

In vivo absolute quantification for mouse brain tumor using an inductively coupled synthetic signal injection method

Donghoon Lee¹, Kenneth Marro¹, Mark Mathis¹, Eric Shankland¹, Cecil Hayes¹, Stacey Hansen², and James Olson²

¹Department of Radiology, University of Washington, Seattle, WA, United States, ²Fred Hutchinson Cancer Research Center, Seattle, WA, United States

Introduction

Medulloblastoma (MB) is the most common pediatric brain tumor. Five year survival rate for children younger than 3 years is in the range of 40 % with current therapy. Prognosis following relapse is so poor that the 5-year survival remains less than 10 %. For preclinical applications, the transgenic Smo mouse model, over-expressing Smoothed receptor in granule cell precursors, has been recognized as a highly effective brain tumor model that resembles human MB. MRI and MRS have been used as key methodologies for clinical brain tumor diagnosis due to their noninvasiveness and good spatial resolution. However, with respect to brain tumors, MRI and MRS have been largely limited to qualitatively detecting symptomatic regions for diagnosis and treatment follow-ups. In this study we used a noninvasive and quantitative MRS method to determine concentrations of ³¹P metabolites for mouse brain tumor in vivo. We used our MR absolute quantification method that injects an inductively coupled pseudo-signal during acquisition of real signal [1-3]. To improve the signal-to-noise ratio, we developed a dual tuned ¹H/³¹P mouse brain probe with an injection coil incorporated for MRI/MRS measurements.

Methods

MRI/MRS data were acquired for normal and Smo mice on a Bruker 4.7 T horizontal bore magnet equipped with a Varian INOVA spectrometer using a dual tuned ¹H/³¹P half volume coil optimized for mouse brain (Fig.1). The probe included an injector to introduce pseudo signals simultaneously with the real signals arising from the tissue. A half volume coil provides high signal sensitivity with a homogeneous region just large enough to cover a mouse brain. Localized ³¹P spectra were acquired using the ISIS (Image-selected *in vivo* spectroscopy) sequence to quantify metabolite contents in 8 μ L volumes (TR= 1.5 s, sweep width = 5 kHz, number of points = 8 k, number of averages = 64 and total acquisition time = 16 min). Calibration measurements were conducted on a phantom containing inorganic phosphate (50 mM) and sodium tripolyphosphate (15 mM).

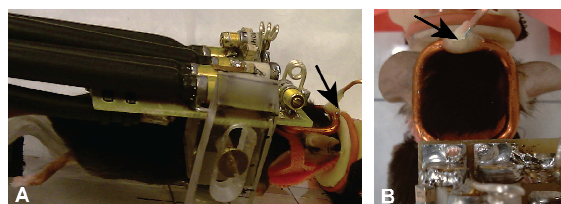


Figure 1. Mouse brain coil in a half volume type for absolute quantification. The brain coil covers the entire mouse head to provide enough RF homogeneity for the brain with high sensitivity. An injector coil was securely mounted on the coil conductor for signal injection.

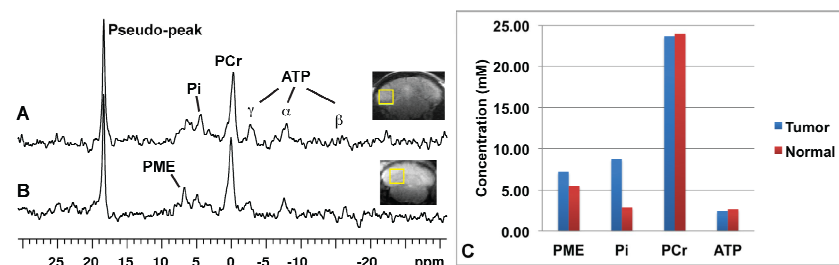


Figure 2. Top and bottom spectra are corresponding to ³¹P ISIS responses obtained at 4.7 T from 2 x 2 x 2 mm³ (or 8 μ L) voxels (yellow squares) localized on tumor (A) and a cerebellum (B) for a Smo mouse and normal mouse, respectively. (C) ³¹P metabolites (in mM) for both Smo and normal mice were quantified based on the synthetic signal injection method.

Results and Discussion

The dual tuned probe allowed ¹H and ³¹P MRI/MRS without changing RF coils and repositioning the animals. Figure 2 shows two localized ³¹P MR spectra (volume elements in yellow squares) localized on a tumor of a Smo mouse and the cerebellum of a normal mouse. Concentrations, in mM, of various ³¹P metabolites are shown in Figure 2C. These results demonstrate that our MR quantification method can be applied to accurately quantify ³¹P metabolites in localized brain regions and may provide noninvasive biomarkers to monitor tumor progression and treatment responses.

Conclusions

We described an absolute quantification approach adapted for metabolite quantification of mouse brain tumor using synthetic signal injection and an optimized dual tuned ¹H/³¹P RF coil. This approach allows reliable ³¹P metabolite determination in mouse brain.

References

1. K. Marro, D. Lee et al. Synthetic signal injection using inductive coupling. *J Magn Reson* **194**, 67-75 (2008).
2. D. Lee, K. Marro et al. Quantitative ¹⁹F imaging using inductive coupled reference signal injection. *Magn Reson Med* **63**, 570-573 (2010).
3. K. Marro, D. Lee et al. Quantitative in vivo magnetic resonance spectroscopy using synthetic signal injection. *PLoS One*, in press.

Acknowledgements

This work was supported by NIH R21EB008166 and R21EB009438.