

# Quantitative Standardization of Volumetric Whole-Brain MR Spectroscopic Imaging

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## Introduction

MR spectroscopic imaging (MRSI) offers considerable potential for detection of alterations in tissue metabolism; however, the use of current techniques for clinical studies and multi-center trials remains limited due to variability of implementations across sites and manufactures scanners; restrictive implementations in terms of the spatial extent over which data is obtained; and relative complexity of the data analysis. To address these limitations a standardized volumetric 'whole-brain' 1H MRSI sequence has been implemented on scanners from three different manufacturers at three sites and combined with a fully automated MRSI processing procedure. Results were compared using a spectroscopic phantom and thirty aged-matched normal subjects.

**Materials and Methods:** A spin-echo volumetric MRSI acquisition was developed on 3.0 Tesla MR scanners from GE, Siemens, and Philips. Pulse shapes, sequence timing, and gradient waveforms were identically implemented. The sequence used lipid inversion-nulling, CHESS water suppression, TE/TR/TI = 70/1710/198 ms, a 135 mm slab excitation, and echo-planar readout plus 2-dimensional phase encoding, for a final sampling resolution of 50x50x18 points. The sequence also included an interleaved water MRSI acquisition with identical spatial and spectral parameters [1]. Standard manufacturer-provided B0 shimming methods and T1-weighted MRI sequences were used at all sites. MRI and MRSI data was converted to a common format and automatically processed using the MIDAS package [1,2] to map N-acetylaspartate (NAA), creatine (Cre), and choline (Cho). Processing included lineshape and B0 correction; determination of grey-matter, white-matter and CSF content at each MRSI voxel; signal normalization of individual metabolite images; and non-linear spatial registration to a reference image that was mapped to a brain atlas with eight lobar regions defined (right and left frontal, temporal, parietal, and occipital). Studies were performed 5 times at each site on an identical spectroscopic phantom and on 30 normal subjects (10 subjects at each site), aged 22 to 30 yo. The inter-site comparisons for the individual metabolite values were performed using percentage errors and one-way ANOVA test (with 5% significance level).

**Results:** Sequences were identically implemented with the exception of excitation pulses and a reduced sweep width on one instrument which were required due to maximum B1 field and sample-size limitations, respectively. Figs. 1 and 2 show the phantom and human results from all sites/scanners, respectively. The 'maximum' differences between metabolite values of the three scanners, relative to mean value, were 1.8%, 1.7%, and 3.6% for Cho, Cre, and NAA, respectively (Fig. 1). Lobar metabolite values were statistically equivalent (ANOVA  $p$ -values > 0.11) between all instruments and sites' normal groups, except in the temporal lobe due to differences in shimming quality. Fig. 3 shows typical metabolite images for NAA. Lack of support for DICOM standard for SI raw data necessitated development of custom software to read data from GE and Philips scanners and to define sequence parameters. Metabolite images and spectral quality were comparable from all instruments, although SNR varied due to differences in RF detection coils.

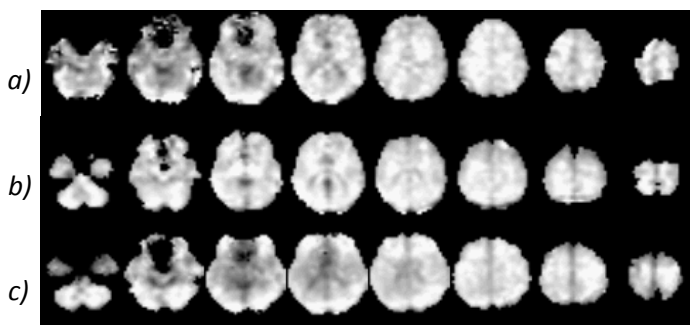


Fig 3: Representative NAA images obtained on a) GE, b) Siemens, and c) Philips scanners.

**Discussion:** This development indicates that volumetric MRSI acquisition can be implemented in a consistent and comparable manner across different scanners, and with standard setup procedures heralding quantitative MRSI comparisons for multi-center studies. The MRSI processing was done remotely from the scanner, but implemented in a fully automated manner following manual initiation of the data transfer. Key factors of this implementation include identical acquisition parameters and processing pipelines, and the use of signal normalization that enables direct comparison of individual metabolite values across instruments and subjects. Further developments will utilize a normative brain metabolite database for analysis of metabolite images from individual subjects for clinical studies [3]. A higher-quality shimming procedure can also enhance the multi-site quantitative standardization.

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**References:** [1] Maudsley AA *et al*, MRM 2009; 61:548–559. [2] Maudsley AA *et al*, NMR Biomed 2006;19:492–503. [3] Govind V *et al*, J Neurotrauma; 2010: 27:483–496.

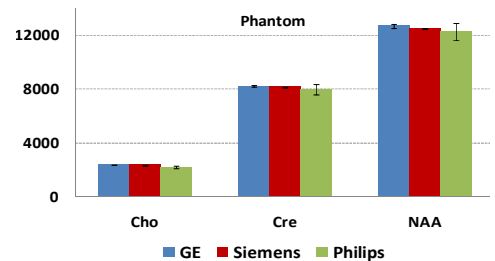


Fig. 1: Means and standard deviations of individual metabolites obtained from a spectroscopic phantom scanned on GE, Siemens, and Philips scanners.

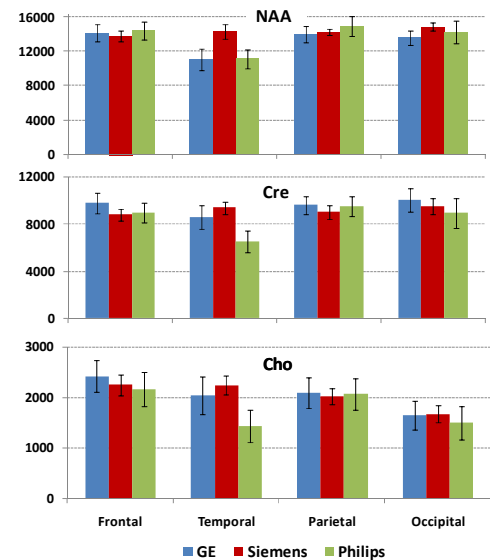


Fig. 2: Mean and standard deviation values (in institutional unit) of individual metabolites at the atlas-defined brain lobes obtained from 30 normal subjects (age 22-30 yo) on GE, Siemens, and Philips scanners. Statistically significant difference ( $p$ -value < 0.05) is only seen at the temporal lobe. For simplicity, only right hemisphere results are shown.