ADC histogram analysis: investigation of treatment response and survival in advanced ovarian cancer

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Target audience Physicists and clinicians interesting in ovarian cancer and diffusion-weighted imaging

Purpose

Diffusion-weighted imaging has been used to assess treatment response in patients with advanced ovarian cancer. For the primary ovarian lesion, the mean ADC of the primary ovarian lesion has been shown to increase significantly after 1–3 cycles of neoadjuvant chemotherapy in responders to the treatment, with no change in non-responders[1,2]. The same pattern has also been seen for histogram parameters C10, C25, C50, C75 and C90 (where Cn is the nth percentile of the ADC distribution within the lesion)[1]. For metastatic disease (omental and peritoneal lesions), no significant difference has been seen in mean ADC[2], while histogram analysis has not yet been reported. This study aims to investigate whether the ADC histogram parameters of both ovarian and metastatic disease: 1) have value in assessing changes during neoadjuvant chemotherapy; 2) are predictive of treatment response; or 3) are related to overall survival.

Methods

20 patients with advanced ovarian cancer were imaged at 3T (Signa HDx, GE Healthcare, Waukesha, WI) after obtaining ethical approval and informed consent. Diffusion-weighted EPI (TE/TR=87/2000 ms, acquisition matrix 128×96, FOV 35×28 cm^2, slice thickness/gap 8/2 mm) was acquired before and after 3 cycles of neoadjuvant chemotherapy (carboplatin ± paclitaxel) prior to 3 further cycles and interval debulking surgery. 7 slices and 9 b-values (0, 100, 150, 200, 250, 350, 500, 750, 1000 s/mm^2) were acquired in a 22-second breath-hold, usually repeated 2–3 times to cover the region of identifiable disease. T2-weighted fast-spin echo images (TE/TR 106/4000+ ms, acquisition matrix 320×256, FoV 28×28 cm^2, slice thickness 5 mm, 4 Nex) were used to evaluate treatment response using the RECIST 1.1 criteria and Ca-125 measurements. ADC maps were calculated using a non-linear fit neglecting b=0. Regions of interest (ROI) for ovarian mass, omental cake and peritoneal implant were defined on the ADC maps by a genitourinary radiologist. The mean ADC values and their relationship with response have been reported previously[2].

Fig. 1: ADC map with outlined ovarian (1), omental (2) and peritoneal (3) lesions.

Histogram analysis of ADC values was performed to calculate these parameters: mean, C10, C25, C50, C75, C90, each calculated over the entire tumour volume. For each parameter and lesion type, paired Student's T-tests were used to compare changes in ADC pre- and post-treatment. Additionally, the ADC changes on treatment (post- minus pre-treatment) was compared between responders and non-responders using an unpaired T-test. To assess the survival data for this relatively small group, Kaplan-Meier plots were produced, and the change in histogram parameter values for 3-year survivors was compared with non-survivors (unpaired T-test). The threshold for statistical significance was p=0.05.

Results

Fig. 1 shows an ADC map with the three lesions. Typical histograms are shown in Fig. 2.

In additional to the ovarian mass (always present), omental cake was identified in 18/20 patients (8 non-responders and 10 responders) pre-chemotherapy and in 16/20 patients (8 non-responders and 8 responders) post-chemotherapy. Peritoneal deposits were identified in 15/20 patients pre-chemotherapy (6 non-responders and 9 responders) and in 8/20 patients post-chemotherapy (5 non-responders, 3 responders).

Fig. 2: Histograms of ADC (in units of 10^{-3} mm^2/s) for the different tumour types, before (blue solid) and after (red dashed) chemotherapy; examples are shown for a non-responding, non-surviving patient (top row) and for a responding, surviving patient (bottom row, patient had no peritoneal deposit).

For the primary ovarian tumour, responders showed a highly significant increase in ADC after treatment for all parameters (p=0.002 for C90, p<0.001 for mean and C10–C75) while there were no significant changes for the non-responders. Correspondingly, the ADC change on treatment was significantly greater for responders than non-responders when comparing mean, C75 and C90 (p<0.05) but no other parameters. However, for omental and peritoneal lesions, no significant changes were found in any parameter, either between pre- and post-treatment ADC values or between the ADC values for responders and non-responders.

