

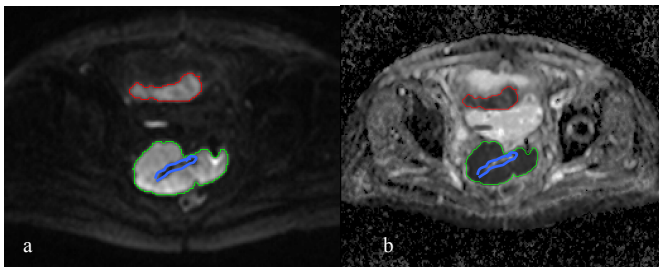
# DIFFUSION-WEIGHTED IMAGING OF OVARIAN-RELATED PERITONEAL CARCINOMATOSIS: ASSESSMENT OF CHEMOTHERAPY RESPONSE IN RELATION TO ANATOMICAL SITE

S. Kyriazi<sup>1,2</sup>, D. J. Collins<sup>1</sup>, V. A. Morgan<sup>2</sup>, S. L. Giles<sup>2</sup>, and N. M. deSouza<sup>1,2</sup>

<sup>1</sup>CR-UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research, Sutton, Surrey, United Kingdom, <sup>2</sup>Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom

**Introduction:** Transperitoneal dissemination is the main pathway of disease spread in ovarian cancer. Standard treatment is neo-adjuvant platinum-based chemotherapy with response assessment relying on serial serum CA125 measurements in combination with morphological imaging criteria. However, these techniques are not sensitive early in the course of treatment and fail to address differential response, which would facilitate surgical planning. The value of Diffusion-Weighted Imaging (DWI) has been established in the qualitative delineation of peritoneal carcinomatosis<sup>1</sup> and site-specific diffusivity profiles have been observed<sup>2</sup>, but changes in diffusivity as a result of cytotoxic treatment have not been reported. The purpose of this study is to evaluate Apparent Diffusion Coefficient (ADC) as a response biomarker in metastatic ovarian cancer and to relate ADC-measured response to anatomical site (peritoneum, omentum).

**Method:** Nineteen females with advanced ovarian or primary peritoneal cancer were examined on a Siemens Avanto 1.5T scanner prior to and after the first and third cycle of platinum-based chemotherapy. Following administration of an antiperistaltic agent (hyoscine butylbromide 20 mg im), standard T1W and T2W imaging and free-breathing axial double spin-echo echo-planar DWI were performed in the abdomen (40 slices) and pelvis (50 slices) with SPAIR fat suppression (TR/TE=6300/69, 5 mm thickness, 5 averages, 128x128 matrix interpolated to 256x256, 380 mm FOV, Grappa = 2, three scan trace with b-values 0, 600, 900, 1050 s/mm<sup>2</sup>). In-house software DiffusionView was used for the pixel-by-pixel extraction of ADC values, whereby non-geometric regions of interest (ROIs) were drawn with computer-assisted segmentation on the high b-value index DW images and copied on the corresponding ADC map (generated from all b-values) (Figure). Mean and median ADCs were calculated for volumes of interest (VOIs) defined as composites of ROIs over multiple slices in order to encompass the entire lesion. Tumour volume was calculated from the total pixel count of each VOI. Lesions with a baseline total pixel count of <50 were excluded from the final analysis. Response was assessed individually for each lesion on conventional volumetric imaging criteria (>65% reduction in volume) after the third cycle of treatment.<sup>3</sup>



ROIs encompassing omental (red) and peritoneal (green) deposits are drawn semi-automatically on the high b-value (b=1050 mm<sup>2</sup>/s) index DW images (a) and copied on the corresponding ADC map (b). Manual segmentation is used to exclude areas of fluid / normal tissue (blue).

