Can the distribution of low b-value and the NEX influence the pseudodiffusion parameter derived from IVIM in brain?

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Target audience Researchers and clinicians interested in brain imaging and diseases, with a particular interest in diffusion imaging

Introduction As an improved MRI technique, diffusion-weighted imaging (DWI) is considered the most sensitive for early pathological changes. Perfusion measurement has been shown to improve sensitivity and predictive value for tumor grading and prognosis, also as a predictor of recovery with reperfusion in patients of acute ischemic stroke [1, 2].To overcome a limitation of DWI, which is that perfusion can substantially confound diffusion measurements because of the incoherent motion of blood, intravoxel incoherent motion (IVIM) based on DWI is proposed [3]. A biexponential model was applied in IVIM imaging to extract the perfusion-related information from a diffusion sequence [3]. The model requires the collection of both low and high b-values as the IVIM effect becomes largely negligible as the b-value is increased beyond approximately 200 s/mm^2 [3-5]. The IVIM model is a two-compartment model and includes terms for the fraction of received signal attributed to moving blood (fractional perfusion, f), the diffusion caused by moving blood (pseudodiffusion, D*), and a diffusion component free of perfusion effects (true molecular diffusion , D).

Our study aims to reveal whether the low b-values distribution and the number of excitation (NEX) for each b value influence the accuracy of pseudodiffusion parameter derived from IVIM in brain.

Method This prospective study was approved by the Ethics Committee and informed consents were obtained from all participants. Twenty-one male healthy volunteers were recruited (mean age, 28 years; range, 25-34) with inclusion standard as follows: no hypertension or cerebral vascular diseases, no systemic metabolic disease; no infection or fever; no use of corticosteroid drugs; no MRI contraindication. Each subject underwent 5 consecutive IVIM DWI sequence on a 3.0-T MRI system (MR750, GE Healthcare, Milwaukee, USA). The details of five different parameter sets of low b-value distribution and NEX were showed in Table 1. Different b values were applied with a single-shot diffusion-weighted spin-echo echo-planar sequence. A local shim box covering the whole brain was applied to minimize susceptibility artifacts. In total, 20 axial slices covering the entire brain were obtained with a 24×24 cm^2 field of view, 5 mm slice thickness, 1.5 mm slice gap, 3,000 ms TR, Minimum TE, 128×128 matrix and acceleration factor 2. The D, D* and f were calculated according to the IVIM bi-exponential model. A freehand oval region of interest (ROI) was placed in bilateral frontal white matter (WM) and the head of caudate nucleus (grey matter, GM) (as shown in Figure A). Numerical variables were denoted as the mean and standard deviation. Parameters D* and f in healthy WM or GM were tested for differences between the different sets of distribution of low b-value and NEX by paired t-test.

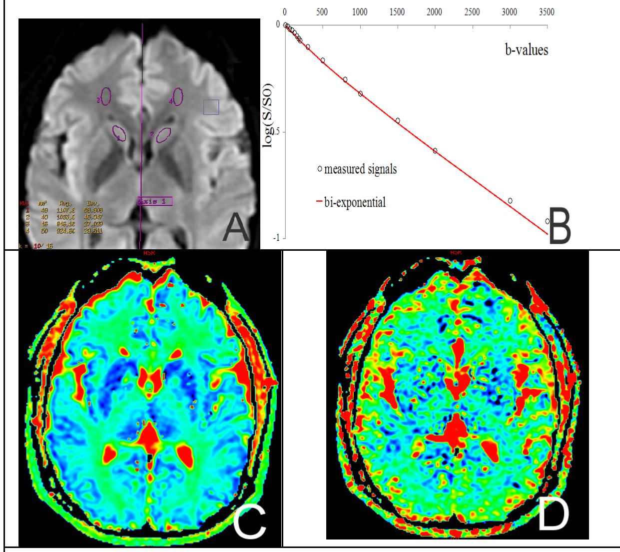

Figure 1. **(A)** Axial diffusion-weighted trace image (b=1000 sec/mm^2) shows ROIs in placed in bilateral frontal white matter (WM) and the head of caudate nucleus (GM). **(B)** The bi-exponential fitting of the diffusion signal decay over a wide-range of b values (up to 3,500). **(C)** Axial f map and **(D)** D* map.

Results The f value of WM or GM were higher in group 3, 4 and 5 than in group 1 and 2 (P<0.05), but no difference exist between group 1 and 2, 3 and 4, or 4 and 5 (all P<0.05) (as shown in Table 1). There were no differences of D* value in WM or GM among each group (all P<0.05) (as shown in Table 1).

Table 1. Compared the pseudodiffusion parameter derived from IVIM among different distribution of low b-value and NEX in brain

	Protocol		D* ($\times10^{-3}$ mm^2)/sec	f (%)
1	Low b=(0,50,150,200)	WM	2.423 ± 0.160	0.3175 ± 0.0113*
	NEX=(1,3,2,2)	GM	2.787 ± 0.494	0.1654 ± 0.0134a
2	Low b=(0,30,50,100,200)	WM	2.475 ± 0.113	0.3181 ± 0.0083*
	NEX=(1,3,3,2,2)	GM	2.955 ± 0.463	0.1658 ± 0.0157a
3	Low b=(0,30,60,90,120,150,180,200)	WM	2.422 ± 0.173	0.3236 ± 0.0082†
	NEX=(1,3,3,3,2,2,2,2)	GM	2.707 ± 0.782	0.1792 ± 0.0284b
4	Low b=(0,30,60,90,120,150,180,200)	WM	2.429 ± 0.156	0.3216 ± 0.0077†
	NEX=(1,1,1,1,1,1,1,1)	GM	2.940 ± 0.758	0.1766 ± 0.0186b
5	Low b=(0,20,40,60,80,100,120,140,160,	WM	2.404 ± 0.197	0.3230 ± 0.0100†
	180,200);NEX=(1,3,3,3,3,2,2,2,2,2,2)	GM	2.921 ± 0.658	0.1884 ± 0.0345b

The units of the b-values are s/mm^2. Each set of low b-values was in addition to a b-value distribution of b= (300, 500, 800, 1000, 1500, 2000, 3000, 3500) s/mm^2. **Note:** WM denotes brain white mater, GW denotes gray mater. The different alphabet and symbol represented a significant difference between the two groups (P<0.05).

Discussion This study suggested that the low b-value distribution affected the f value derived from IVIM sequence, and the f value of WM or GM in more low b-values were significantly larger than in less b-values, similar with the previous study in the liver [6] . However there was no significant difference of f value derived from IVIM sequence using the same b-values and different NEX. In addition, paradoxically, this study showed no significant difference in D* between different distribution of low b-value and the NEX, further research is warranted to clarify this issue.

Conclusion This study showed that f tended to be underestimated when there were less low b-values distribution (0<b<200 s/mm^2). Eight low b-values might be the optimal set when performing IVIM studies in evaluating the pseudodiffusion parameter. We also identified that the NEX might not affect the f value derived from IVIM in brain.

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