Characterising heterogeneity of stage 1 cervical cancers using histogram analysis from diffusion weighted images.

K. Downey[1,2], S. F. Riches[1,2], V. A. Morgan[1,2], S. L. Giles[1,2], C. Simpkin[1,2], D. P. Barton[3,4], and N. M. deSouza[1,2]

[1]Clinical MRI Unit, Institute of Cancer Research, Sutton, United Kingdom, [2]Clinical MRI Unit, The Royal Marsden Hospital, Sutton, United Kingdom, [3]Gynaecology Unit, The Royal Marsden Hospital, Sutton, United Kingdom, [4]Gynaecology Unit, Institute of Cancer Research, Sutton, United Kingdom

Introduction: Prognosis of patients with stage 1 cervical cancer is dependent on primary tumor histology: adenocarcinoma tumour types, poorly-differentiated tumours and those with invasion of the microvasculature have a higher incidence of metastases and therefore a poorer prognosis than their squamous cell, well-differentiated counterparts with no evidence of lymphovascular space invasion (LVSI). Apparent Diffusion Coefficient (ADC) values in cervical cancer have been shown to be significantly lower than non-malignant cervical epithelium and cervical intraepithelial neoplasia and a mean tumour ADC has shown potential as predictive biomarker. This study aims to use histogram analysis to establish whether ADC values are significantly different in cervical tumours according to their histological characteristics.

Methods: From March 2006 to May 2009, 60 patients with stage 1 cervical cancer were scanned at 1.5T (Philips Intera) with a 37mm diameter endovaginal coil. T2-weighted images (TR/TE = 4500/80 ms) were acquired to identify the tumor followed by diffusion-weighted imaging (TR/TE = 2500/69 ms; 5 b values 0, 100, 300, 500 and 800 s/mm^2). Regions of interest around the tumor were drawn on ADC maps by an expert observer with reference to the T2-weighted images. ADCs were calculated using a mono-exponential fit of data from all b values. ADC histograms obtained from the entire tumor volume had their 10th, 50th and 90th centile pixel values documented and the skewness of the histogram recorded. Data was analyzed using the SPSS (version 18 for windows). An independent samples t-test was used to compare differences in the mean centile ADC values and the skewness of the distribution between squamous vs. adenocarcinoma, well/moderately differentiated vs. poorly differentiated tumors and the absence vs. the presence of lymphovascular space invasion.

Results: 20 patients were subsequently excluded from the analysis (19 no visible tumor, 1 non-comparable b values). There was no statistically significant difference in the ADC centiles in adenocarcinomas compared to squamous carcinomas but the 50th centile ADC values were significantly higher in well/moderately differentiated compared to poorly differentiated tumors. The skewness was significantly different between tumor types. There was no significant difference between any parameter with regards to absence or presence of lymphovascular space invasion.

Histology	Category	No. Patients	Mean+/-SD ADCx10^{-6} (mm^2/s) 10th C	Mean+/-SD ADCx10^{-6} (mm^2/s) 50th C	Mean+/-SD ADCx10^{-6} (mm^2/s) 90th C	Mean+/-SD Skewness
Tumour type	SCC	26	826(+/-197)	1018(+/-189)	1326(+/-206)	0.97(+/-0.67)
	AC	13	885(+/-204)	1101(+/-187)	1407(+/-243)	0.30(+/-0.97)
P value			0.38	0.20	0.28	**0.02**
Differentiation	Well/Mod	18	911(+/-192)	1113(+/-177)	1418(+/-224)	0.48(+/-0.94)
	Poor	22	797(+/-189)	996(+/-184)	1302(+/-200)	0.92(+/-0.71)
P value			0.07	**0.049**	0.92	0.99
LVSI	Yes	18	839(+/-185)	1042(+/-154)	1354(+/-181)	0.72(+/-0.70)
	No	22	856(+/-210)	1054(+/-216)	1354(+/-246)	0.72(+/-0.95)
P value			0.78	0.84	0.99	0.99

Table 1.Mean + standard deviation (SD) of centile ADC values by tumour type, differentiation and LVSI

Discussion and conclusions: The increased cellularity of poorly differentiated tumors is reflected in their lower median ADC. ADC distribution however, does not appear to be associated with lymphovascular space invasion. The increased skewness of the histograms in the adenocarcinomas is likely to reflect the mixture of glandular and cellular content of these tumors. A prospective study to determine sensitivity and specificity of ADC in determining poor histological features in cervical cancer is warranted.

Figs.1a&b. Example ADC histograms in individual patients according to tumor differentiation (a) and tumor type (b).

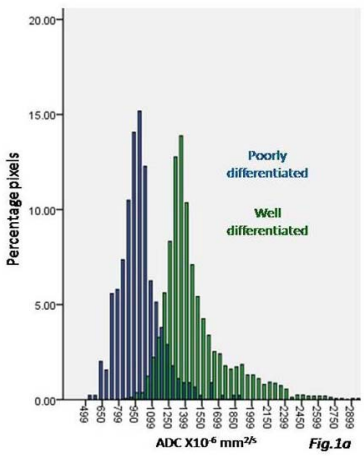

Fig.1a

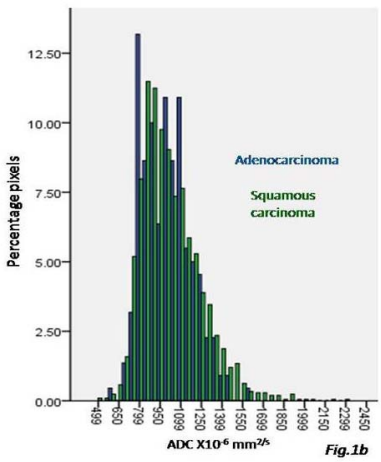

Fig.1b

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