Effects of Gd-DTPA on *In Vivo* ^{1}H MRS Choline Signals Observed in HT-29 xenografts.

B. Madhu[1], S. P. Robinson[1], J. R. Griffiths[1]

[1]Cancer Research UK Biomedical Magnetic Resonance Research Group, St. George's, University of London, London, England, United Kingdom

INTRODUCTION:

Routine clinical protocols for cancer diagnosis include the use of contrast agents to enhance the tumour region. Choline signals have shown potential for diagnostic and prognostic value in ^{1}H MRS clinical cancer research. In human brain tumours, earlier reports showed a 12-15% decrease in Cho/Cr after Gadolinium - Diethyl Triamine Penta Acetic acid (Gd-DTPA) at long TE (135 ms) in CSI examinations,[1] whereas short-echo (TE=30ms) time investigation with single voxel localization methods (STEAM/PRESS/both) revealed no contrast agent-induced decrease in signal[2]. Some other studies focused on T_1 weighting showed changes in choline peak area and line shape[3]. In a combined Dynamic contrast enhanced Breast MR and proton spectroscopic imaging study using long echo times of 272ms it was found that choline SNR was significantly different between benign and malignant lesions[4]. Hence it is important to estimate accurately any change in choline signal after the administration of Gd-DTPA. In this study we have used a wide range of echo times and post observation time points to follow the modulation of choline and water signals following the administration of contrast agent.

METHODS:

HT-29 xenografts, grown subcutaneously to 500 mm^3 on female MFI nude mice (n=5), were studied *in vivo* by ^{1}H MR using a 15 mm diameter two-turn RF coil in a 4.7T Varian Unity Inova MR spectrometer. PRESS localisation (250 – 400 mm^3 voxels) with water suppression was used with a repetition time of 2 sec, 64 transients and varying echo times from 20 - 272 ms[5]. MRS acquisitions were carried out pre and post administration of 0.2 mM/kg Gd-DTPA(Magnivist) through a cannulated tail vein. All the spectral processing and quantification of signal peak areas was done by using the MRUI software package. Percentage of intra voxel enhancement (IVE) has been calculated by using the ratio of post admininistration of contrast agent Peak area to Pre administration peak area [Percentage of IVE =100 * (Post-peak area/Pre-peak area)].

RESULTS:

There were changes in choline peak area after bolus injection of Gd-DTPA at 20ms, 68ms 136ms echo times but none of them showed any statistical significance. Relatively long echo times (TE=272ms) clearly showed 13%, 27% and 17% reduction of choline peak areas at 10, 22.5 and 35 mins after the Gd-DTPA administration(Figure 1). Though there was some signal recovery at long echo time at 35 min after contrast agent administration, but it was still significantly lower than the pre-contrast choline peak area. There were also increased choline line widths observed due to the contrast agent administration at all the echo times and at various post observation times, but none of them were found to be statistically significant. Water peak area also showed a significant increase (about 20%) at 20 and 136ms echo times after contrast agent administration but did not show any change at 272 ms echo time (Figure 1). There was a significant linear correlation (R=0.62, p<0.0001) found between the percentage of IVE of choline and water signals (Figure 2).

DISCUSSION:

The short echo time (20 and 68ms) observations of the choline signal confirm earlier reports[2]. Significant decrease in the choline peak area and observation of increased choline signal line widths at long echo time (TE=272) are a consequence of the contrast agent shortening the relaxation times and inducing susceptibility effects. The enhancement of water peak areas at short echo time may also a consequence of this same phenomenon. The effects on quantification indicate that caution should be exercised when choline estimations are performed using water as a reference and/or acquisitions at long echo times if the signal is acquired after administration of a contrast agent. The significant correlation between the choline and water IVEs indicates a direct contact of choline with the contrast agent[3], implying that the choline observed in these tumours mostly resides in the interstial and extracellular space.

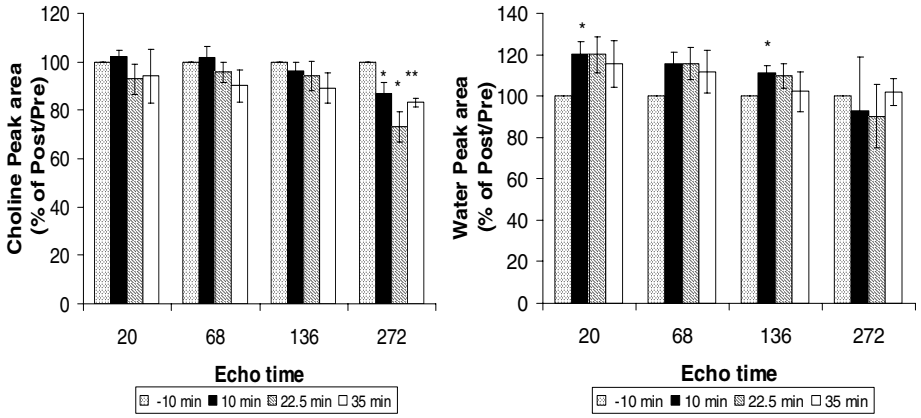

Figure 1. Choline and water peak areas (as % of post/pre administration of Gd-DTPA) at various echo times, pre and post Gd-DTPA administration observation time points. (Paired student's t-test, *p<0.05, **p<<0.005)

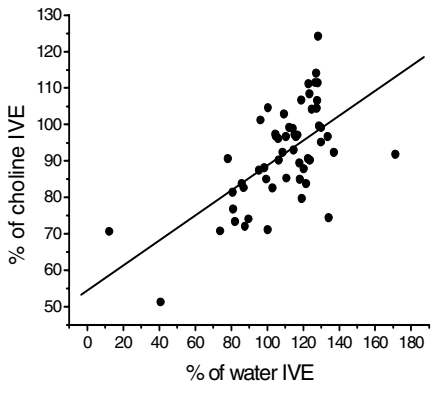

Figure 2. Correlation of Choline and water signals IVE.

REFERENCES:

1) Sijens PE, *et al*, Magn Reson Med. 37(2):222-5. 1997; 2) Lin AP, Ross BD. J Comput. Assist Tomogr. 25(5):705-12. 2001; 3) Murphy PS *et al*, , Magn Reson Imaging. 20(1):127-30. 2002; 4) Jacobs MA,*et al.*, J Magn Reson Imaging. 21(1):23-8, 2005; 5) Madhu B *et al*, Proc ISMRM 2045, 2005.

This work was supported by Cancer Research UK.