Measurement reproducibility of ADC for liver metastases using multi b value diffusion weighted imaging: preliminary results.

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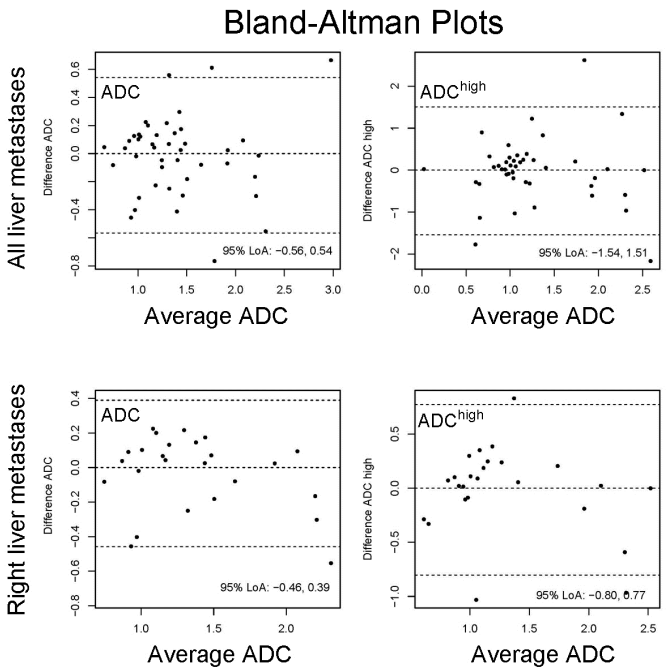
Target audience: Oncologists, radiologists and medical physicists interested in the reproducibility and potential use of diffusion weighted imaging in the liver for tumor response assessment.

Purpose: Diffusion weighted magnetic resonance imaging (DWI) is increasingly promoted in oncologic imaging as a potential biomarker to assess treatment response (1). However, limited data exist on the reproducibility of apparent diffusion coefficients (ADC) of liver metastases using multi b value DWI (2,3). The purpose of this study is to assess the measurement reproducibility of ADC for liver metastases in a patient population with metastatic neuroendocrine tumors.

Methods: Fourteen consecutive patients with metastatic neuroendocrine tumors were recruited in a prospective IRB approved study and underwent two MRIs on the same day, leaving the MR unit between examinations. A breath-hold fat suppressed DWI was performed with each MRI on one of two 3.0 Tesla GE MR 750 scanners with a phase array body coil. Parameters were: TR/TE 3000/47ms, 12 slices per acquisition with a slice thickness of 7 mm, 400 to 440 mm FOV, 128x128 matrix, 1 signal average, 20s acquisition time, the following b values: 0, 50, 250, 350, and 500 s/mm^2, with all three diffusion encoding directions applied simultaneously. Liver metastases greater than 2.0 cm were randomly selected in both hepatic lobes (up to 5 per patient) and their signal intensities (SI) at each b value were recorded by one radiologist. Diffusion coefficients were calculated by linear least squares estimates for each liver metastasis, based on SI from every b value (ADC) or using only high b values > 100 s/mm^2 (ADC^{high}). For statistical analysis, intra-class correlations (ICC) were calculated and Bland-Altman plots were constructed for both ADC and ADC^{high}. The limits of agreement (LoA) were calculated as: average difference ± 1.96 * standard deviation difference.

Results: 14 patients (7 male, 7 female, mean age 53 years) were recruited with a total of 44 liver metastases (mean size 4.3 cm; range 2.0-15.9 cm). For the initial and repeat MRIs, the calculated mean ADC were 1.40 and 1.41 x 10^{-3} mm^2/s, while the ADC^{high} were 1.26 and 1.27 x 10^{-3} mm^2/s, respectively. When including all liver metastases, ADC ICC was 0.845 (CI 0.733,0.912) and ADC^{high} ICC was 0.380 (CI 0.093,0.608). For right hepatic metastases, ADC ICC was 0.895 (CI 0.778,0.952), while ADC^{high} ICC was 0.766 (CI 0.535,0.890). Among all liver metastases, the confidence intervals for ADC and ADC^{high} do not overlap, indicating significantly higher agreement for ADC than ADC^{high}. The 95% LoA were calculated for ADC and ADC^{high} for all versus right hepatic metastases (Figure).



Discussion: Our preliminary results show excellent measurement reproducibility for ADC of neuroendocrine tumor liver metastases and poor measurement reproducibility for ADC^{high}. The measurement reproducibility for ADC^{high} improved when we limited our analysis to lesions in the right hepatic lobe. However, our preliminary results suggest that for monitoring treatment response, large absolute changes in ADC, greater than 0.4-0.6 x10^{-3} mm^2/s, are required to be considered significant. The lower reproducibility of ADC^{high} may be due to our limited number of b values acquired and only 1 signal average, given the constraints of breath-hold DWI technique.

Conclusion: ADC of liver metastases have higher measurement reproducibility than ADC^{high} with breath-hold DWI. An absolute change in ADC of greater than 0.56 x10^{-3} mm^2/s for hepatic metastases (or 0.46 x10^{-3} mm^2/s for right lobe metastases) following therapy may be needed to be considered a true change.

References: **1**. Padhani AR and Koh DM. Magn Reson Imaging Clin N Am. 2011. **2**. Heijmen L, Verstappen MC, Ter Voert EE et al. Crit Rev Oncol Hematol. 2012. **3**. Andreou A, Koh DM, Collins DJ et al. Eur Radiol. 2012