Assessment of variability of region of interest (ROI) delineation on diffusion weighted MRI (DW-MRI) using manual and semi-automated computer methods

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Introduction: Diffusion-weighted magnetic resonance imaging (DW-MRI) has the potential to become a biomarker in anti-cancer drug development for assessment of tumour response [1]. In chemo-radiotherapy treated tumours, early ADC change has been shown to predict response to therapy, with an increase in tumour ADC correlating with cell death [2]. A major challenge for implementing DWI in multicentre clinical trials is in measuring changes in individual patients reliably and reproducibly. Along with the acquisition parameters, the delineation of the region of interest (ROI) has a great impact on final reproducibility. Drawing ROIs manually is time consuming and highly operator dependent. This study compares ADC values obtained using in-house computer ROI drawing software (Diffusion View) to segment tumour with those obtained from a manual free drawing technique.

Methods: Ten patients with metastatic disease referred for phase I trials were studied. Seven patients were scanned twice 7 days apart to assess reproducibility. Patients were imaged using an 1.5T Avanto MR Siemens system (Siemens Medical Systems, Erlangen, Germany). DW-MRI measurements were acquired with a free-breathing, multiple-averaging technique, using single-shot echo-planar MR imaging (TR/TE 3500/69ms, 5mm thickness, 340-mm FOV, 128×104 matrix, images interpolated to a 256×208 matrix, 7 b-Values of 0, 50,100, 300, 600, 900 and 1050 s/mm^2 in three orthogonal directions). Morphological images were also acquired using breath-hold gradient-echo T1-weighted and turbo spin-echo T2-weighted sequences. Isotropic ADCs were calculated using all trace diffusion weighted images.

An experienced radiologist drew ROIs for each axial image using the trace/index b-1050s/mm^2 image. The same region was drawn manually and using the Diffusion view software. Fifteen lesions were analysed twice by each method 1-269 days apart. The location of the lesions was liver (7), pelvis (3), adrenal gland (1), kidney (1), peritoneum (1), lymph node (1) and subcutaneous nodule (1). For each lesion, the distribution of the ADC pixel values was asymmetric, and median values were used to summarise the distribution. The distribution of the median values of all tumours conformed to a normal distribution and a Bland–Altman analysis was performed to test variability [3]. For the reproducibility cohort the ROI's were drawn using both techniques interchangeably. The within-patient coefficient of variance (wCV) and the coefficient of repeatability expressed as % of baseline average were calculated. The value of the coefficient of repeatability (r) indicates that the difference between the two measurements for the same ROI will be less than the "r" value for 99% of the pairs of observations.

In four out of 15 lesions (26.6%; 3 liver and 1 pelvic) the ROI generated by the computer did not include the lesion entirely. This was due to high lesion heterogeneity with a wide spectrum of ADC values which resulted in computer segmentation of tumours into more than one ROI. Therefore, only 11 of the 15 lesions described by a single ROI were included in the comparison between manual and computer drawn ROIs.

Results: Manual drawn ROIs were larger than computer generated ones (p =0.001). Median ADC values were lower on computer generated ROIs (p = 0.04). The wCV and r values were low for the median ADC per ROI with both techniques but significantly lower for the computer generated ROI's (see table). The wCv for the pixel numbers were 0.03 for manual and 0.07 for the computer technique with a coefficient of repeatability of 9.2% for the manual drawn ROIs and 2 for the computer generated ROIs. The computer generated approach was associated with a significant reduction in the time used to obtain ROIs.

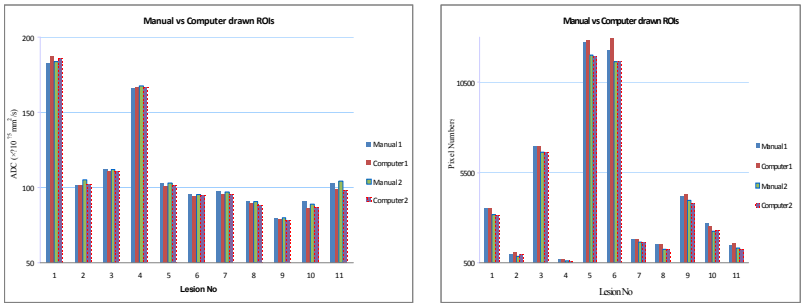

Fig.1Median ADC (right) and pixel numbers (left) at 2 time points for each technique.

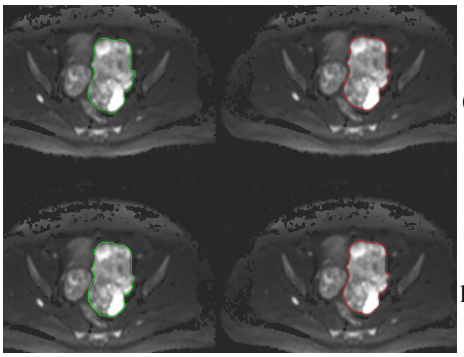

Fig.2 Manual (green) and computer (red) generated ROI's at 2 time points (upper and lower rows)

Median ADC	wCV	r (%)
Manual	0.008	2.37
Computer	0.04	1.16
Reproducibility Cohort	0.024	6.8

Table 1. Median ADC

Discussion and Conclusion:
ROIs drawn on DWI images using in-house software are highly reproducible in terms of median ADC and number of included pixels. Computer generated ROIs have the advantage of less variability, operator independence and significant time saving and support the feasibility of use of automated DWI measurements in clinical trials. However, the method cannot be used reliably when the tumours have a wide range of ADC or if ADC values are similar to those of the adjacent normal tissue; further development is needed to address this.

References: [1]Padhani et al (2009). Neoplasia 11(2): 102–125[2]Charles-Edwards et al (2006) Cancer Imaging 13;6:135-43 [3]Galbraith SM, Lodge MA, Taylor NJ et al (2002) NMR Biomed 15:132–142

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