Pathological tissue classification by multiparametric MRI: Technical Development and Application in Renal Masses Characterisation.

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INTRODUCTION: The non-invasive characterisation of heterogeneous tumours is a recognised goal for MR multiparametric analysis. Such an approach offers an alternative to RECIST criteria for treatment response, but could also provide biologically meaningful tissue characterisation that aids targeted biopsy. Moreover, early depiction of the cell transformations during tumour progression could be valuable for treatment planning and response prediction. Researchers in various studies have demonstrated the benefits of Diffusion-Weighted MRI (DWI) [1,2] and Dynamic Contrast Enhanced (DCE) MRI [3,4] in helping characterise renal masses. Their findings brought forward biological interpretations in terms of different tissue subtypes for the ranges of DCE enhancement and apparent diffusion coefficient (ADC) values (axes of **Fig 1**). However, a lack of tools for advanced analysis of combinations of quantitative measures has, to date, limited the scope of investigations in this area.

AIMS: We have developed an interactive framework [5] that allows spatially synchronised 3D visualisation and analysis of anatomical, diffusion-weighted and dynamic contrast enhanced MR data in multi-planar orientations. Our aim is to use this methodology to establish correlations between parametric maps derived from MRI (ADC and Area Under the concentration Curve - AUC), and the corresponding characteristics measured from paired histological sections. We thus hope to provide biologically meaningful interpretations of non-invasively measured imaging parameters as well as a computer aided tissue classification scheme for the RCC model.

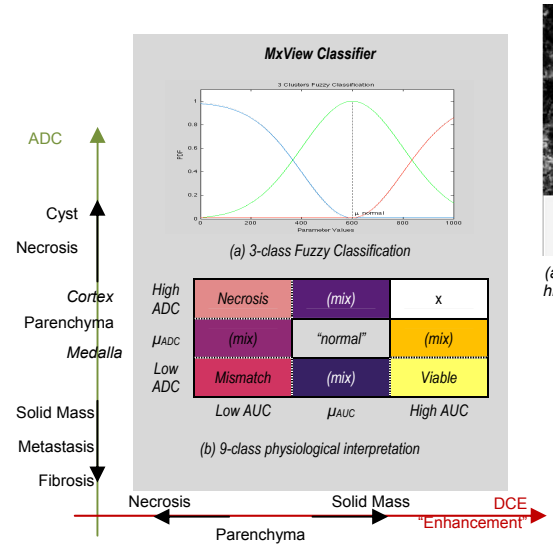
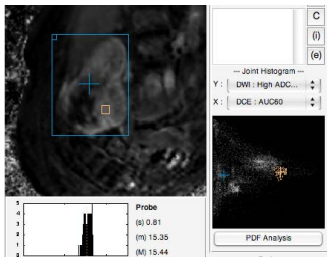
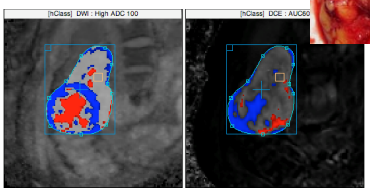


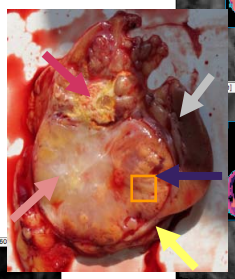
Fig 1: ADC-DCE Correlations & Physiological Interpretations



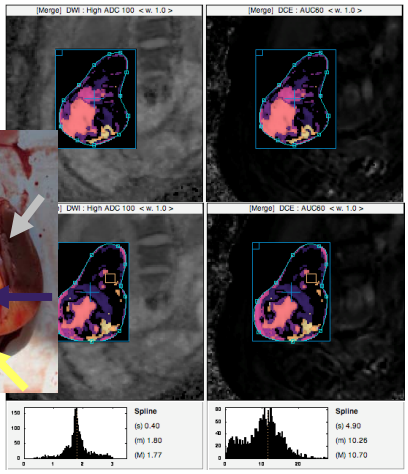
(a) Data Exploration: Matching samples from histology, parametric images (software probe – orange box) and multiparametric space (orange scatter plots on joint histogram).



(b) 3-class split for ADC and AUC.



