NAAG Detection in the Human Brain by Wiener Filtering and TE Optimization at 7T

Li An[1], Shizhe Li[1], Emily T Wood[2,3], Daniel S Reich[2,3], and Jun Shen[1]

[1]*National Institute of Mental Health, National Institutes of Health, Bethesda, MD, United States,* [2]*NeuroImmunology Branch (NINDS), National Institutes of Health, Bethesda, MD, United States,* [3]*Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, United States*

Target audience: Physicists and clinicians who are interested in brain magnetic resonance spectroscopy (MRS).

Purpose: N-acetyl-aspartyl-glutamate (NAAG), a dipeptide neurotransmitter, is often measured by LCModel fitting of short echo-time (TE) PRESS (point-resolved spectroscopy) spectra. The accuracy and precision of NAAG measurements are often limited because the NAAG singlet at 2.05 ppm overlaps with the n-acetyl-aspartate (NAA) singlet at 2.01 ppm and the NAAG multiplet at 2.19 ppm is buried by other signals. In this work, we optimize the TEs of the PRESS sequence to improve NAAG detection at 7T. In addition, we develop a water reference deconvolution algorithm to enhance spectral resolution by reducing lineshape distortions due to B_0 inhomogeneities and residual eddy currents.

Methods:

TE optimization: Density matrix simulations, programmed using the GAMMA C++ library, were conducted to optimize TE_1 and TE_2 of a PRESS sequence for the detection of NAAG at 7T. It was found that TE_1 = 26 ms and TE_2 = 72 ms generate optimal NAAG signal. At these TEs, the multiplet of NAAG glutamate moiety at 2.19 ppm becomes a well defined positive peak, which benefits NAAG quantification. Meanwhile, the C4 proton multiplet of Glu at 2.35 ppm is a narrow peak with high amplitude. In addition, the C3 proton multiplet signals of Glu between 1.95 - 2.2 ppm are very small, thus minimizing interference to the detection of NAAG signals. The effects of other low concentration metabolites (e.g. glutamine, glutathione, and γ-Aminobutyric acid) on NAAG quantification are negligible at this set of TEs.

Water reference deconvolution: Wiener filtering can be incorporated into QUALITY (Quantification Improvement by Converting Lineshapes to the Lorentzian Type) [1] for water reference lineshape correction [2,3]. The corrected free decay induction (FID) signal FID'(t) is given by: $FID'(t) = FID(t)\, W(t)^* S(t) / (|W(t)|^2 S(t) + \sigma^2)$, where FID(t) is the FID before deconvolution; W(t) is the water reference signal divided by the T_2 decay curve of water; $W(t)^*$ is the complex conjugate of W(t); σ^2 is the noise variance in FID(t); S(t) is the mean squared magnitude of the ideal distortion-free signal, which needs to be estimated. The original Wiener filtering method uses $|W(t)|^2$ as S(t). To minimize errors in NAA and NAAG measurements, we propose to use the squared magnitude of the ideal T_2 decay curve as the ideal signal: $S(t) = [2\, Area_{NAA} \exp(-t/T_{2NAA})]^2$, where $Area_{NAA}$ is the area of the NAA peak in the spectrum reconstructed from the uncorrected signal FID(t) and T_{2NAA} is the estimated T_2 value of NAA. A factor of 2 was multiplied to $Area_{NAA}$ according to ref. [4].

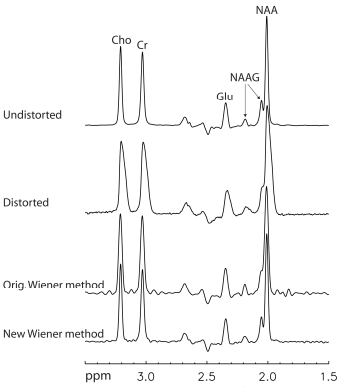

Fig. 1. Comparison of spectral resolution of the original and new Wiener filtering method using simulated data.

