^{31}P MRS of human brain tumors at 3T using ^{1}H –^{31}P polarization transfer

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Introduction:
It is well known that tumors have an abnormal phospolipid metabolism[1]. This is typically reflected in the higher phosphomonoester and total choline compound levels observed by in vivo ^{31}P and ^{1}H MRS respectively, which may be used as biomarkers for diagnosis and treatment evaluation [1,2,3,4]. For practical and sensitivity reasons ^{1}H MRS has been used most extensively in the clinic to assess higher choline compound levels in brain tumors. However, the choline resonance in ^{1}H MR spectra of these tumors may be quite variable as the intensity of this signal also depends on other factors such as cell density. From extract and cell studies it appears that in particular the phosphocholine (PC) over glycerophophocholine (GPC) and phosphoethanolamine (PE) over glycerophosphoethanolamine (GPE) ratios are potential biomarkers for tumor presence and malignancy [1,5]. Unfortunately, the resonances for these compounds are not resolved in ^{1}H MR spectra obtained in vivo. With ^{31}P MR spectroscopy the options to observe these compounds separately are much better, however this comes with a lower sensitivity. Moreover, the spectral region with these resonances is contaminated with signals of other phosphomonoester and diester substances.
To increase sensitivity we have developed a ^{1}H - ^{31}P polarization method that achieves a high efficiency of polarization transfer for the signals of PE, GPE, PC and GPC by using chemical shift selective refocusing pulses [6]. This ^{31}P MR method of using refocused insensitive nuclei enhanced by polarization transfer (RINEPT) has the additional advantage of a distinct selection of the resonances of these compounds.
Aim: to explore the potential of this new approach in the assessment of human brain tumors at 3T.

Methods:
In this study 3 patients with a glioblastoma multiforme were included. We used an in-house developed ^{31}P coil (two slightly overlapping surface coils in quadrature operation) shifted into a quadrature ^{1}H birdcage coil (Fig.1) in a 3T whole body scanner (TRIO TIM, Siemens, Erlangen) [7]. We used localized RINEPT [6] by adding an Image Selective In vivo Spectroscopy (ISIS) pulse sequence. Voxels of 50x50x60mm were selected on a T2-weighted background image (Fig. 1) ^{31}P MR acquisition parameters: TR=1500ms, 296 averages, 400ms WALTZ16 decoupling. Total acquisition:

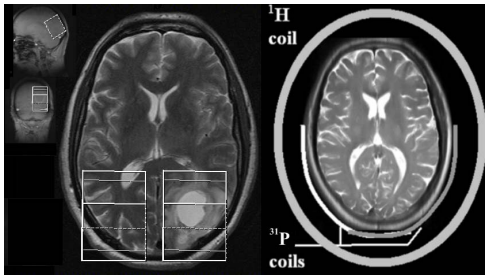

Figure 1:*Left, position of the tumor and a contra lateral 'normal' voxel. Right, coil concept shown with a normal brain.*

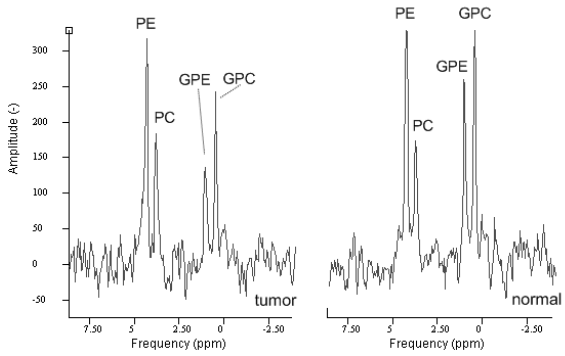

Figure 2*: ^{31}P MR spectra of the voxel in the tumor and the 'normal' voxel in which the resonances of PE, PC, GPE and GPC are well separated.*

7:24 min. Furthermore, a 3D ^{1}H MRSI was acquired using the body coil for excitation and a 12-channel receive only head coil for signal reception with the semi-LASER sequence [8]. Scan parameters; TR 1500ms, TE 30ms, elliptical k-space acquisition with 2 weighted averages, FOV 140x160x80mm, matrix size 12x14x8 (Fig 3.) The ^{1}H MRSI data was analysed by LCModel version 6.1-4F [9] and color maps of the metabolite levels were overlaid on post-Gd T1-weighted images using in-house developed software.

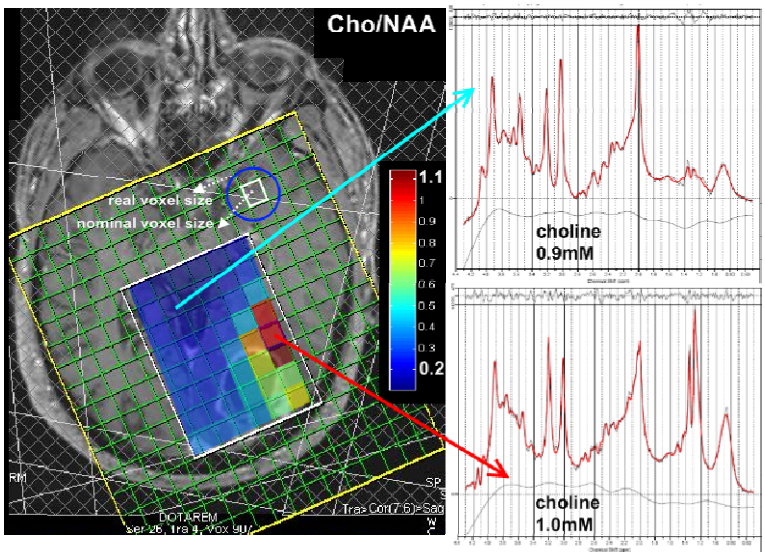

Figure 3*: Metabolite map of the ratio choline over NAA in the patient, overlaid on a post-Gd T1-weighted image. The combination of the weighted acquisition and filtering of k-space reduced contamination from neighboring voxels, but increased the real voxel size to a sphere with a cross section size of the blue circle, whereas the nominal voxel size is a cube with dimensions equal to the white square. Metabolite levels were scaled to the water signal; the LCModel basis set included simulated MR profiles based on the semi-LASER sequence.*

Results and Discussion:
The ^{31}P MR spectra obtained from a tumorous and contralateral normal region in the brain of a 60 year old patient (Fig 1) show well-resolved signals of PE, PC, GPE and GPC with high SNR (Fig. 2). A comparison of the spectra reveal an increase in the tumor of the ratios of PC/GPC (0.75 and 0.55 respectively) and PE/GPE (2.17 and 1.64 respectively) as would be predicted from studies of brain tumor extracts and cells [1]. Similar results were obtained in two other patients with a glioblastoma multiforme. This patient was also subjected to an ^{1}H MRSI examination, which showed only a minimal increased total choline signal in the tumor region (Fig 3). In this study a high SNR was obtained in only 7 min. acquisition time. This allows to obtain ^{31}P MR spectra from smaller voxels with less partial volume effects, for instance using a multi-voxel RINEPT, which also allows to spatially localize difference in phosphorylated compounds. With the ability to implement multi-voxel RINEPT at a field strength of 7T, we anticipate to be able to study this metabolism at a resolution and sensitivity approaching that of ^{1}H MRS at 1.5T.

Conclusion:
In this study we demonstrate the feasibility of ^{31}P RINEPT to examine the in vivo metabolism of selected phosporylated compounds in brain tumors. The changes observed in the ratios of individual phosphomonoester and diester compounds are more informative than changes in the signal of total choline compounds and may be valuable biomarkers for tumor diagnosis and treatment follow up.

References:
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