Combined ^{31}P and ^{1}H Magnetic Resonance Spectroscopic Imaging of phosphomono and -diesters in human brain tumors at 3T.

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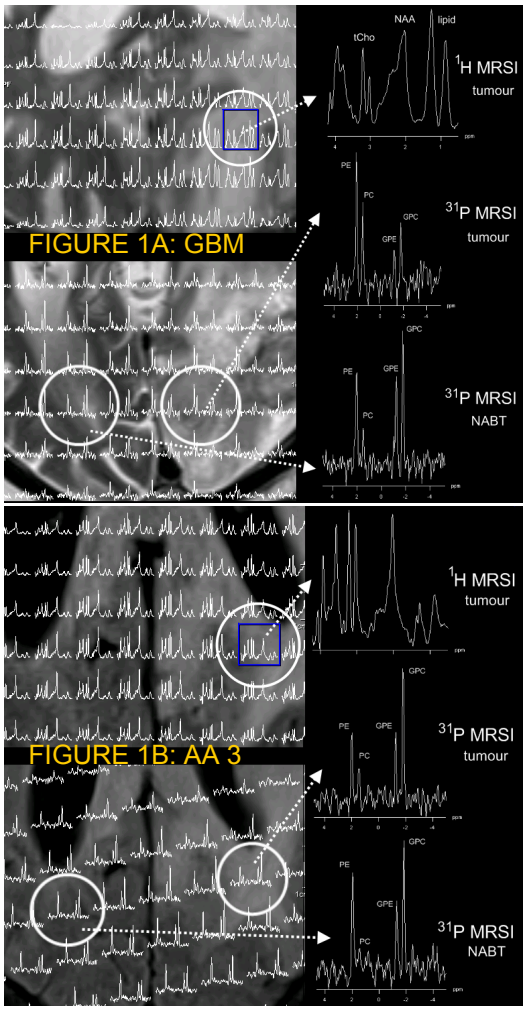

Introduction: The peak of methyl protons in choline compounds in ^{1}H MRSI of tumours is a hallmark of malignant growth [1,2]. It is assumed to reflect abnormal metabolism of membrane lipids and cell density. However, this peak is composed of phosphocholine (PC), glycerophosphocholine (GPC), and free choline and assessment of their individual contribution is not possible. PC and GPC can be monitored by ^{31}P MRSI with polarisation transfer (sRINEPT for enhanced sensitivity [3,4]). Thus the combination of ^{1}H and ^{31}P MRSI has the potential to provide a more complete view of choline compounds present in tumours than with either approach alone. In addition the sRINEPT sequence detects signals of phosphoethanolamine (PE) and glycero phosphoethanolamine (GPE), compounds also involved in metabolism of membrane phospholipids of tumour.

Aim: to explore the clinical feasibility of combined ^{1}H and ^{31}P MRSI of human brain tumours at 3T to uncover the composition of choline and phosphorylated ethanolamine compounds.

Methods:

Four patients participated in this study after informed consent was obtained; a 59 year old male and a 38 year old female with glioblastoma multiforme (GBM), a 30 year old female with grade 3 astrocytoma, and a 38 year old female with grade 3 oligodendroglioma. Patients were measured at a 3T MR system (Magnetom Trio, Siemens, Erlangen) using an optimised coil concept for multi-nuclear MRS of the human brain [5] (a volume TxRx ^{1}H birdcage coil and a quadrature TxRx surface coil for ^{31}P). First T1 and T2 weighted MR imaging was performed followed by ^{1}H MRSI using semi-LASER [6] with TE=30ms and TR 1500=ms. The field of view (FOV), matrix size and number of acquisition-weighted averages (n_acq) were adapted to obtain a real voxel size of 3-4cc within an acquisition time of 8 minutes. For each patient one acquisition without water suppression was used as a reference measurement for quantification. Subsequently, ^{31}P MRSI was performed with sRINEPT MRSI using a relatively short TR of 1500ms (during polarization transfer, T1 relaxation is dominated by ^{1}H). The FOV, matrix size and n_acq were adapted to obtain voxels with a real size of 15-17cc within a total acquisition time of 18 min. A hamming filter in 3 spatial directions was applied before spatial Fourier transformation. ^{1}H MRSI data was analysed with LCModel (simulated basis set). ^{31}P MRSI data was analysed with JMRUI 3.0 software, using Gaussian singlet's with equal line widths (derived from the line width of PE). Voxels were selected inside the tumour and in the normal appearing brain tissue (NABT). As the ^{1}H coil has a homogenous B1 field individual signal intensities can be compared, the ^{31}P coil is not homogenous, but phantom and volunteer studies showed that the signal intensity differences between the selected voxels is < 20%. Voxel locations in ^{1}H and ^{31}P data were manually matched taking into account differences in voxel volume: the average of 4 ^{1}H MRSI voxels were compared with one ^{31}P MRSI voxel.