Monte Carlo simulations were performed to compare the performances of the original and the new method. The density matrix simulated FIDs of NAA, NAAG, Glu, creatine (Cr), and choline (Cho) were multiplied by trial concentration values and T_2 decay curves to generate the ideal FID. The trial concentration values for NAA, NAAG, Glu, Cr, and Cho were 13, 2.6, 10, 10, and 3, respectively. The trial T_2 value of NAA was set to 130 ms according to the literature [5]. This ideal FID is distorted by 3-dimensional linear and quadratic B_0 inhomogeneities and added with random noise to simulate a realistic metabolite FID. The water reference signal was also generated with the same B_0 inhomogeneities. The FID was lineshape corrected using the two different methods. To test the new method for tolerance to T_{2NAA} estimation error, T_{2NAA} values of 100 ms and 160 ms, along with the trial value of 130 ms, were used to compute S(t). The reconstructed spectra were fitted by a linear combination of the basis spectra of NAA, NAAG, Glu, Cr, and Cho to quantify the metabolite concentrations. This whole process was repeated 100 times with the same spatial B_0 inhomogeneities and same level but different realizations of random noise.

In vivo experiments: Eight normal volunteers (one woman and seven men; aged 20 - 39 years), who gave informed consent in accordance with procedures approved by local institutional review board, were scanned on a Siemens 7T scanner equipped with a 32-channel receiver head coil. The voxels were all located in the white matter of the right frontal lobe of the subjects. The PRESS sequence had TR = 2.5 s, TE_1 = 26 ms, TE_2 = 72 ms, voxel size = 2×2×2 cm^3, spectral width = 4000 Hz, number of data points = 2048, and number of averages = 128. Water suppression was accomplished using eight RF pulses which had ~350 Hz bandwidth. In addition, eight interleaved unsuppressed water acquisitions were performed, one after every 16 water-suppressed acquisitions. The 32-channel data were combined into a single FID by a generalized least square method and then lineshape corrected using the new Wiener filtering method. The NAA, NAAG, and Glu signals were quantified using a linear combination fitting program.

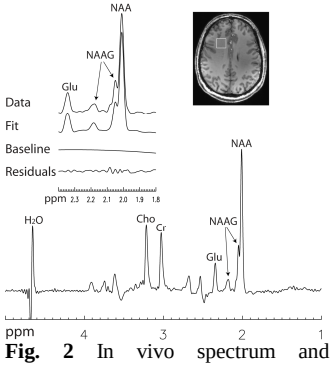

Fig. 2 In vivo spectrum and corresponding linear combination fitting results.

Results: Simulation results are shown in Fig. 1 and Table 1. The new Wiener filtering method clearly shows the NAA-NAAG singlet split and also correctly reconstructed the NAAG peak at 2.19 ppm, whereas the original Wiener filtering method generates large spectral artifacts and does not resolve the NAAG singlet. The proposed method offers significantly lower error in NAAG quantification, and is not sensitive to the T_{2NAA} value used to estimate the ideal signal. The spectrum and fitting results from one volunteer are plotted in Fig. 2. The NAA-NAAG split is clearly shown in the reconstructed spectrum. The mean value of NAAG/NAA in the eight normal volunteers is 0.22±0.04 with Cramer-Rao lower bound (CRLB) being (0.9±0.2)%. The mean value of Glu/NAA is 0.55±0.04 with CRLB being (1.2±0.1)%.

Discussion and Conclusion: Simulation results demonstrate that the new Wiener filtering method offers higher spectral resolution, smaller spectral artifacts, and higher accuracy in NAAG quantification compared to the original Wiener filtering method. The in vivo spectra results confirm that proposed TE optimized PRESS and the new Wiener filtering method lead to improved spectral resolution and accuracy in measuring NAAG.

Table 1. Simulation results of the original and new Wiener filtering method.

	NAA		NAAG		Glu	
	Mean ± SD	Error(%)	Mean ± SD	Error(%)	Mean ± SD	Error(%)
True concentration	13.0		2.6		10.0	
Original Wiener method	12.64±0.06	2.8	2.49±0.03	4.2	10.0±0.2	0.17
New Wiener (recon. T_{2NAA} = 130 ms)	12.92±0.07	0.61	2.64±0.03	1.5	10.0±0.2	0.31
New Wiener (recon. T_{2NAA} = 100 ms)	12.85±0.07	1.2	2.64±0.03	1.5	10.0±0.2	0.38
New Wiener (recon. T_{2NAA} = 160 ms)	12.95±0.06	0.38	2.64±0.04	1.5	10.0±0.2	0.24

References:

1. de Graaf AA, *et al*., MRM 1990;13:343–357.
2. Bhat H, *et al*., JMR 2006;183:110-122.
3. Dong Z, *et al*., JMRI 2009;29:1395-1405.
4. Starcuk Z, *et al*., JMR 1994;108:177-188.
5. Marjanska M, *et al*., NMR Biomed 2012;25:332-339