Correlating prospective and histology-matched ADC histograms with extra-capsular extension in prostate cancer

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Introduction: One of the challenges for the imaging of prostate cancer is in correlating imaging results with clinical data. Of particular interest is an evaluation of whether the tumour has extended beyond the borders of the prostate. In the past research has shown the possibility of using traditional T1/T2-weighted MRI for predicting pathologic stage (1), but to date possible benefit from the addition of DW-MRI has remained largely unknown. Recently histogram analysis using ADC maps has been shown to aid in the assessment of tumour response to treatment (2), and it is hypothesized that such analysis could prove valuable for the local staging of prostate cancer. Therefore the aim of this study was to investigate the value of histogram analysis of ADC maps, using ROIs from both a prospective reader and from a histology-matched session, in relation to extra-capsular extension (ECE) status.

***Methods*:** The initial twenty-five patients, all with biopsy-confirmed prostate cancer and scheduled for prostatectomy, from a current prospective study were studied with a 3T Signa HDx scanner (GE Healthcare, Waukesha, WI) using an 8-channel cardiac coil. Ethics committee approval was obtained and all patients gave informed consent. T2-weighted FSE images (TE/TR=85/4000ms) were acquired along with diffusion-weighted spin echo EPI (TE/TR=77/2000ms; b values: 150, 1000 s/mm^2; ASSET factor-2, Matrix 128x128; 4mm slice thickness, 1mm gap). Regions of interest around the suspected lesions were drawn on ADC maps by an intermediate experience reader (T.B.) with reference to T2-weighted and DW-MR images. All suspected tumour regions were correlated to subsequent whole-mount pathology. A second group of regions was drawn retrospectively on the same ADC maps with reference to the whole-mount pathology slides. Volumetric histogram parameters, in particular interquartile range (IQR) and mean ADC, were analyzed for all tumour regions according to ECE status. A student's T-test was used for statistical analysis. Statistical independence between tumours was assumed although in a few cases multiple tumours were present per patient (mean: 1.2, range: 1-3). The performance of mean ADC for evaluation of ECE was determined by constructing Receiver Operating Curves (ROC) of sensitivity against 1-specificity. The optimal cut-off values were defined as the shortest Euclidean distance between the curve and the point representing 100% specificity and sensitivity. Linear discriminant analysis (LDA) was also completed using all eligible cases for training, on both data sets separately, to look at the effect of the inclusion of IQR for the evaluation of ECE.

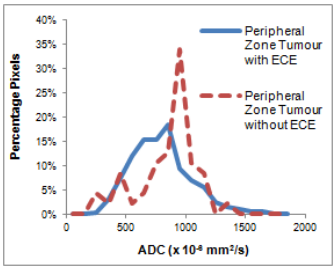

Fig 1. Example ADC histogram for individual tumours according to ECE (Histo-matched)

***Results and Discussion*:** Evaluation included 20 peripheral zone tumours (6 with ECE, 14 without) for the histology-matched session and 20 peripheral zone tumours (9 with ECE, 11 without) for the prospective reader due to differences in prospective detection and availability of full histo-pathology slides. The prospective reader had a sensitivity of 64.5% (20/31) for detection of peripheral zone tumours. For the histology-matched tumour regions a significant difference was identified between ECE status groups for mean interquartile range (IQR) but not mean ADC (Table 1). For the prospectively drawn tumour regions mean ADC and mean interquartile range were both significantly different between the two groups (Table 1). This difference in IQR is shown visually, in a comparison between representative histograms from each group of the histology-matched data set (Fig 1), as a broader spread of ADC values in the tumour with ECE and a sharper focus of ADC values near the mean value for the tumour without ECE. The performance of mean ADC, as determined through ROC curve analysis, was better for the prospective data set (AUC- 0.767) than for the histology-matched data (AUC-0.524). For the prospective data set, using the optimum cut-off of 926.5 x10^{-6} (mm^2/s), this translated to a sensitivity and specificity of 66.7% and 80.0%, respectively. Similar to the analysis of mean ADC alone, with the addition of IQR the performance of the prospective data set (Fig 2b) was better than the performance of the histology-matched data set (Fig 2a) with each data set having a mis-classification rate for ECE of 10% and 25%, respectively. Using the LDA function developed for the prospective reader set (Fig 2b), a combination of IQR and mean ADC showed improved sensitivity and specificity (88.9% and 90.9%, respectively) for ECE when compared to mean ADC alone. While limited by study size, the difference in ECE status groups, highlighted by the increased IQR with ECE, hints at a difference in tumour heterogeneity correlated with subsequent increased ADC pixel heterogeneity (Fig 3).

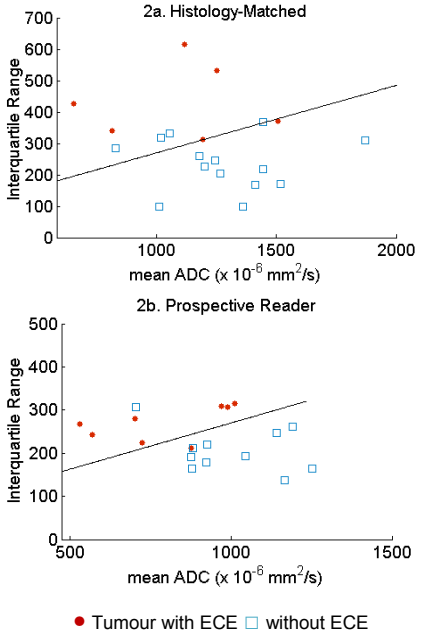

Fig 2. Linear Discriminant Analysis for ECE status using mean ADC and IQR (with classification boundary- black line)

Table 1: Correlating ADC parameters and extra-capsular extension

	Extra-capsular extension		
Histology-Matched	Present (n=6)	Absent (n=14)	*P value*
Mean ADC (±SD) [x10^{-6}mm^2/s]	1090 (±309)	1275 (±262)	0.185
Mean IQR (± SD) [x10^{-6}mm^2/s]	434 (±118)	236 (±83)	**<0.001**
Prospective Reader	Present (n= 9)	Absent (n= 11)	*P value*
Mean ADC (±SD) [x10^{-6}mm^2/s]	755 (±219)	1000 (±171)	**0.01**
Mean IQR (± SD) [x10^{-6}mm^2/s]	268 (±38)	207 (±50)	**0.007**

Conclusion: These initial results show a promising relationship between interquartile range and extra-capsular extension in both a prospective and retrospective data set. Interestingly they also highlight the possible relationship between mean ADC and ECE, but only in the prospective set. Further research using a more robust data set and more sophisticated analysis is warranted.

References

1. Augustin H et al. Acta Radiol 2009; 50:562-569.
2. Kyriazi S et al Radiology 2011; 261:182-192.

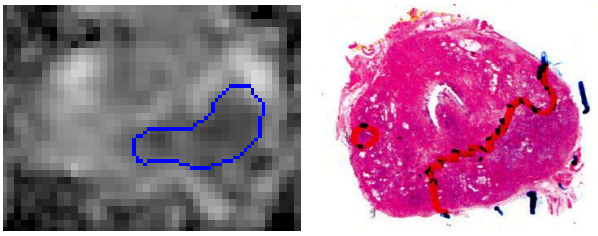

Fig 3. Patient with peripheral zone tumour with established ECE. **a|** ADC map (b-values 150,1000) **b|** Histopathology