Diffusion-Weighted MRI of the Liver: Parameters of Acquisition and Analysis and Predictors of Chemotherapy Response

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Introduction: Diffusion-weighted (DW) MRI is sensitive to the microscopic random motion of water molecules which can be quantified via the apparent diffusion coefficient (ADC). The method allows for the characterization of biological tissue as it provides unique information regarding cellularity, cell membrane integrity and alterations in intra- vs. extra-cellular compartments prior to changes in tumor volume that occur with chemotherapy[1]. In hepatic metastases, baseline ADC values have been shown to potentially predict treatment response [2] and disease survival [3] in colorectal patients. There are currently no accepted methods or standardized protocols for acquisition and image analysis of liver metastases[4]. The aim of this study was to optimize a protocol for obtaining reproducible results for DW-MRI of liver metastases including choice of b values, lesion segmentation and percent region of interest (ROI) segmentation for predicting chemotherapy responses. Baseline ADC, lesion size, and the number of prior treatments were also evaluated as possible predictors of chemotherapy response.
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Materials and Methods: Conventional T1-weighted imaging was performed at 1.5T, along with single-shot echoplanar DW-MRI using b-values of 0, 150, 300 and 450 s/mm^2. DW-MRI image pairs (b=0 and 150, 300 or 450 s/mm^2) were collected within a single breath-hold (**Figure 1**). MR imaging was performed at baseline, day 4, 11 and 39 following the commencement of cytotoxic therapy for 46 hepatic metastases in 19 female breast cancer patients. Following data acquisition, an automated segmentation and an ADC estimation algorithm were applied to achieve improved image analysis compared to standard methods such as manual segmentation and the diffusion map approach. Receiver operating characteristic (ROC) analysis was performed to identify the threshold ADC value of potential responders and non-responders.

Results: The b value pairs of b0-300 and b0-450 s/mm^2 were statistically different from b0-b150 and provided the most reproducible measure of the apparent diffusion coefficient for all days except day 4 (all $p \leq 0.05$). A semi-automated segmentation scheme was employed that produced reliable and reproducible ADC measures comparable to manual segmentation. The comparison of a 100% ROI to progressively smaller ROIs including 90%, 80% and 65% of the ROI area revealed that there was no significant difference in mean values. ROC analysis identified a threshold ADC value of 1.22 $\mu m^2/ms$ as 62% sensitive (5 out of 8) and 89% specific (8 out of 9) for identifying non-responding metastases. Using this ADC value as a cut point, 76% of the lesions were correctly classified. Our results demonstrated that a low baseline ADC (≤ 1.22 $\mu m^2/ms$) was a better predictor of therapy response in patients with one or no prior treatments (**Figure 2**). A lower ADC threshold was needed to comparably predict responses in patients more heavily treated.
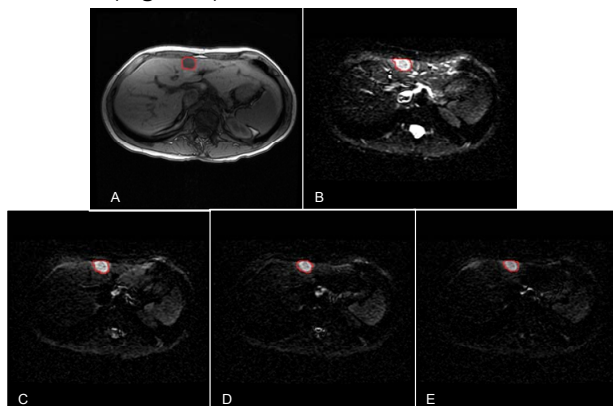

Figure 1. Liver metastases. **A.** T1 weighted image **B.** b=0 s/mm^2 **C.** b=150 s/mm^2 **D.** b=300 s/mm^2 **E.** b=450 s/mm^2. ROI (red circle) represents an example of a lesion of interest used to calculate the ADC value.
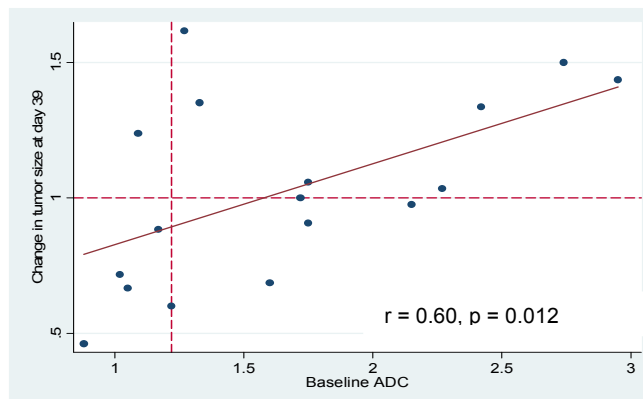

Figure 2. Patients with 0 or 1 prior treatments (n = 17 lesions, 9 patients) with a linear regression line. Responding lesions are those with change less than 1 and ADC ≤1.22 $\mu m^2/ms$.

Conclusions: Both tumor and imaging parameters affect ADC measurements in metastatic liver lesions from breast cancer. Our study suggests that liver lesions in patients with 0-1 prior treatments are best analyzed using the b value pair of b0-b450. Moreover, lower baseline ADC values predict for a higher likelihood of tumor response, but only in patients who had received one or no prior chemotherapy treatments for their liver metastases.

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