Combined $^{31}$P and $^1$H Magnetic Resonance Spectroscopic Imaging of phosphomonopho and -diesters in human brain tumours 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 glycerophosphoethanolamine (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 $T_xR_x$ $^1$H birdcage coil and a quadrature $T_xR_x$ 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 1500ms. The field of view (FOV), matrix size and number of acquisition-weighted averages (n_acq) were adapted to obtain a realistic voxel size of 3x3x3 mm and 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. $^{31}$P 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 but 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 [7] 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 presence of PE, PC, GPE and GPC and free choline in different human brain tumours.

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The increase in PE/GPC 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.

References:
[5] Scheenen, MRM 2008;59:p1