Differentiation of High-grade and Low-grade Diffuse Gliomas by Intravoxel Incoherent Motion MRI

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Target audience: Researchers and clinicians interested in IVIM imaging or/and diffusion/perfusion imaging of brain tumors.

Purpose: Intravoxel incoherent motion (IVIM) has been proposed as a method to measure diffusion and perfusion using a single diffusion-weighted (DW) acquisition scheme[1]. The diffusion property is related to cellularity, and the perfusion property is determined by neoangiogenesis of tumors. The both properties are major features in determining glioma grades[2]. ADC, frequently calculated with a pair of b values (e.g. 0 and 1000 s/mm^2), includes contributions from microcirculation in capillaries (perfusion), and it can be overestimated especially in tumors with high vascularity. IVIM model applies bi-exponential fitting to signal decay obtained with multi-b values and then separates true diffusion and capillary perfusion. IVIM imaging allows us to simultaneously obtain both diffusion and perfusion imaging with complete geometrical matching. The purpose of this study was to prospectively evaluate the diagnostic performance of IVIM parameters (perfusion fraction f, and true diffusion coefficient D) in differentiating high-grade gliomas (HGGs) from low-grade gliomas (LGGs).

Methods: *Subjects:* Consecutive 35 patients with histologically proven diffuse glioma (50.5±22.0 years old, 21 males and 14 females) were included. The number of patients for grade II, III, and IV was 10, 4, and 21, respectively. The histological types of gliomas were as follows: 7 astrocytomas, 2 oligodendrogliomas, 1 oligoastroctyoma, 2 anaplastic astrocytomas, 2 anaplatic oligoastrocytoma, 21 glioblastoma multiforme (GBM).

MRI: IVIM imaging was conducted on a 3T clinical scanner (Achieva TX, Philips Healthcare, Best, The Netherlands) with an 8-channel head coil. IVIM imaging was performed in axial planes by using a single-shot echo-planar imaging diffusion sequence, with 13 values of b (0, 10, 20, 30, 50, 80, 100, 200, 300, 400, 600, 800, 1000 s/mm^2) in 3 orthogonal directions. The other imaging parameters were: repetition time (TR) = 2,500 ms; echo time (TE) = 70 ms; matrix = 128 × 126 (reconstructed to 256×256); slice thickness=5 mm, field of view=230×230 mm; number of slices=11, sensitivity encoding factor=1.5; scan time=2min 7s. The standard IVIM 2-compartment diffusion model was employed, with a capillary perfusion component and a nonvascular compartment. Signal decay was estimated by using the following the bi-exponential equation:

$$SI/SI_0 = (1 - f) \times exp(-bD) + f \times exp(-bD^*),$$

Where D and D* are the true diffusion coefficient and the pseudodiffusion coefficient, respectively, SI and SI_0 are the signal intensity at a given b value and b=0, respectively, and f is the fractional volume of the capillary perfusion. The signal decay was fitted in the 2 steps as follows; First the single parameter D was obtained by fitting with b > 200 s/mm^2, and then D* and f was obtained by fitting with all b values while keeping D constant. This fit was performed on a voxel-by-voxel basis to create each parameter map (D and f) by using the interactive data language (IDL)-based software program (DWI Tool R1.5, Philips Medical Systems, Best, Netherlands). In addition, conventional ADC maps were created with a pair of b values (b=0 and 1000 s/mm^2). Relative cerebral blood volume (rCBV) was measured with dynamic susceptibility contrast (DSC) perfusion-weighted imaging. Two experienced placed independently placed regions-of-interest (ROIs) in the tumor and measured minimum D and maximum f. ADC was measured in the same ROIs for D. Student's t-test and receiver-operating characteristics (ROC) analysis were performed to evaluate their diagnostic performance in grading gliomas.

Table: Diagnostic Performance for discriminating HGG from LGG.

