Quantitation of Human Hepatic Tumors In Vivo by Phantom Replacement Method of Proton MR Spectroscopy at 3 Tesla

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Synopsis: Quantification of choline-containing compounds in herpatic tumors using ^{1}H MRS technique is of great interest since such compounds have been linked to malignancy. In this study, we demonstrate a practical external phantom replacement method for absolute quantification of hepatic metabolites at 3 T using a body coil. In phantom studies, results showed good accuracy compared with the known concentrations. In normal brain studies, after corrections for coil loading and T_1 and T_2 effects, results showed good consistency with those published before. This technique was further applied to two patients with hepatocellular carcinoma (HCC) to demonstrate the feasibility of this technique.

Introduction: Several studies have indicated that in vivo ^{1}H MR spectroscopy can be utilized for the differentiation of benign and malignant lesion based on the quantitative measurement of the signal intensity detected from choline-related compounds[1-3]. However, quantification of choline-related compounds by ratio method using an internal standard is difficult, since the background of liver tissue is highly variable[4]. Conventional phantom replacement method, however, is not directly applicable for clinical diagnostics based on the current practice in many clinical sites due to the complicated procedures. The aim of this study is to establish a practical external phantom replacement method for absolute quantification of metabolites observed in ^{1}H MR in vivo spectra of liver tumors by using a body coil.

Material and Methods: The experiments were performed on a GE Signa 3.0 T whole-body system equipped with the standard ^{1}H MR spectroscopy acquisition software. The body coil was used for both imaging and spectroscopy. The spectroscopic data data were processed by MR spectroscopy analysis package provided by the manufacturer (SAGE 7.1). The raw data was zero filled once, apodized with a 5 Hz Gaussian filter, Fourier transfer, phase correction and baseline correction. Marquatt curve fitting with Gaussian line shape were used to calculate the area under the peak. A standard spectroscopy phantom provided by GE Medical Systems (25 cm in diameter) was used for a regular system stability check and also served as the concentration calibration phantom in the quantification procedures. This phantom contains 3.0 mM of Choline chloride and other compounds. Choline chloride inside the standard phantom was selected as the reference compound since the choline metabolite (at 3.2 ppm) is the most important marker of tumors. Coil performance including long-term system stability, spatial sensitivity homogeneity, signal linearity with VOI size, and coil loading effect were tested. To test the calibration strategy, the data were collected about once per month from the standard phantom to check if the strategy for concentration measurement is appropriate in the long run. Five volunteers were studied on the brain in order to check the accuracy of this technique. A VOI containing primarily white matter was then selected in parietal lobe of the brain. T_1 and T_2 values were measured. In normal liver, five volunteers were studied. A VOI of 2x2x3 cm3 was placed in the right herpatic lobe with care taken to avoid the large intrahepatic vessels. No reparation gating was used during the MRS study. The quantification technique was further used in two patients. A VOI of 2x2x3 cm^3 located at solid portion of the tumor was selected with parameters of TE 30 ms, TR 1500 ms, 256 acquisition, 2500 Hz spectral width and 2048 data points. No resparation gating was used during the MRS study. We have also measure the value of saturation factor and T_2 of choline signal from HCC patients. These parameters could not be found in the literature and the measured values will provide the much more accurate in-vivo quantification than those deduced based on assumed T_1 and T_2 values.

Results & Discussion:

In phantom studies, The coefficient of variance (CV) of the detected intensity for Cho signals from the GE standard phantom were 9% within an 8-month period. Good linearity with the r^2 value near 0.98 was obtained from VOI that ranged from 3 to 64 cc. The T_1 value of Cho, Cr and NAA was determined to be 235, 489, 775, respectively, and the T_2 value of Cho, Cr and NAA was determined to be 167, 231 and 301 ms, respectively. The concentration of Cho, Cr and NAA in the standard phantom was determined to be 3.1, 9.7, and 13.9 mM, respectively(n= 11), which were consistent with the values, 3, 10, and 12.5 mM for Cho, Cr and NAA, respectively, provided by the manufacturer. In brain studies, T_1 of Cho, Cr and NAA was measured to be 1320, 1500 and 1410 ms respectively. T_2 of Cho, Cr and NAA was measured to be 348, 220 and 354 ms respectively. The concentration of Cho, Cr and NAA from white matter in the normal head a was determined to be 1.8 ± 0.4 mM, 7.2 ± 1.8 mM, and 11.9±1.8 mM, respectively. Rresults are in a good agreement with those published[5-6]. In normal livers studies, Fig. 1 shows typical spectra from the normal live. The metabolite concentrations of Cho compound in the liver of the five adults were determined to be 0.3, 0.7, 1.2, 1.8, 2.5 mM, respectively. Apparently, the intensity varied significantly among different volunteers, which could be due to many factors such as the respiration motion of each individual and would need to be carefully considered. In HCC patients studies, total cholines concentration was estimated to be 4.8 and 10.6 mM in the malignant liver leisions of two HCC patients and Fig. 2 shows the spectra obtained from one of the HCC patients. Compared to the value obtained from the healthy volunteers, these determined values from HCC patients were substantially higher. Fig 3(a). shows spectra obtained under different TE with the same TR of 1500 ms. The T_2 values were determined to be 88 ms and 148 ms from two HCC patients, respectively, with a r^2 value greater than 0.99. Fig 3(b). shows spectra obtained under TR of 1500 ms and 8000 ms, respectively. The saturation factors were estimated to be 1.76 and 1.91, respectively.

Conclusions: We have demonstrated the feasibility of MRI-directed localized ^{1}H MRS of choline compound in vivo in the liver of human subjects. By frequently ensure the stability of the MR system, take advantage of the good sensitivity homogeneity of the body coil, and using an external water bottle to correct the coil loading effect, an appropriate and easy to perform quantification procedure can be established in the routine clinical MRS study. Our approach may permit one to obtain molar concentrations of choline compound in herpatic cancers and the surrounding liver.

Reference

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Fig. 1. Example of *in vivo* liver choline compound concentrations study in a normal volunteer.
Fig. 2. Example of *in vivo* liver choline compound concentrations study in an HCC patient.
Fig. 3. Example of the measurement of the T_2 and saturation factor of coline compound signal from herpatic tumor in one of the patient. (a). spectra under TE of 30 ms, 90 ms, 150 ms, and 300 ms with the same TR of 1500 ms. (b). spectra under TR of 1500 ms and 8000 ms with the same TE of 30 ms from one of the patient.

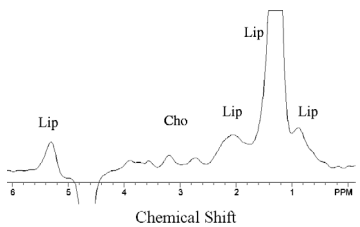

Fig. 1

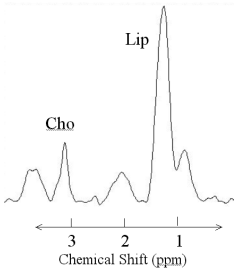

Fig. 2.

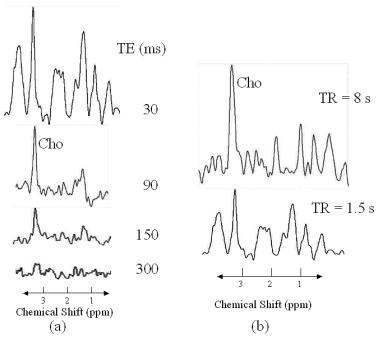

Fig. 3.