

Towards Repeatable ADC Mapping of the Liver: Some Guidance for Clinical Use

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Introduction. While qualitative analysis of diffusion weighted MRI (DWI) of the liver by visual assessment is increasingly for lesion detection, characterization and therapeutic monitoring [1], clinical application of quantitative DWI through apparent diffusion coefficient (ADC) measurement, is limited due to unacceptable variability of quantitative results. In the literature on diffusion weighted imaging (DWI) of the liver, one is faced with more than two-fold differences between publications [2, 3] in the reported mean ADC values in healthy controls. These inconsistencies have implications for our ability to detect pathological changes, or therapeutic response, as well as to work collaboratively between centers. In this study, we examined the impact on inter and intra-subject repeatability of whole liver ADC measurements of some factors known or suggested to affect liver ADC: prandial status [4], choice of b-values and directions [5], and ROI definition.

Materials and Methods. Ten healthy volunteers (age: 33 ± 11 years, 2 F) underwent DWI after at least 4 hours of fasting and between 45 and 75 minutes after consuming a meal. A T2-weighted scan was acquired in the pre-meal session to rule out pathology. DWI were acquired in both sessions with the following parameters: 30 axial slices, FoV 340 x 280mm, matrix 256 x 192 (after interpolation), Thickness/gap 7/1mm, TE/TR, 71/3200ms, b-values: 0, 50, 100, 200, 400, 500, 700, 900, 1000 s/mm², with 4 averages and fat suppression performed during gentle free breathing. In half of the subjects, DWI was acquired with 3 diffusion encoded directions was acquired twice in the pre-meal session and once in the post-meal session. For the other half of the subjects, 3 direction DWI were acquired once prior to the meal and twice in the post-meal session. Further, single diffusion encoded direction acquisitions were performed to ring the total number of DWI scans to 3 per session (6 per subject).

Of the 502 possible combinations of 9 b-values that could be used in ADC calculations, we examined the following combinations:

8 ADC maps obtained starting with the highest two b-values and progressively incorporating the next highest (see table),

ADC calculations made use of in-house software based on the Insight Toolkit version 3.10 and programmed in C++. ADC values of < 0 and < 20 mm²/s were excluded from reconstruction and did not contribute to subsequent measurements.

For each acquisition, a whole liver regions of interest (ROIs) was manually traced on the b=0 image using imageJ software (Figure 1, top right). In drawing the "whole liver" ROI, the hepatic trunk was avoided. Based on the b=0 image intensities within the whole-liver ROI, a threshold range of ± 2 standard deviations about the median value was used to create a "masked ROI" that excluded the majority of resolved duct (low signal) and vascular (high signal) structures. Mean and standard deviation of AD values for all of the inclusive and masked ROIs were computed from each of the ADC maps calculated from their associated scan.

Results. All DW images acquired had liver signal visibly above noise level even for b=1000. One subject included in the results had a haemangioma that was excluded when drawing the ROIs.

The most pronounced effect on ADC came from the choice of b-values (Figure 1, all panels), with the inclusion of the b=0 image in ADC calculation or limiting the b-values used to those greater or equal to 700 s/mm² significantly increased ($p < 0.01$) both the estimated mean ADC and its variability between subjects. Excluding these extreme cases, the intra- and inter subject standard deviations were similar ($\sim 10\%$, and 15-22% respectively) and mean values indistinguishable for both 1 and 3 direction diffusion encoding for all choices of b-value combination (combinations 2-6, Figure 1 Left).

The prandial state (Figure 1 Centre) and the use of the whole liver or masked ROIs (Figure 1 Right) both yielded relatively small differences in ADC that were most pronounced when extreme b-values (combinations 1 and 8 Table).

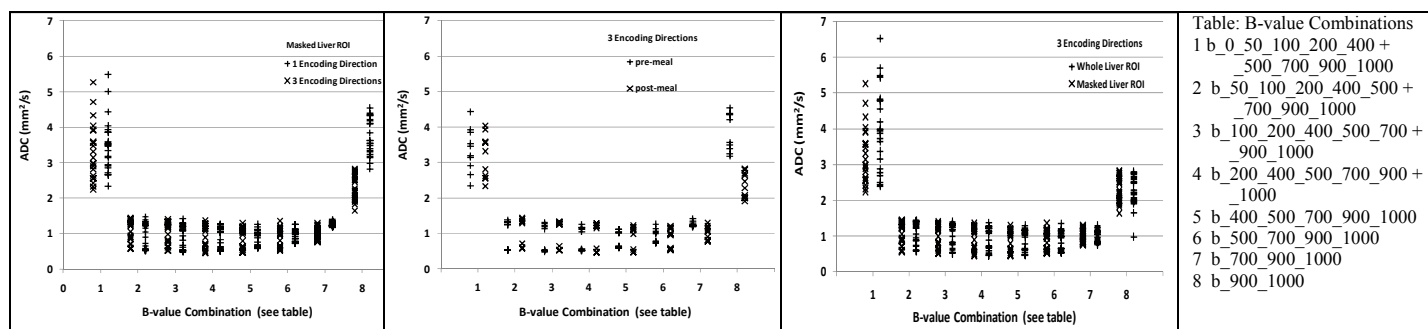


Figure 1. Left) Comparison of ADC values between 1 and 3 encoding direction acquisitions for masked liver ROI. Centre) Masked liver ROI ADC values before and after a meal. Right) Comparison of mask liver ROI and whole liver ROI ADC values for 3 direction encoding.

Discussion. While the small number of subjects and possible scanner specific considerations must be kept in mind, our study suggest some guidance for clinical and research scanning of the liver:

1. The near equivalence of 3 and 1 directional encoding suggests that scan times can be kept minimal by using just 1 direction)
2. Consistency of ADC measurements can be maximized by avoiding the inclusion of b values of 0 and 50 s/mm² and the use of more than 4 b-values less than 1000 s/mm² does not appear necessary. Optimization for fewer b-values may be possible.

As well, when following the above guidance on choice of b-values,

3. Prandial status has limited impact on ADC.
4. The exclusion of isolated visible vessel and ducts in large ROI definition is not necessary.

The co-involvement of microvessel blood flow in the diffusion weighted MR signal is well recognized [6]. As flow effects are most strongly manifested at low b-value images, care should be taken when interpreting ADC values that rely exclusively on b-values less than 500 s/mm² and / or include b-values less than 100 s/mm² in the ADC calculation. Many of the early reports of liver ADC violate one or both of these cautions, likely leading to the extreme variability of ADC in early reports. The prospect of obtaining a measure of flow in the liver by using low b-value DWI remains to be fully explored, and is only hinted at by the significantly higher ADCs obtained when making use of very low b-values in the present study.

In our subjects we obtained a mean intra-subject variation of less than 10%, a level better than most previous reports. We consider this a reasonable point of reference for both individual patient examinations and multi-centre clinical trials, with the application of respiratory gating [7]. or breath-holding holding promise to further reduce variation.

References.

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