Histology



(c) Ternary bit combination Classification: 2 consecutive slices automatically segmented into 9 classes colour coded and labelled as described on fig 1.b.

Fig 2: MxView Tissue Description and Classification Scheme

MATERIALS & METHODS: *Data:* 5 patients with advanced RCC undergoing a clinical trial were scanned pre and post treatment, and then had surgical excision. Each study included two anatomical scans (T1w, T2w), a quantitative DWI scan with 8 b-values (0, 25, 50, 75, 100, 200, 500, 900 s.mm^{-2}), a pre-contrast PD and an 80-dynamic DCE-MRI scan (0-280 s). A double oblique imaging plane was used to align all datasets to the long axis of the kidney to facilitate radiological-pathological matching. *Processing:* Our framework allowed us to co-register all datasets and derive quantitative maps. ADC was computed from all b-values, as well as from high b-values (≥ 100 s.mm^{-2}) using mono-exponential fit. Onset time and AUC maps were derived from the DCE data. *Biology vs. Multiparametric Space:* Data Exploration was enabled by Software Probing, which displayed the location in multiparametric space of samples in image space, that were mapped to histology (orange box & scatter plots in **Fig 2.a**). The 3-way mapping provided correlative information for biological classification, as shown on **Fig 1.b**. *Classification:* ADC and AUC maps were each partitioned into 3 fuzzy classes based on the "normal kidney" distributions (**Fig 1.a, 2.b**), then merged using ternary bit combination to obtain a 9-classes tissue classification map (**Fig 1.b, 2.c**) [5] and mapped onto the histology data (arrows on histology, **Fig 2**). "Normal kidney" distributions were determined by an expert radiologist, by probing multiple slices of normal renal areas on image sections, pre and post treatment.

RESULTS: *"Normal kidney":* Normal ADC distribution was computed from all patients. $\mu_{ADC,\ full\ b\text{-}values}$ showed too large overlap between tissues, as well as overestimation. On the other hand, $\mu_{ADC,\ High\ b\text{-}values}$ gave more accurate discrimination between classes. $\mu_{ADC,\ High\ b\text{-}values} = 1.85 \pm 0.15 \times 1e^{-3}.mm^2.s^{-1}$ (cortex + medalla). AUC had to be determined for each patient. For the patient of **Fig 2**, $\mu_{AUC} = 12.2 \pm 4.5$. Across all patients, μ_{AUC} ranged from 6.5 to 14.6. *Parametric Space vs. Histology:* Definition of tissue types such as *necrosis* (high ADC/low AUC), and *viable* (low ADC/high AUC) corroborated global consensus. Of particular interest was the *Mismatch* class (low ADC/low AUC), which we hypothesize could represent a microenvironment in which a more aggressive phenotype may arise. *Classified tissues vs. histology:* Our automatically classified tissues matched histology findings, within the margins of sampling inaccuracies. In the example presented, a region of *necrosis* on maps was matched to 80 – 90% necrosis at histology, while a *viable* region showed < 10% necrosis. Areas of *mismatch* demonstrated the highest Fuhrmann grades scores (3 to 4) suggesting increased aggressiveness.

CONCLUSION: These preliminary results show that combining quantitative maps in a multiparametric analysis framework can provide useful biological information. Not only can we explore the correlations and relationship between these parameters and pathology, but we can also step further into "virtual biopsy" and advance towards gene expression correlations. Further work is being carried out to automate the analysis process and build a knowledge base. At the current state, our framework simplifies mix classes, but further investigation is required to further validate our initial observations and better understand the complexity of the tissues.

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[1] Sandrasegaran et al. Usefulness of DWI in the Evaluation of Renal Masses. AJR 2010. **[2] Paudyal et al.** Role of ADC value in the Characterization of Renal Carcinoma by DWI. BJR 2009. **[3] Hecht et al.** Renal Masses: Quantitative v.s Qualitative Analysis of Enhancement for Diagnosing Malignancy. Radiology 2004. **[4] Taouli et al.** Renal Lesions: Characterization with DWI vs. Contrast Enhanced MRI. Radiology 2009. **[5] Andriantsimisvona et al.** MR Multiparametric Analysis for Tumour Heterogeneity Characterisation. Framework & Initial Experiment in Liver Metastases. Proc. ISMRM 2011.