Figure 3 shows example Kaplan-Meier plots for median (C50) ADC of the ovarian lesion (both baseline value and change on treatment), comparing the survival of patients with values greater and less than the group median (no significant differences were found). There was no significant difference between the ADC change for 3-year survivors and non-survivors for any lesion or for any histogram parameter.

Discussion

Our study confirms the highly significant changes previously seen using histogram analysis of the primary ovarian mass in responders but not in non-responders[1]; this technique may therefore have value in predicting treatment response. A similar pattern does not seem to apply in metastatic disease, although in the case of peritoneal deposits there were too few patients with both pre- and post-treatment lesions to allow robust statistical comparisons. Future studies with larger patient cohorts might be able to assess this further or to show benefits from a combined analysis of all tumours together.
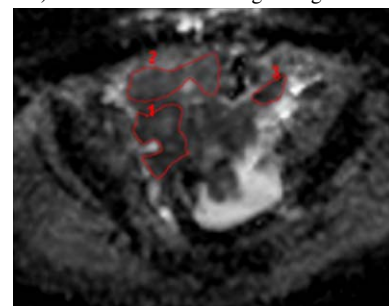
The shapes of the histograms, and their changes on therapy, often vary substantially between the different lesions for a given patient, which may reflect the differing natures of these lesions.
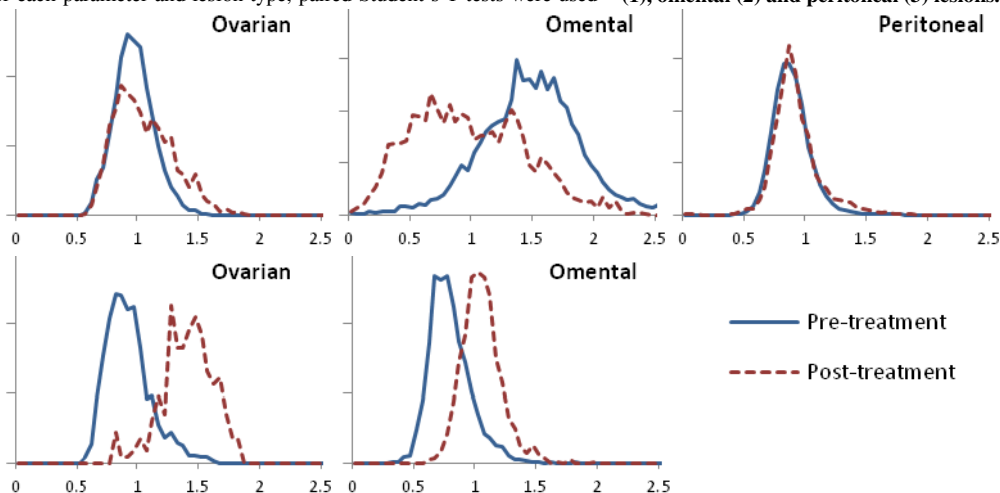
Conclusion

ADC histogram analysis may have value predicting chemotherapy response in advanced ovarian cancer, but this small study found no evidence of a corresponding difference in survival.
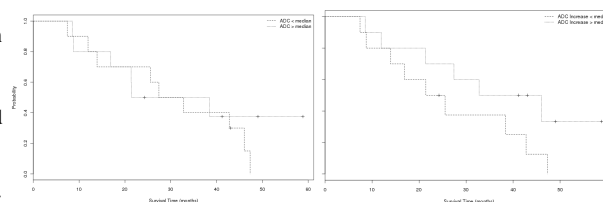
References

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2. Sala E, Kataoka MY, Priest AN, et al. Advanced ovarian cancer: multiparametric MR imaging demonstrates response- and metastasis-specific effects. Radiology. 2012;263(1):149–59.

Figure 3: Kaplan-Meier plots comparing above-median and below-median values of (a) pre-treatment ADC and (b) ADC change (post- minus pre-treatment).