Parameters	Cutoff Value	Sensitivity (%)	Specificity (%)
D	≤1.19 × 10^{-3} mm^2/s	92	80
ADC	≤1.20 × 10^{-3} mm^2/s	80	80
f	≥5.4 %	96	80

Results and Discussion: HGG showed lower D in HGG (0.96 ± 0.18 × 10^{-3} mm^2/s) than in LGG (1.35 ± 0.43 × 10^{-3} mm^2/s, P < .001), and lower ADC in HGG (1.05 ± 0.19 × 10^{-3} mm^2/s) in HGG than in LGG (1.37 ± 0.40 × 10^{-3} mm^2/s, P < .001) (**Fig. 1**). D was lower than ADC in HGG (P < .0001) while no difference was found in LGG. HGG showed higher f values in HGG (15.6 ± 6.2 %) than in LGG (5.4 ± 4.2 %, P < .0001, **Fig. 2**). Diagnostic performance of each parameter in differentiating HGG from LGG is shown in **Table.** The parameter f showed the best sensitivity in differentiating HGG from LGG. D showed better sensitivity compared with ADC while their specificity was equivalent. ROC analysis for discriminating these two statuses demonstrated that f showed high diagnostic performance with area under curve (AUC) values of 0.91. The D and ADC showed moderate diagnostic performance with AUC of 0.80 and 0.78, respectively (**Fig. 3**). The f correlated with rCBV (R^2 = 0.71; P <. 0001). **Figure 4** shows a representative case of grade III (anaplastic astrocytoma). Lower D and higher f are observed in the tumor. IVIM imaging could simultaneously obtain diffusion and perfusion imaging, and both parameters were useful in grading gliomas.

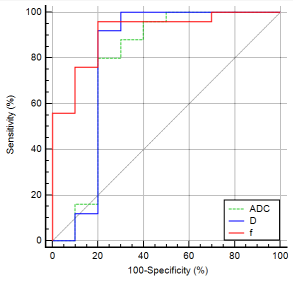

Figure 3: ROC analysis for discriminating HGG from LGG.

Conclusion: IVIM imaging can be used as a noninvasive quantitative imaging method in differentiating HGG from LGG.

References: 1. Le Bihan D et al., Radiology (1988), 2. Louis DN et al., Acta Neuropathol (2007)

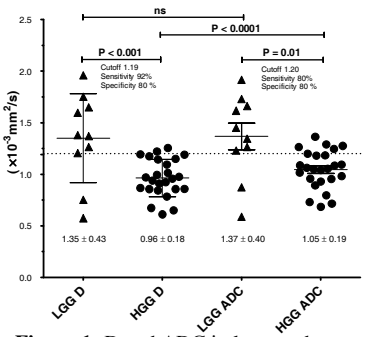

Figure 1: D and ADC in low-grade glioma (LGG) and high-grade glioma (HGG). HGGs show lower D and ADC than LGGs.

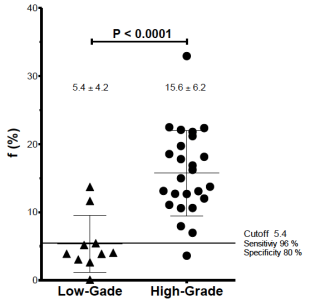

Figure 2: f in LGG and HGG. HGGs show larger f value than LGGs.

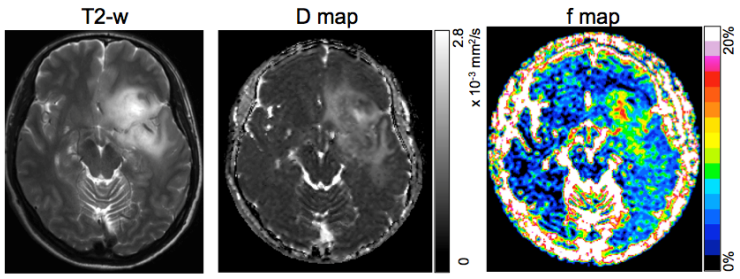

Figure 4. 38-year-man with anaplastic oligoastrocytoma, Grade III (HGG). The D map shows increased D value (1.10 × 10^{-3} mm^2/sec) in the lesion compared with that in normal white matter (0.74 × 10^{-3} mm^2/sec). The f map shows increased f value (12.7 %) in the lesion compared with that in normal white matter (4.5 %).