Quantitative Assessment of Amide Proton Transfer (APT) and Nuclear Overhauser Enhancement (NOE) Imaging with Extrapolated Semi-solid Magnetization Transfer Reference (EMR) Signals - an Accurate and Straightforward Measurement Approach

Hye-Young Heo[1], Yi Zhang[1], Shanshan Jiang[1], Dong-Hoon Lee[1], and Jinyuan Zhou[1]
[1]*Russell H Morgan Department of Radiology and Radiological Science, Johns Hopkins University, Baltimore, Maryland, United States*

Target audience: Basic scientists and clinical scientists who are interested in the development of APT and CEST imaging technology.

Introduction

CEST imaging is an important molecular MRI technique that allows detection of endogenous, low-concentration biomolecules in tissue. Although promising in terms of the feasibility and potential clinical values, the quantitative explanation of many results in detecting proteins, amino acids, and metabolites, as well as pH changes is still highly controversial in the literature[1,2].In addition to the magnetization transfer ratio (MTR) asymmetry analysis, several alternative quantitative image analysis methods, such as the three-offset method[3] and multiple Lorentzian shape fitting[4,5], have been introduced to assess downfield APT and upfield NOE signal contributions. Here, we propose a new quantitative approach that is based on the extrapolated semi-solid MT model reference (EMR) signals for measuring pure APT and NOE signals accurately.

Methods

Eleven patients with high-grade glioma were scanned on a Philips 3T MRI scanner. CEST image data were obtained using a fat-suppressed fast spin-echo pulse sequence, using the following parameters: TR = 3 s; FOV = 212 × 190 mm^2; matrix size = 256 × 256; slice thickness = 4.4 mm; and single slice acquisition. The RF saturation used was four block RF saturation pulses (total 800 ms duration and 2 μT amplitude). The frequency sweep corresponded to a full z-spectrum with 64 frequency offsets: off (S_0 image), 0, ±0.5, ..., and 14 ppm, at an interval of 0.5 ppm.

Three possible EMR approaches (**Fig. 1**) were assessed. The first **(aEMR)** is based on the modified asymmetric MTC model (6) (assuming the chemical shift center mis-match between bulk water and semi-solid macromolecules, using two-side z-spectrum data). Alternatively, one can divide the conventional asymmetric z-spectrum into the symmetric semi-solid z-spectrum and the upfield asymmetric NOE effects of aliphatic and olefinic protons of various relatively less mobile molecules. Thus, based on a Henkelman's symmetric semi-solid MTC model (7), we have two more EMR approaches: using two-side z-spectrum data **(sEMR^2)** or one-side z-spectrum data **(sEMR^1)**. The one- or two-side data were fitted with the super-Lorentzian lineshape. Data points of small frequency offsets between 7 and -7 ppm (aEMR, sEMR^2), or between 7 and -14 ppm (sEMR^1) were excluded to avoid possible APT and NOE contributions. Based on the fitted MTC model parameters, the EMR signals (Z_{EMR}) in the offset range from +6 ~ -6 ppm were obtained, and the differences between Z_{EMR} and experimental data at 3.5 ppm and -3.5 ppm were used to calculate the APT and NOE signals (called **APT$^{\#}$ and NOE$^{\#}$**, respectively).

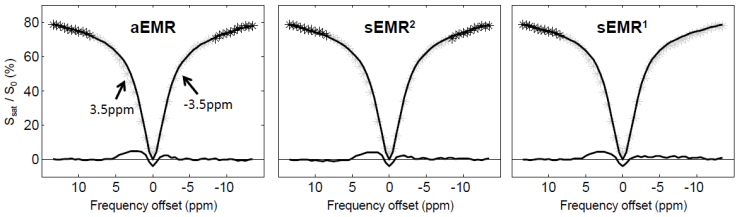

Fig. 1. Three possible EMR models. Experimental data (from the glioma, black asterisks) used for fitting the EMR curves (solid line).