Results and Discussion:

We compared the total choline (tCho) signal as measured by ^{1}H MRSI (which mainly consists of signals of PC, GPC and free choline) with the PC+GPC signal as measured by ^{31}P MRSI. When normalising the values from a voxel inside the tumour to a NABT voxel (Fig.2) we observed that in GBM the tCho is much higher than PC+GPC, suggesting that the high tCho signal in the proton spectrum of the tumour has its origin in an increased free choline pool, rather than higher levels of (glycero-)phosphorylated choline. This is in contrast to findings of ^{1}H high resolution magic angle spinning (^{1}H HRMAS) of tumour specimens, where usually the intensity of PC is the largest amongst resonances in the "choline area" (3.2ppm) [7]. It remains to be seen if this is due to some exceptional condition of these 2 GBMs or to artefacts that may occur in HRMAS tissue analyses [8]. The situation in the grade 3 astrocytoma (AA3) and the grade 2 oligodendroglioma (OA2) is different, here the PC+GPC is larger in the tumour than in the NABT (ratio>1 Fig.2), this would agree with HRMAS findings. However, even when accounting for 20% variation of the PC+GPC level due to the coil profile of the ^{31}P surface coil, the PC+GPC level remains lower in GBM compared to NABT and higher in AA3 and OA2 compared to NABT.

Different patterns were observed for the ratio PE/GPE and PC/GPC averaged over 5 independent voxels in tumour or NABT. PE/GPE and PC/GPC were higher in the tumour voxels of the GBM of the 59-year old male (PE/GPE 4.3±1.9 in tumour vs 1.3±0.3 in NABT), and OA2 (not significant in OA2 due to large standard deviation). In the AA3, the PC/GPC was higher in the tumour (0.3±0.04 vs 0.11±0.04 in NABT) but the PE/GPE was lower in the tumour (1.0±0.2 vs 1.5±0.1 in NABT). In the GBM of the 38-year old female no obvious differences in PC/GPC and PE/GPE between tumour and NABT were observed.

For all patients, the ratio PE/GPE and PC/GPC in the NABT were similar to these ratios found in healthy volunteers of similar age [4] (except for PE/GPE in OA2). In tumour however, these ratios differed from the ratios in healthy volunteers and varied between the patients.

The increase in PE/GPE and PC/GPC ratios, both accommodated by a high tCho, in GBM and OA2 might be explained by an increased PME and PDE turnover and cell proliferation [9]. Obviously, a larger patient group needs to be studied for a full understanding of the variable presence of PE, PC, GPE and GPC and free choline in different human brain tumours.

Conclusion: We demonstrated the clinical feasibility of combined ^{1}H and ^{31}P MRSI with sensitivity enhancement by polarisation transfer of ^{1}H to ^{31}P spins of human brain tumours at 3T to uncover the composition of choline and phosphorylated ethanolamine compounds. This opens a window on a detailed view of the levels of some key metabolites in membrane phospholipid metabolism of human tumours.

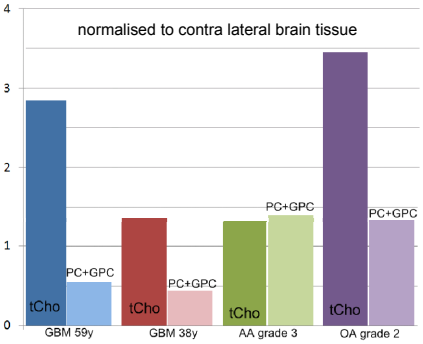

Figure 2: total choline level (measured with ^{1}H MRSI) and the PC+GPC level (measured with ^{31}P MRSI) displayed as ratios of the MR signal in tumour to normal appearing brain tissue, for each patient.

References:

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