Predicting lesion subtype and response to chemotherapy in paediatric Wilms' tumours using ADC histogram analysis

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Target audience Clinicians and scientists interested in oncology and diffusion weighted imaging.

Purpose Wilms' tumour is the second most common abdominal tumour in childhood, with approximately 80 children diagnosed in the UK each year. Patients in Europe are treated with pre-operative chemotherapy, to reduce the volume of tumour tissue prior to nephrectomy. Chemotherapy response has traditionally been assessed by change in tumour volume, however, this can be unreliable in the presence of substantial necrosis, and tumours which shrink may still be composed of predominantly malignant cells[1]. Alternatively, the Apparent Diffusion Coefficient (ADC) derived from Diffusion Weighted Imaging (DWI) has been shown to be negatively correlated with tumour cellularity/malignancy[2], and it has been suggested that shifts in ADC distributions towards higher values might be indicative of good therapy response[1]. We aimed to investigate if the distribution of ADC values measured in a Wilms' tumour on initial diagnosis could be used to predict: (a) the histological subtype of the lesion, and (b) the lesion's response to chemotherapy. Two definitions of tumour response were investigated: increase in median ADC within the tumour, and shrinkage in tumour volume.

Methods DWI was performed in 22 paediatric Wilms' tumour patients (mean age 38±38 months), using a free-breathing 2D EPI protocol[1]. Imaging was performed in all patients pre-chemotherapy; 16 patients also received imaging post-chemotherapy, with a mean scan interval of 48±24 days. Following nephrectomy, histological slices from the surgically resected tumours were reviewed by a consultant paediatric histopathologist to determine lesion subtype. Regions of interest (ROIs) defining the tumour volume were drawn on the ADC images, and histograms of ADC values were produced for each lesion, at both time points (when available). Each lesion's ADC histogram was parameterized in terms of its median (M), full width at half maximum (FWHM), excess kurtosis (K) and skewness (S). Multinomial logistic regression was then used to test if these histogram parameters at scan 1 could be used to predict the histologically-determined subtype of the lesion. Following this, multiple regression analysis was performed in patients with imaging data at both time points, in which the lesion response to chemotherapy, *y*, was defined as either median ADC at scan 2 ($y=ADC_2$, model #1) or percentage change in lesion volume ($y=\delta V$, model #2), with M, FWHM, K, S of the ADC histogram at scan 1 as regressors in both models.

Results

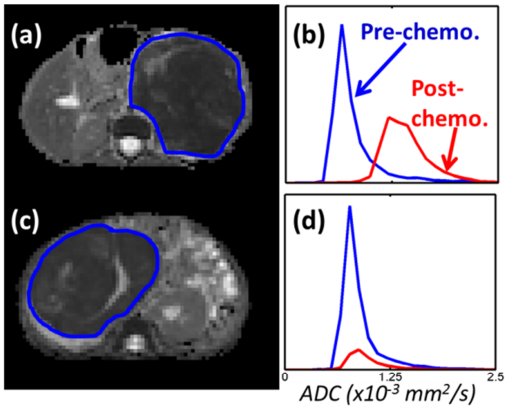

Figure 1 ADC maps from a stromal (a), and epithelial (c) Wilms' tumour, prior to chemotherapy (tumour outlined in blue). Histograms of ADC values pre- and post-chemotherapy are shown for the stromal and epithelial lesions in (b) and (d) respectively.

Table 1: Results from multiple regression analysis of model 1 ($y=ADC_2$) and model 2 ($y=\delta V$; β=regression coefficient).

Regressor	**Model #1**: R^2=0.59, p=0.046		**Model #2**: R^2=0.63, p=0.018	
	β	p value	β	p value
Intercept	-3.8×10^{-3}	0.12	-12.5	0.005
Median	-0.023	0.95	2049.4	0.005
FWHM	2.60	0.048	4673.6	0.024
Kurtosis	-4.0×10^{-4}	0.014	-0.56	0.026
Skewness	2.5×10^{-3}	0.024	4.45	0.013

Histological analysis revealed the 22 Wilms' tumours were comprised of the following subtypes: 9 mixed, 5 stromal, 3 blastemal, 2 completely necrotic, 1 epithelial, 1 regressive, 1 diffuse anaplastic. Due to low numbers of some subtypes, only the mixed, stromal and blastemal lesions were considered for logistic regression (N=17). Of these, the logistic regression model correctly identified 8/9 mixed, 4/5 stromal, and 3/3 blastemal lesions (based on the M, FWHM, K, and S values of the ADC histogram at scan 1). The results of the multiple regression analysis are shown in Table 1. All ADC histograms had positive excess kurtosis and positive skewness at scan 1. Excess kurtosis was the most significant regressor in model #1, with increase in median ADC (i.e. reduction in tissue malignancy) being associated with lower excess kurtosis at scan 1. In model #2, skewness was the most significant regressor, and lesions whose ADC histogram had the lowest skew at scan 1 showed the greatest chemotherapy-induced shrinkage.

Discussion & Conclusion Our analysis suggests ADC histogram properties pre-treatment show good potential for predicting both Wilms' tumour subtype, and response to chemotherapy, in terms of predicted change in tumour cellularity (model #1) or volume (model #2). This could be a valuable tool when assessing the risk/benefits of pre-operative chemotherapy in paediatric patients.

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References 1. McDonald K, Sebire NJ, Anderson J, Olsen OE. Patterns of shift in ADC distributions in abdominal tumours during chemotherapy-feasibility study. *Pediatr Radiol*. 2011;41(1):99–106. 2. Humphries PD, Sebire NJ, Siegel MJ, Olsen ØE. Tumors in Pediatric Patients at Diffusion-weighted MR Imaging: Apparent Diffusion Coefficient and Tumor Cellularity. *Radiology*. 2007;245(3):848 –854.