Volumetric MR Spectroscopic Imaging with Reduced k-Space Acquisitions: Variability and Pathologic Detectability in Mild Traumatic Brain Injuries

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Introduction: Several parallel imaging (PI) techniques have been developed for MR spectroscopic imaging (MRSI) (*e.g.*,[1-4]) to reduce data acquisition times in clinical settings. Unlike MRI, MRSI methods are often sensitivity-limited, and only a few reports (mainly, in patients with brain tumors) [5] have studied the resultant impact that PI may have when applied to MRSI on the outcome of diagnostic accuracy. However, for these studies the relative performance of the PI variants remained well within that required for the target pathologies, where large alterations of the brain metabolites can occur, and the moderate spatial resolutions used for which good SNR values could still be obtained. It therefore remains unknown whether the clinical diagnostic value is maintained for PI-enabled MRSI to detect subtle pathologies? We address this question by implementing a GRAPPA-MRSI method within a fully-automated MRSI data processing pipeline and evaluating it using studies of subjects with mild traumatic brain injury (mTBI) that represents a patient group for which the metabolic changes are relatively diffuse and frequently can only be determined using quantitative assessments [6].

Materials and Methods: Twenty-five mTBI subjects (Glasgow Coma Score of 13 to 15) were selected from an existing group of subjects. Details of the subject enrollment criteria are described in a previous report [6]. Additional studies were carried out on 25 age-matched control subjects. All subjects provided signed written consent before participation. A spin-echo volumetric 'whole-brain' echo-planer spectroscopic imaging (EPSI) acquisition was developed on 3.0 T Siemens Trio scanner that used lipid inversion-nulling, CHESS water suppression, TE/TR/TI = 70/1710/198 ms, a 135 mm slab excitation, with a final k-space sampling resolution of 50x50x18 spatial and 1000 spectral points. The sequence also included an interleaved water MRSI acquisition with identical spatial and spectral parameters [7]. A T1-weighted MRI (MPRAGE; TE/TR= 4.43/2150 ms, 160 slices, 1-mm slice thickness, FOV: 256x256mm^2) was also collected. A reduced k-space acquisition was simulated on the fully sampled 3D EPSI raw data obtained from all 50 subjects by acquiring only 32 phase-encoding lines (with a subsampling factor of 2 and 7 ACS lines) reducing the total scan time to ~ 16 min. A low-resolution central k-space MRSI - with same scan time as GRAPPA - was also evaluated for comparisons. A spectral phase corrected GRAPPA-EPSI reconstruction algorithm [2] was implemented as part of the fully-automated MIDAS MRSI data processing package [8] that also converted MRI and MRSI data to a common format to map N-acetylaspartate (NAA), creatine (Cre), and choline (Cho). Processing included lineshape and B0 correction; determination of GM, WM, 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 nine lobar regions (right and left frontal, temporal, parietal, and occipital; and cerebellum). The fully sampled 3D EPSI data were reconstructed and used as a gold standard. The metabolite values were compared between groups and reconstruction methods using linear regressions and a two-way analysis of variance (ANOVA) (factors: method and group; with 5% significance level) on Cho, NAA, and Cho/NAA. The specificity, sensitivity, and diagnostic accuracy were calculated and compared against the gold standard.

Results: Fig 1 shows representative GRAPPA and full k-space spectra from a 22-yo male mTBI subject (initial GCS score of 13, scanned 53 days after injury) both demonstrating similar altered NAA and Cho concentrations compare to a normal subject. Fig 2 illustrates the regression results analyses of the mean metabolites at all brain lobes for the mTBI group. GRAPPA and the gold standard yielded strong correlation coefficients (R^2's > 0.924) for the normal subjects and for the mTBI group (R^2's shown in Fig 2a) demonstrating a small variability induced by the GRAPPA method. The variability of the central k-space was noticeably larger than GRAPPA (see Fig 2b). Table 1 lists spectral quality measures for each method and group with no significant difference in fitted volume between all three methods. The mean metabolites concentrations obtained from the WM of a representative lobe (the parietal) are also listed in Table 1 together with the mean SNR values calculated from all voxels at a middle slice of the NAA maps. Both acquired GRAPPA and central k-space results yielded metabolite values similar to those of the gold standard dataset (*p*-values>0.20). The ANOVA results in 54 segments (2 tissue types (GM/WM) x 9 brain regions x 3 metabolites and ratio) indicated: i) non-significant differences between the three methods in 23 segments; ii) significant differences between the control group and the mTBI group in 16 segments; iii) only 5 significant interactions between method used and the specific group under investigation. Compared to the gold standard findings [6], a sensitivity of 88.23% and 88.23%, specificity of 95% and 91.9%, and accuracy of 92.6% and 90.7% were obtained for the GRAPPA and the central k-space reconstruction, respectively.

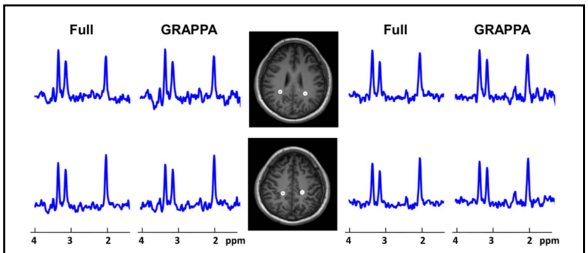

Fig 1: Sample spectra from GRAPPA and full k-space EPSI in a mTBI patient at four voxels labeled on MRI.

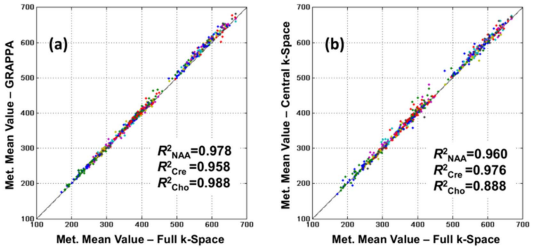

Fig 2: Mean metabolites concentrations in institutional unit from the nine atlas-registered brain lobes of all mTBI subjects from (a) GRAPPA-EPSI and (b) central k-space plotted against those obtained with fully k-space EPSI.

Conclusions: Although the reduced encoding method is associated with lower SNR that impact the quality of spectral analysis, the use of PI method can lead to robust and similar results in terms of MRSI quantitation, spectral fitting, and diagnostic accuracy with that of fully sampled data when using the sensitivity-limited volumetric MRSI. Additional improvements can potentially be obtained by using a receive coil with a higher number of elements and/or MRSI acquisitions with shorter echo times [3,4] that would enable the 3D EPSI GRAPPA acquisition to be further sped up.

Table 1: Spectral quality in terms of fitted volume, mean metabolite concentrations, averaged over all voxels of WM tissue in parietal lobe, and SNR for full k-space, GRAPPA, and central k-space EPSI data.

Data	Acquisition	Fitted Volume (%)	NAA	Cre	Cho	SNR
Normal	*Full k-space*	71.7+2.35	585±35.6	338±23.9	97±9.6	20.0±2.39
(n=25, age=27.7±3.2)	*GRAPPA*	69.1+2.44	591±35.2	343±23.6	99±9.0	14.7±2.08
	Central k-space	68.6+2.46	589±37.1	342±24.2	98±9.6	19.0±2.74
mTBI	*Full k-space*	64.3+3.35	577±42.5	357±26.4	110±11.1	18.7±1.48
(n=25, age=25.8±4.2)	*GRAPPA*	65.5+2.63	585±39.4	360±28.1	111±11.7	15.1±1.39
	Central k-space	65.6+2.36	584±39.6	359±25.7	110±11.0	18.5±1.71

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