# Correlation of MRS water proton resonance frequency with ADC in childhood brain tumours

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**Purpose:** To investigate the MRS water proton resonance frequency (PRF) differences found among childhood brain tumours by combining with ADC measures from DWI.

**Introduction:** The rate of improvement in survival, among children with brain tumours, has decreased in recent years. Novel prognostic markers that may contribute to associated treatment stratification and improved outcomes are required. Non-invasive measures of tumour microenvironment, which may provide such markers, have been relatively unexplored. In addition to metabolite levels, Magnetic Resonance Spectroscopy (MRS) can provide a measure of the water Proton Resonance Frequency (PRF) relative to reference metabolite peaks, which is sensitive to temperature and micro-environmental factors including fast proton exchange and ionic concentration. This measurement could be useful for the characterisation of childhood brain tumours. A previous study showed differences in water PRF between two broad categories of childhood brain tumours [1]. However, further investigation into the main drivers of these differences is required. In this study, the water PRF relative to reference metabolite peaks was compared to corresponding ADC values measured using DWI, which has been shown to be a marker for cellular density [2]. Differences in cellular density may affect the water PRF in opposite directions through potential temperature and protein content changes (fast proton exchange) [3,4]. The aim of this study was to investigate the correlation between the water PRF and ADC as a proxy for cellular density to aid in understanding the underlying mechanisms and clinical potential of the water PRF measure.

**Method:** Single-voxel MRS data (PRESS, TR 1500ms, TE 30ms) and DWI (b values 0.1000 s/mm$^2$, mean TR 7500ms, mean TE 100ms ) were acquired using either a 1.5T Siemens or GE system in 38 childhood brain tumour patients. The cohort consisted of 16 medulloblastomas (MB) and 22 gliomas (twelve grade I, six grade II, one grade III, four grade IV), which were retrospectively analysed. The MRS voxel was placed within the solid part of the tumour. Spectra were analysed using jMRUI (AMARES tool [5]) and the water PRF shift relative to total choline, $\delta_{(H20\text{-}tCho)}$ was measured [1]. ROI analysis was performed on the ADC maps derived from the DWI using T2 imaging as a point of reference for tumour location. Obvious cyst and oedema regions were excluded to compare with the MRS voxel. The mean ADC and $\delta_{(H20\text{-}tCho)}$ values were plotted for all tumours and Pearson correlation analysis was performed (figure 1). Differences in the mean ADC and $\delta_{(H20\text{-}tCho)}$ values between the MB and glioma groups were evaluated using unpaired two-tailed Student t-tests. Statistical significance was deemed for $p<0.05$.

**Results & Discussion:** The mean water PRF difference between the glioma and MB group was significant, 4.677 ±0.011 ppm and 4.689 ±0.009 ppm, respectively. The mean water PRF values are comparable to a previous study [1]. The mean ADC value difference was also significant between the glioma and MB groups, 157.66 ± 39.41 mm$^2$/s and 90.78 ± 51.17 mm$^2$/s, respectively. The ADC results are comparable to the literature for the same tumour types [6]. A higher ADC value was expected in the glioma group due to the micro-cystic nature of the tumours and the predominantly low grade population in this study. A significant negative correlation was found across all tumours between the ADC and the water PRF value, $p<0.05$. This suggests that increases in cellular density are associated with increases in water PRF. Based on previous results, an increase in water PRF could result from a lower temperature or an increase in protein content and associated fast proton exchange. The correlation of water PRF with cellular density suggests that fast chemical exchange is likely to be the major driver in the water PRF difference observed [3,4]. However, the observed correlation could also reflect lower temperatures due to increased perfusion, leading to more efficient dissipation of heat.

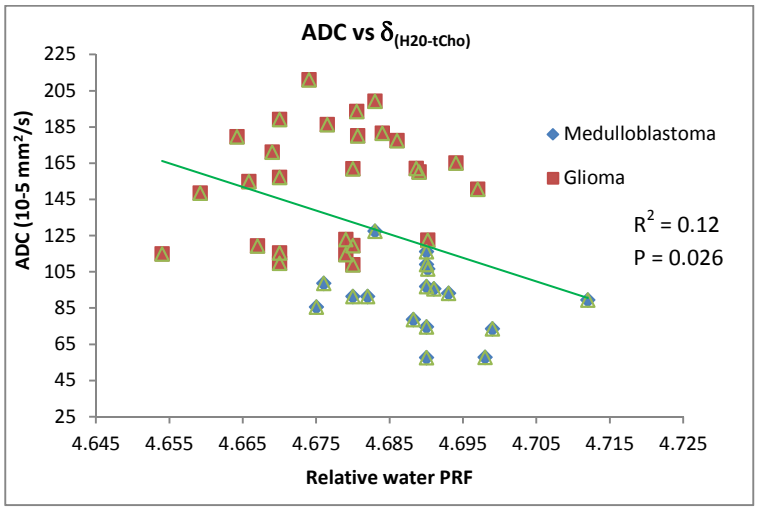


Figure 1: A scatter plot of water PRF (Cho referenced) measures vs ADC values for the glioma and medulloblatoma patient groups.

**Conclusion:** A significant negative correlation of water PRF with ADC was found in this cohort of childhood brain tumours. Further investigation is required to determine the clinical significance of these findings.

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