**Results:** Twelve omental (6 responding, 6 non-responding) and 27 peritoneal (15 responding, 12 non-responding) lesions were evaluated. Pretreatment mean ADCs were not significantly different between sites (omental [115±22] vs peritoneal [108±25] x 10<sup>-5</sup> mm<sup>2</sup>/s, p=0.328, Mann Whitney U test). After the first cycle of chemotherapy, responding peritoneal tumours demonstrated a significant increase in mean and median ADC (p=0.031 and p=0.017 respectively) in contrast to responding omental tumours (p=0.465 and p=0.433 respectively) (Table). Non-responding lesions did not display significant ADC change irrespective of site. No significant volume change occurred after one cycle in responders or non-responders for both sites (responding p=0.295, non-responding p=0.865, Wilcoxon's signed ranks test). After the third cycle of treatment, eleven (4 omental, 7 peritoneal) out of 21 responding lesions could not be assessed due to volume reduction below the threshold of measurability, thus precluding late ADC analysis of responding omental deposits. Among the remaining evaluable lesions significant late ADC change compared to baseline values was observed in the responding peritoneal group but not in non-responding tumours. There was no significant correlation between percentage volume change after the third cycle and percentage ADC change after the first (r<sup>2</sup>=0.007, p=0.681) or third (r<sup>2</sup>=0.102, p=0.065) cycle.

Site / Response	Mean ADC (± SD) (x 10 <sup>-5</sup> mm <sup>2</sup> /s)					Median ADC (x 10 <sup>-5</sup> mm <sup>2</sup> /s)				
	PreTx	PostCycle1	p <sup>a</sup>	PostCycle3	p <sup>a</sup>	PreTx	PostCycle1	p <sup>a</sup>	PostCycle3	p <sup>a</sup>
<b>Peritoneal Responding</b>	<b>104±24</b>	<b>115±26</b>	<b>0.031</b>	<b>127±34</b>	<b>0.048</b>	<b>100</b>	<b>114</b>	<b>0.017</b>	<b>125</b>	<b>0.048</b>
<b>Omental Responding</b>	109±15	113±12	0.465	NA	NA	106	112	0.433	NA	NA
<b>Peritoneal Non-responding</b>	114±15	115±15	0.239	117±20	0.182	108	109	0.439	113	0.182
<b>Omental Non-responding</b>	122±28	127±14	0.465	127±20	0.465	120	125	0.715	126	0.728

Parameters (mean ± SD) for responding (R) and non-responding (NR) lesions according to site. Statistical significance (p<0.05, Wilcoxon's signed ranks test) is highlighted by bold typeface. Omental responding lesions were not included in the analysis after the 3<sup>rd</sup> cycle because of their small number (n=2). (°): Comparison to pre-treatment values.

significant ADC change irrespective of site. No significant volume change occurred after one cycle in responders or non-responders for both sites (responding p=0.295, non-responding p=0.865, Wilcoxon's signed ranks test). After the third cycle of treatment, eleven (4 omental, 7 peritoneal) out of 21 responding lesions could not be assessed due to volume reduction below the threshold of measurability, thus precluding late ADC analysis of responding omental deposits. Among the remaining evaluable lesions significant late ADC change compared to baseline values was observed in the responding peritoneal group but not in non-responding tumours. There was no significant correlation between percentage volume change after the third cycle and percentage ADC change after the first (r<sup>2</sup>=0.007, p=0.681) or third (r<sup>2</sup>=0.102, p=0.065) cycle.

**Discussion & Conclusion:** Pretreatment ADC values of peritoneal and omental metastases are not site-specific. An early increase in mean/median ADC after the first cycle of chemotherapy may indicate subsequent macroscopic tumour shrinkage in peritoneal lesions. Volume reduction of omental lesions after three cycles despite no significant ADC change indicates that ADC is poorly predictive of response in the omentum. This may be explained by treatment-induced return of fat into omental tumours, resulting in a decrease of ADC values.

**References:** [1] Low RN et al. *Am. J Roentgenol.* 2009;193:461-470, [2] Sala E et al. *Eur Radiol.* 2009 doi:10.1007/s00330-009-1543-y, [3] Therasse P et al. *J Natl Cancer Inst.* 2000;92:205-216.

**Acknowledgements:** This work is supported by Marie Curie Early Stage Training programme (contract no 020718) and CRUK and EPSRC Cancer Imaging Centre in association with the MRC and Department of Health (England) grant C1060/A10334. We also acknowledge support of NHS funding to the NIHR Biomedical Research Centre.