# Multinuclear MRS Screening of Untreated Pediatric Brain Tumors

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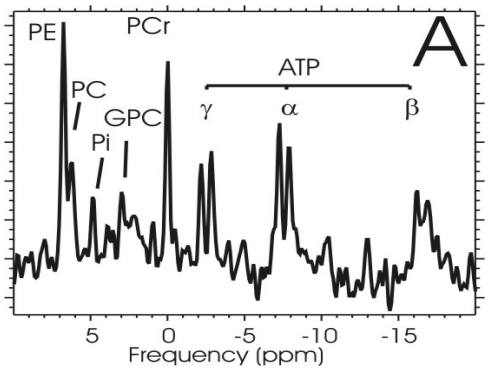
**Synopsis:** Proton-decoupled 31P (31P-[1H]) and 1H MR spectroscopy was combined with MR imaging to assess the metabolic profile of untreated pediatric brain tumors. Five patients with tumors of different pathologies were studied. Striking differences between tumors of different pathologies were seen in 31P-[1H] and 1H MR spectra. A quantitative cross-check of 31P-[1H] and 1H tumor spectra revealed additional information about the composition of the choline peak, an important marker of tumor malignancy. Multinuclear MRS allows a more complete screening of the molecular basis of tumors *in vivo* and may improve the predictive value of non-invasive tests.

## Introduction

Phosphorylethanolamine (PE), glycerophosphorylethanolamine (GPE), phosphorylcholine (PC), and glycerophosphorylcholine (GPC), are precursors and catabolites of phospholipids and are associated with cell membrane synthesis and cellular growth (1-3). Quantitation of these compounds in vivo in humans may aid in tumor classification and provide prognostic information. These chemicals cannot be separated and quantified with 1H MRS or with conventional 31P MRS. We therefore integrated proton-decoupled 31P (31P-[1H])MRS into the routine work-up of patients with newly diagnosed tumors scheduled for brain surgery.

## Methods and Materials

Five patients with newly diagnosed, untreated brain tumors (1 primitive neuroectodermal tumor (PNET), 2 ependymomas, 1 astrocytoma, 1 fibrous histocytoma) were studied. A clinical 1.5 T GE scanner was equipped with a stand-alone decoupler MRI, 1H MRS, and 31P-[1H] MRS were acquired using a double-tuned head coil (AIRI, Cleveland, Ohio). A 2D-CSI spinecho sequence was used for 31P MRS with TE = 2.5 ms, TR = 1.5s, NEX = 24, 6× 6 phase encoding steps, and FOV=180-200 mm. Slice thickness was 30 mm resulting in nominal voxel resolutions of 27–33 $cm^3$. Spectra were analyzed using the Sage/IDL program provided by GE. The pH of tumors was calculated from the chemical shift difference between inorganic phosphate (Pi) and phosphocreatine (PCr).Gaussian lines were fitted to the resonances of PE, PC, Pi, GPE, GPC, PCr, γ-ATP (two lines), α-ATP (two lines), dinucleotides (DN), and β-ATP (one line) and peak ratios were calculated. Single voxel 1H spectra of the tumors were acquired using a PRESS sequence with TE = 35 ms and TR = 1.5s. Proton spectra were processed using the LCModel software (4) and absolute concentrations were determined. 31P-[1H] and 1H MRS from five subjects with MRI reported to be normal were used to generate preliminary "normal" data. To estimate concentrations of phosphorylated metabolites, PCr was used as an internal reference. It was assumed that PCr ≈ ½ total creatine. Total creatine (Cr) concentration was determined by 1H MRS.




## Results

PCr/ATP, GPC/ATP, and GPE/ATP were statistically significantly reduced in tumors (Table). Mean PE/ATP was also reduced but did not reach statistical significance due to large variations of PE/ATP in tumors. In particular in PNET, PE was the most prominent peak (Fig. 1). The quantitative comparison of 1H and 31P-[1H] MRS revealed that total choline in ependymomas (Fig. 2) is close to the sum of PC+GPC whereas in the PNET and astrocytoma most of the choline (≈ 70%) is not accounted for by the phosphorylated cholines PC and GPC. Cr was depleted in 1H MRS of fibrous histocytoma (not shown).

## Discussion and Conclusion

The individual components of the phosphomonoester (PME) and phosphodiester (PDE) resonances in 31P MRS were studied in untreated pediatric brain tumors with 31P-[1H] MRS and 1H MRS and significant abnormalities were detected and quantified. We speculate that the analysis of these metabolites *in vivo* will provide relevant and specific information regarding the molecular basis of brain tumors. Variations with tumor type may be important for grading and outcome prediction based on non-invasive tests.

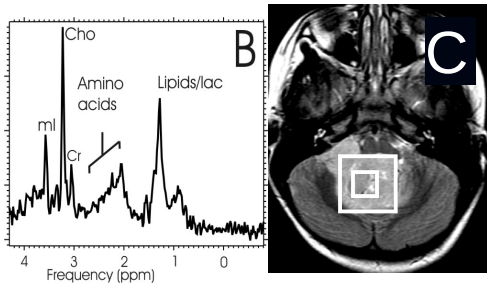



**Fig. 1:** 31P-[1H] MRS (A), 1H MRS (B), and MRI (C) of a PNET in the posterior fossa.

**References**

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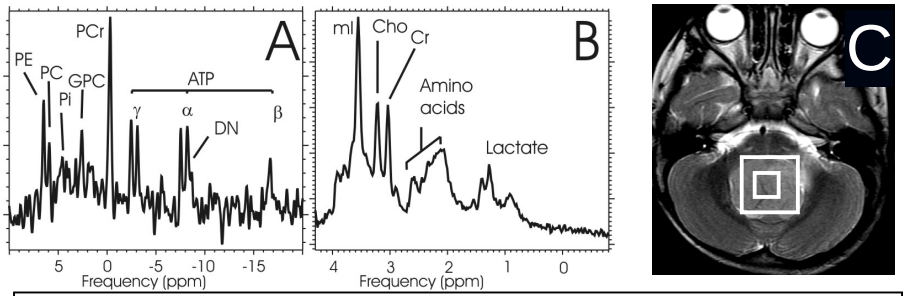


**Fig. 2:** 31P-[1H] MRS (A), 1H MRS (B), and MRI (C) of an ependymoma (C).

**Peak ratios of phosphorylated metabolites**

| | Tumor (n=5) | Control (n=5) |
|---|---|---|
| PE/ATP | 0.69±0.27 | 1.15±0.35 |
| PC/ATP | 0.35±0.10 | 0.33±0.07 |
| GPE/ATP | 0.21±0.15* | 0.56±0.22 |
| GPC/ATP | 0.34±0.14** | 0.78±0.15 |
| PCr/ATP | 1.25±0.25*** | 2.22±0.23 |
| Pi/ATP | 0.36±0.19 | 0.53±0.16 |
| PCr/Pi | 4.23±1.97 | 4.34±0.78 |
| pH | 7.06±0.04 | 7.03±0.04 |

*p<0.05, **p<0.01, ***p<0.001