Diffusion-weighted MR imaging of Colorectal Liver Metastases: Repeatability and Reproducibility of Apparent Diffusion Coefficients and Implications for Therapeutic Monitoring

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Introduction

A number of novel targeted therapies are available for the treatment of colorectal hepatic metastases. Diffusion-weighted imaging (DWI) of the liver allows quantitative apparent diffusion coefficients (ADCs) of metastases to be derived (1), which may be useful for detecting early treatment response. However, little is known about ADC measurement variability. Repeatability analysis assesses observer variability in drawing regions of interests (ROIs) for quantifying ADC on one set of images. Reproducibility analysis, in addition, reflects measurement and biological variability by comparing ADC results obtained from two DWI studies performed on different days. These analyses inform the magnitude of ADC change that may be ascribed to therapeutic effects rather than biological variations, observer errors or instrumental errors; and are thus important for therapeutic assessment.

Purpose

The purpose of this study was to determine the repeatability and reproducibility of ADC measurements derived from regions of interests (ROIs) drawn within colorectal hepatic metastases at DWI performed on two consecutive days.

Materials and Methods

18 consecutive patients (12 males, 8 females; mean age 64 years) with potentially resectable colorectal metastases > 1 cm in size were prospectively evaluated. DWI of the liver was performed on a 1.5T MR system (Philips Intera, Software version 11) using breath-hold single-shot echo-planar imaging with three *b* values (0, 150 and 500 sec/mm^2) applied along three directions. Twelve axial sections were acquired during each 20 seconds breath-hold (*TR = 1850 ms, TE =72 ms, α = 90 degrees, 7 mm thickness, 1mm gap, FOV = 340 cm, Matrix = 112 x 256, SENSE factor = 2*) and the entire liver was evaluated in two breath-holds. DWI performed on day 1 was repeated 24 hours later on day 2. All images were reviewed in consensus by two experienced readers at the same session to minimise observer error (2). An IDL-based software (DiffusionView, ICR, UK) was used for image registration and to generate maps of apparent diffusion coefficient (ADC0-500) and flow insensitive apparent diffusion coefficients (ADC150-500 using only *b* = 150 and 500 sec/mm^2 trace images).

For each patient, a marker metastasis was selected and its maximum transverse diameter and location recorded. An ROI was drawn just within the border (~1 pixel) of each metastasis on the b= 0 sec/mm^2 image and copied onto the ADC0-500 and ADC150-500 maps to record their mean values. This was repeated to enable two mean ADCs to be recorded for each metastasis. DWI images of metastases in the same scan position acquired the following day were similarly analysed. Bland-Altman analysis was used to calculate the coefficients of repeatability (CR*day1* and CR*day2*) from mean ADCs obtained on the same day, and the coefficient of reproducibility from averaged mean ADCs obtained on different days (CR*day1&2*). Larger coefficients of repeatability/reproducibility indicate larger measurement variability. Same day ADCs were also compared using the paired t-test, as were the averaged ADCs of day1 and day2.

Results

18 metastases were evaluated (14 right lobe, 4 left lobe). The mean size of metastasis was 4.3 cm (1.0-16.5cm). ADCs were normally distributed (D'Angustino Pearson test, p > 0.05). No significant difference was found in the mean ROI size, ADC0-500 or ADC150-500 of metastases measured on the same day or 24 hours apart (p > 0.05, paired t-test). ADC0-500 and ADC150-500 were highly repeatable (CR*day1* and CR*day 2* < 10%). However, ADC0-500 was more reproducible than ADC150-500 (CR *day1&2;* 19.5% vs 33.5%) (Table 1). Figure 1 shows the Bland-Altman plot of ADC0-500 (Day1&2). Sub-analysis by lesion size indicated that the ADC measurement was more reproducible in lesions measuring ≥ 4 cm (n =9) than those measuring < 4 cm (n =9).The CR*day1&2* for lesions ≥ 4 cm and < 4 cm were as follows: ADC0-500 10.6% vs 26.5%; ADC150-500 32.5% vs 36.4%.

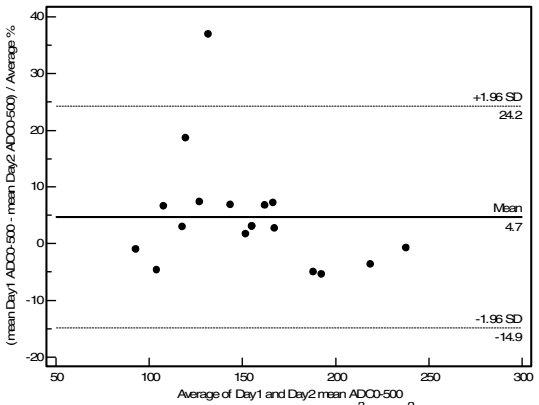
Table 1. Measurement variability of ADC0-500 and ADC150-500 of colorectal metastases on day 1 and day 2

	DAY1	DAY2	DAY1	DAY2	DAY1 & 2	DAY 1 &2
	ADC0-500	ADC0-500	ADC150-500	ADC150-500	ADC0-500	ADC150-500
Mean difference (%)	0.77	-1.26	0.55	-1.57	4.67	0.48
SD of difference (%)	4.40	2.95	4.04	5.08	9.97	17.11
Coefficient of repeatability or reproducibility (%)	8.62 (CR*day1*)	5.79 (CR*day2*)	7.92 (CR*day1*)	9.96 (CR*day2*)	19.5 (CR*day1&2*)	33.5 (CR*day1&2*)

Discussion

Our results demonstrate that ADC measurements are highly repeatable. The CR*day1* and CR*day2* indicate that up to 10% mean difference between the ADCs obtained on the same day could be due to observer errors in drawing ROIs. The ADC reproducibility CR*day1&2* showed larger variations, indicating additional measurement errors when comparing ADC calculations from different days. The reproducibility of ADC150-500 was poorer than ADC0-150, which could be explained by the use of only two b-values images for calculating ADC150-500, resulting in lower signal-to-noise and more susceptibility to data errors. Future work should investigate if the use of more b-values at image acquisition further improves reproducibility. Not surprisingly, ADC measurements were more reproducible in larger (≥ 4 cm) than smaller metastases.

Figure 1. Bland-Altman plot of day1 and day 2 ADC0-500



(Units of ADC in x 10^{-3} mm^2/s)

Conclusions

ADC measurements in colorectal hepatic metastases are highly repeatable. For serial assessment of therapeutic response of colorectal metastases in the liver, using ADC0-500 and larger target lesions ≥ 4 cm in diameter minimises measurement variability. Reproducibility appears to be SNR limited, which offers the potential for improving study precision.

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References: (1)Koh DM et al. Eur Radiol 2006; 16:1898-1905;(2) Beresford MJ et al. J Magn Reson Imaging 2006.