

Demonstration of whole body DWI characterisation of tumour heterogeneity for serial response assessment.

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Target audience: Physicists and clinicians using whole body diffusion-weighted MRI in oncology

Purpose. Tumour heterogeneity, within the same lesion or between different lesions of the same patient, is a major challenge for anticancer treatment. Whole-body diffusion-weighted MR imaging (WBDWI) may offer a viable means of measuring therapy response in disseminated disease. Our work demonstrates a novel WBDWI analysis methodology to assess longitudinal tumour behaviour throughout the course of therapy at multiple sites of metastatic disease exemplified on a patient with metastatic ovarian cancer.

Methods. Patient: Our example is a 49-year-old woman with advanced ovarian cancer with liver and peritoneal metastases enrolled in a phase II trial of a novel anticancer targeted agent. The research study received local ethics approval. The patient was scanned on a 1.5T Siemens Avanto at baseline and every 6-week interval during treatment until disease progression (total time points n=10). **MR image acquisition:** A 3-station (chest, abdomen, and pelvis) diffusion weighted imaging (DWI) was acquired. The DWI parameters for each station were: 2D EPI imaging sequence, 46 axial slices, slice thickness 5mm, TR/TE=12700/69 ms, FOV=380 x 380 mm², NeX = 4, 150x150 imaging matrix, phase partial Fourier 6/8, parallel acquisition (Grappa acc. factor 2, ref. lines 32), b =50/900 s/mm², acq. time ~6 min/station. **Segmentation:** Volumes of interest (VOIs) were drawn automatically on computed high-b-value images (in-house software¹) and reviewed by a senior radiologist. Lesions were spatially separated following segmentation using a blob detection algorithm ('Label_Region', IDL, Exelis Inc). Histogram analysis of Apparent Diffusion Coefficient (ADC) values were performed for each lesion using kernel density estimation to smooth the resulting distributions (see Fig.2) and changes occurring in each lesion were visualised by colour-coding the regions according to their median ADC along a sliding scale (Fig.2, panel A).

Results and discussion. Four main sites of metastatic disease (located in the liver and pelvis) were segmented for this patient. Lesions less than 100 voxels in size were not included in the analysis to improve statistical support of the results. The overall temporal evolution of lesion volume and median ADC are shown in Fig.1. Figure 2 shows colour-coded ADC histograms and spatial distributions of these lesions at beginning, middle and end of therapy. Panel A (baseline) clearly demonstrates inter-

lesion heterogeneity of ADC values: the liver metastases are predominantly highly cellular whilst the pelvic lesions are predominantly cystic. Differential response of lesions is observed throughout the treatment (Fig.2, all panels): the liver metastases show continuous rise in ADC and the cystic pelvic lesion show a decreased ADC with complete response to therapy in the inferior lesion and slow reduction in size of the lateral pelvic metastasis. The initial difference in response of individual lesions seems to converge towards a stabilization of the ADC values across all lesions by the last study (Fig.2, panel C) indicating a more homogeneous sub-population of disease. However, the broad ADC histogram (panel C) suggests that the remaining tumoral tissue is a mixture of solid and cystic tumour. In addition, this quantitative method allows measurement of tumour volume for each individual site, as exemplified for two lesions in Fig. 2, all panels. By considering each lesion separately, it is apparent that WBDWI can be more sensitive to changes occurring throughout treatment rather than investigating global properties of disease (black dotted curve in Fig.1). Further interrogation of lesion histograms may also demonstrate heterogeneous response occurring within lesions².

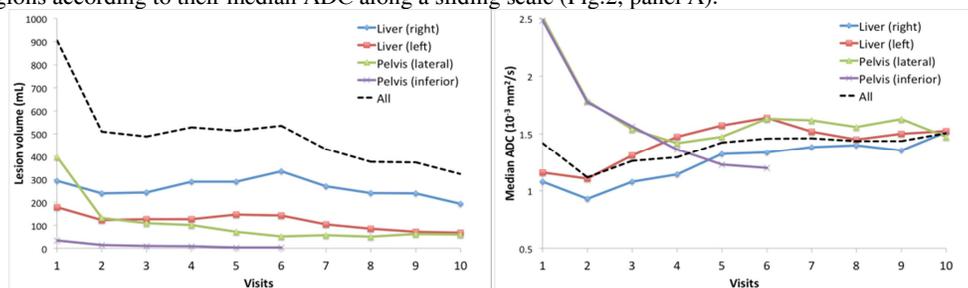


Figure 1. Temporal evolution of tumour volume (left) and median ADC (right) for all individual lesion and the combined evaluation (dotted line). One of the pelvic lesions (purple line) was completely resolved after 6 visits.

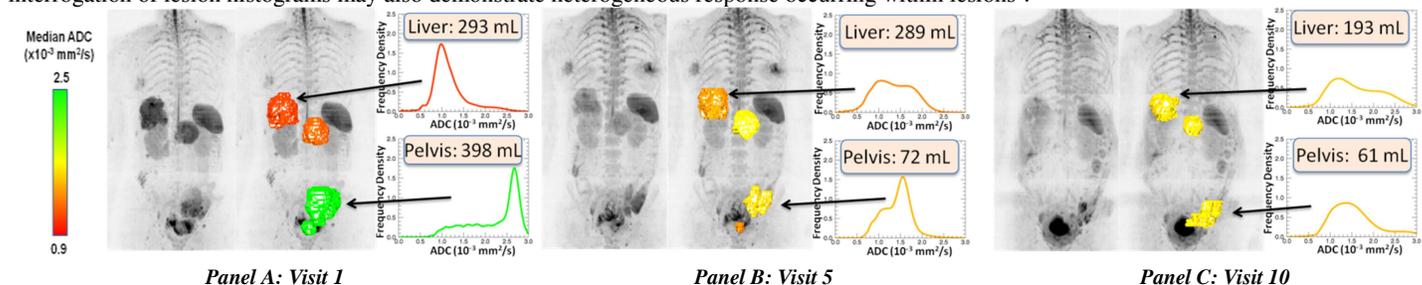


Figure 2. Pre and post treatment coronal maximum intensity projections ($b = 900 \text{ s/mm}^2$) with overlaid segmentation surfaces colour-coded according to the median values of the underlying ADC distribution. Plots show the ADC histogram distribution and the tumour volume evolution for two main lesions.

Conclusion. This methodology successfully demonstrates pre and post-treatment tumour heterogeneity in a patient with metastatic ovarian cancer. Such analysis allows full characterization and visualisation of disease burden and observation/quantification of individual tumour response to therapy at each individual site. Histogram and volumetric assessment of individual lesions provides additional information regarding treatment compared to overall assessments of total tumour burden and global ADC distributions¹.

References. ¹Blackledge *et al.*, Proc. 20th Annual Meeting ISMRM 2012, 255; ²Rata *et al.*, Proc. 21st Annual Meeting ISMRM 2013, 592.

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