Caloric Intake Influence on Hepatic MR Diffusion Measurement

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Introduction: Studies have sought to use changes in hepatic apparent diffusion coefficient (ADC) as an imaging biomarker for the assessment of the degree of fibrosis (1-2). Portal venous blood flow and hepatic sinusoidal blood flow increase after meal ingestion (3). ADC, as measured in conventional clinical practice with two *b*-values (0, and another 'high b' value), reflects the combined contribution from both perfusion and diffusion, and therefore, may be affected by meal ingestion. In this study we sought to assess: (a) the reproducibility of hepatic ADC measurements from a multi- *b* value breath-held acquisition, (b) the effect of a high-caloric food intake on ADC using a compartmental analysis of multiple '*b*' values, and (c) perfusion volume ratio *f* of intravoxel incoherent motion (IVIM) model was obtained by asymptotic method (6).

Methods: *Subjects and Study Design:* In this IRB approved prospective study, 20 healthy subjects (8 f/12m, age: 48.5 ±11.6yrs, BMI: 24.67±7.84 kg/m^2) provided written informed consent. After overnight fasting, subjects were imaged twice (experiments B_1 and B_2), and twice after a 1090 kcal meal (carbs: 111g, protein: 36g, fat: 56g) (experiment A_1: 30mins after taking meal; experiment A_2: 45mins after taking meal). The subjects were removed from the scan bed, and repositioned between imaging sessions.

MRI data acquisition: All imaging was done at 3.0T (Philips, Ingenia 3.0T) with a 32 channel coil for signal reception. DWI images of three axial slices centered around the largest extent of the liver visible in scout images were acquired using a SE-EPI sequence: 4-*b* values (0, 40, 200 and 1000 s/mm^2); TR/TE: 1500/67 ms; acquired voxel size: 3.5 x 3.5 x 8mm^3; NEX: 1; and scan time: 18s.

Data Analysis: All processing was done offline using custom-written software in MATLAB^{TM}. Pixel-wise ADCs were calculated by different combinations of *b*-value: (1)$ADC_{b0\text{-}b40}$; (2) $ADC_{b200\text{-}b1000}$ (3)$ADC_{b0\text{-}b1000}$. All continuous variables are reported as mean±std. Test-retest reproducibility was assessed using coefficient of variation (CV), as well as Bland-Altman analysis for the imaging sessions before and after meal ingestion. Student's T-test was used to assess the statistical significance of difference between two means. A p-value of < 0.05 was assumed to be statistically significant.

Results: The coefficient of variation (CV) for the estimation of ADCs was about 20%, and was higher for the estimation of *f* via IVIM model (Table 1). Bland-Altman analysis showed that there was a slight elevation in the mean bias between the two measurements performed after meal ingestion (A_1 vs A_2), but this difference did not rise to the level of statistical significance.

The $ADC_{b0\text{-}b40}$, which reflects the perfusion contribution, did not change appreciably before or after meal. $ADC_{b200\text{-}b1000}$, which reflects the diffusion contribution, increased after meal ingestion, and this difference was statistically significant. Conventional measure of ADC, $ADC_{b0\text{-}b1000}$ which reflects contributions from both diffusion and perfusion (*f*) terms (4), also increased after meal ingestion. IVIM based estimate of *f*, did not show any difference.

Table 1.

	Before Meal (Mean ± Std)	After Meal (Mean ± Std)	T Test (P value<0.05)
$ADC_{0\text{-}40\ s/mm^2}$ (10^{-3} mm^2/s)	7.50 ± 2.19	8.16 ± 2.41	*p*=NS (p=0.1740)
$ADC_{200\text{-}1000\ s/mm^2}$ (10^{-3} mm^2/s)	1.03 ± 0.24	1.16 ± 0.24	0.0007
$ADC_{0\text{-}1000\ s/mm^2}$ (10^{-3} mm^2/s)	1.43 ± 0.31	1.67 ± 0.33	0.0001
f (%)	30.03 ± 9.26	32.57 ± 11.21	*p*=NS (p=0.2092)

Table 2.

	Reproducibility (%)		Bland-Altman (Mean ± 1.96 Std)	
	Before Meal	After Meal	Before Meal	After Meal
$ADC_{0\text{-}40\ s/mm^2}$ (10^{-3} mm^2/s)	24.25	20.41	-0.947 ± 4.814	-0.168 ± 4.721
$ADC_{200\text{-}1000\ s/mm^2}$ (10^{-3} mm^2/s)	17.02	17.39	0.006 ± 0.498	0.004 ± 0.572
$ADC_{0\text{-}1000\ s/mm^2}$ (10^{-3} mm^2/s)	19.44	14.15	-0.019 ± 0.790	-0.065 ± 0.657
f (%)	22.70	25.67	-2.047 ± 19.018	4.713 ± 21.415

Discussion: Although portal venous, and hepatic sinusoidal blood flow increase after meal ingestion, perfusion related metrics such as $ADC_{b0\text{-}b40}$, and *f*-values do not show an appreciable difference, while diffusion (largely) driven $ADC_{b200\text{-}b1000}$, and both diffusion and perfusion driven $ADC_{b0\text{-}b1000}$ do increase post meal ingestion. The large CV in the estimation of *f*, suggests that the SNR of the b=0 image needs to be higher to reduce the uncertainty in the estimation of *f*. It is also possible that, to detect perfusion changes due to food-intake, it is necessary to use b-values < 40 s/mm^2. In a similar study, Shila Pazahr et al. found that ADC values were unaffected after ingesting a protein based or a carbohydrate based meal adjusted to body weight (5). In another study, Hollingsworth reported ADC values increased after food ingestion which is the same with our results (6). We speculate that this may be related to the amount of fat content in the ingested meal in our study (56 g), study (6) (41g) versus (< 2 g) in study (5).

Conclusions: The reproducibility of hepatic ADC values is around 20%, and diffusion contributions to $ADC_{b200\text{-}b1000}$ increase following a 1090 kcal high fat meal ingestion. The $ADC_{b0\text{-}b1000}$ which includes both diffusion information and perfusion information (*f*) also increased after such high calorie high fat meal ingestion.

Reference: [1] Koinuma M et al. JMRI 22:80-85, 2005 [2] Li H et al. ISMRM 2002: 1966 [3] Iwao T et al. Radiology 201: 711-715, 1996 [4] Le Bihan D et al. Radiology161 (2): 401-7.1986 [5] Shila Pazahr et al. Investigative Radiology 49(3): 138-146, 2004. [6] Hollingsworth KG et al. NRM Biomed 19: 231-235, 2006 [7] James Pekar et al. MRM 23: 122-129, 1988