimage 61(4); 1000-1016, 2012