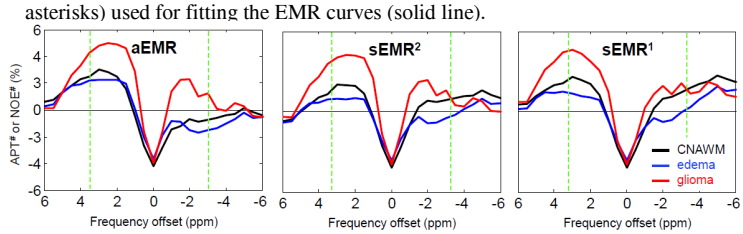

Fig. 2. Downfield CEST$^{\#}$ and upfield NOE$^{\#}$ signal features of the CNAWM, edema, and glioma obtained from the three EMR approaches.

Results and Discussion

Fig. 2 demonstrates CEST$^{\#}$ and NOE$^{\#}$ signal features obtained. The downfield CEST$^{\#}$ signals may be contributed by amide protons (APT$^{\#}$, 3.5 ppm downfield from water), amine protons (2 ppm downfield from water), and other possible sources. The upfield NOE$^{\#}$ signals may be contributed by mobile biomolecules (T_2 ~ 10 ms), and, for sEMR^1 and sEMR^2, some less mobile biomolecules (T_2 ~ 0.1-1 ms; namely, between semi-solid and mobile).

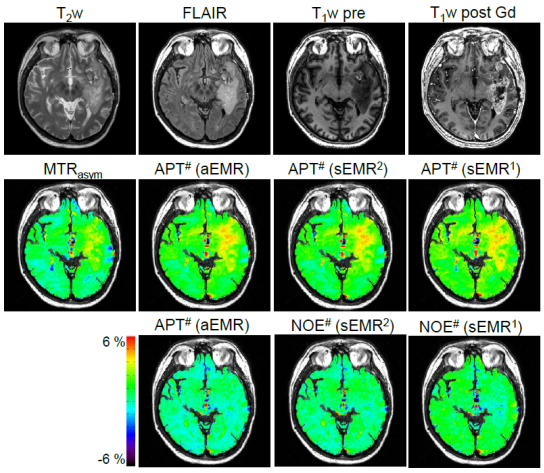

Fig. 3. Conventional MR images and MTR$_{asym}$(3.5ppm), APT$^{\#}$, and NOE$^{\#}$ maps for a patient with GBM obtained from the three EMR approaches.

The APT$^{\#}$ signals of the glioma were significantly higher than those of the edema and CNAWM for all EMR models. However, the NOE$^{\#}$ signals were slightly lower in the edema relative to the glioma and CNAWM, but the differences were small among them. In the aEMR approach, the chemical shift centers were found to be at 1.4, 1.2, and 0.5 ppm upfield from the water signal for CNAWM, edema, and glioma, respectively, at which the NOE$^{\#}$ quantification were problematical. It seemed that sEMR^1 (using the data points of 14-7 ppm only) that excluded most APT and NOE contributions would be the best choice.

Fig. 3 shows MTR$_{asym}$(3.5ppm), APT$^{\#}$, and NOE$^{\#}$ maps for a patient with GBM. As reported before (8), the Gd-enhancing area (tumor core) on the post-Gd T_1-weighted image was hyperintense on the MTR$_{asym}$(3.5ppm) and APT$^{\#}$ maps, but the glioma was seemingly isointense on the NOE$^{\#}$ maps. Therefore, the APT effect was the major contributor to the APT-weighted image contrast (based on MT asymmetry analysis) between the tumor and the normal brain tissue.

Conclusions

Our EMR provides a relatively accurate approach for quantitatively measuring pure APT and NOE signals. The quantitative results would provide some insight into the origin of the APT-w eighted image contrast in malignant gliomas.

References

(1) Xu J et al. NMRB 2014; (2) Scheidegger R et al. NeuroImage 2014; (3) Jin T et al. MRM 2013; (4) Zaiss M et al. JMR 2011; (5) Desmond KL et al. MRM 2014; (6) Hua J et al. MRM 2007; (7) Henkelman RM et al. MRM 1993. (8) Zhou et al. JMRI 2013.