Towards Robust Reproducibility Study for MRSI via Fully Automated Reproducible Imaging Positioning

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Introduction: In vivo MR spectroscopic imaging (MRSI) is a noninvasive tool for measuring spatial variations in tissue metabolite levels. With increasing use for clinical research studies, it is critical to have robust and reproducible methodology for acquiring and analyzing such data. A key factor that influences the ability to obtain comparable results for repeat examinations and across populations is the current manual positioning of the region used to obtain the data. Another limitation is that few studies have presented results in a standard template space, which makes it difficult to generalize and compare between them. One approach to addressing these concerns is to use an atlas-based automated positioning technique[1]. The purpose of the current study was to examine the repeatability of predefining both the imaging volume and fat saturation bands on a standard image atlas, and automatically transforming the prescription to individual subject space.

Methods and Subjects: *Positioning on atlas* The MNI152-1mm standard-space average structural T1-weighted image was used as the atlas, on which a target PRESS box and 16 fat saturation bands were prescribed (Fig.1a). The PRESS box had a size of 8 (RL)×10(AP)×5(SI) cm^3, which covers most of the deep gray matter structures. *Image registration* The atlas image was linearly registered to the T1 image of the subject during the imaging using FSL FLIRT with 12 degrees of freedom. To accelerate the computation, both images were downsampled to an isotropic resolution of 2mm, and no skull stripping or T1 image intensity correction was performed. Following a similar process to that described in (1), the output transformation matrix was applied to the normal vectors of PRESS box and saturation bands to generate their locations in the subject imaging space. The entire process was performed on the scanner console within 1 minute. *MR Imaging* Data acquisition used a GE 3T scanner with a 32-channel head coil. An axial 3D IR-SPGR T1 image was acquired using TE/TR of 2.5/7ms and a resolution of 0.5×0.5×1.5mm. EPSI flyback 3D multi-voxel MRSI with PRESS volume selection was performed using a TE/TR of 80/1800ms, 16×16×16 phase encodings, an isotropic nominal resolution of $1cm^3$, and a total acquisition time of 7.8mins. A shorter TE than usual long-echo time was used to boost SNR in lower regions of brain. The MRSI sequence was tailored to accept parameters generated after the registration, including size, center and rotation angles of both the PRESS box and saturation bands[2]. An overpress factor of 1.2 was used to reduce chemical shift artifacts[3]. *Subjects* Eight healthy volunteers were scanned twice in separate sessions that were a week apart to study the reproducibility of the results obtained. While the T1 image was acquired once in each session for registration, the MRSI scan was repeated twice without repositioning to look at its intra-scan variation. *Data analysis* The MRSI and metabolite peak ratios were reconstructed and quantified as previously proposed method[4]. The reproducibility of the automated positioning was assessed by measuring the percentage of PRESS box volume overlap between scans. This was done by rigidly registering the follow-up high resolution T1 image to its baseline counterpart, and sampling at 0.1mm intervals inside the baseline box to determine how many of samples also lay in the follow-up box[5]. The reproducibility of the ratios of NAA/Cre, Cho/Cre and NAA/Cho was measured by the coefficient of variance (CoV = standard deviation/mean). CoVs of the ratios were calculated for each voxel and then averaged for each subject. To exclude regions with low signal to noise ratio, only voxels with Cho/Cre>0 for all 4 scans were included. The test-retest reliability was evaluated for intra-scan and inter-scan (between the very first scans from both scan sessions) by the intra-class correlation coefficient (ICC) based upon a two-way mixed model that treats voxels as a random factor.

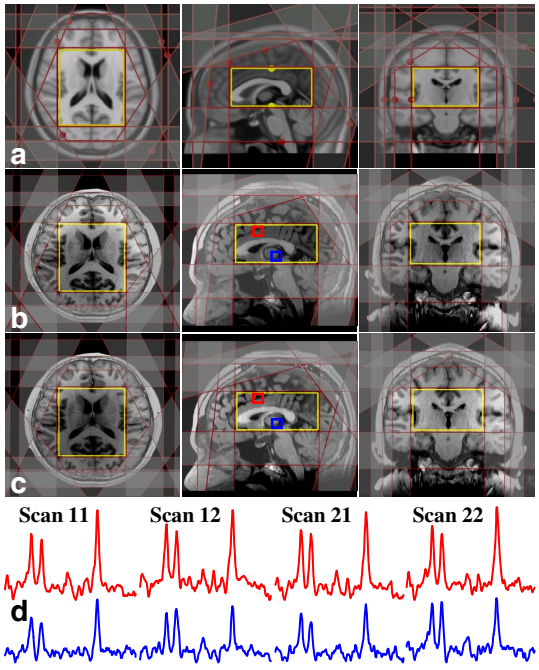

Fig 1. (a) The MNI atlas images with predefined PRESS box and 16 fat saturation bands. (b&c) Transformed boxes and saturation bands overlaid on T1 images from the baseline (b) and follow-up scans (c) of a subject, where both T1 images were realigned to the box axis. (d) The spectra in the red and blue voxels in b&c from all scans.

Results: The average percent of PRESS box overlap between follow-up and baseline scans was 98.1%±0.5%, with a range of 97.3%~98.5%. The average box size shift between the scans was no larger than 0.5mm in all 3 imaging planes. Fig.1(b&c) shows the positioning of box and saturation bands for a subject in two serial scans. Visually, it is hard to discern the difference in the locations of both box and saturation bands. Spectra in two voxels from all scans of the subject are also shown in the figure with no significant difference from one scan to the others. On average 90% of the voxels in the box were included in the analysis of CoV and ICC. The group averages of the mean inter-scan CoV from 8 subjects were 0.10±0.01, 0.11±0.01, and 0.12±0.01 for NAA/Cre, NAA/Cho, and Cho/Cre, respectively (Fig.2). Paired t-tests showed no significant difference in CoVs for inter-scan and intra-scan comparisons (p>0.13). For voxels in the most superior slice, the CoVs were below 0.10 for all ratios. The values for the most inferior slice were larger but no more than 0.15. The average ICC between inter-scans was 0.74±0.05, 0.78±0.04 and 0.66+0.09 for NAA/Cre, NAA/Cho and Cho/Cre, respectively. Paired t-tests again showed no difference in ICC between the inter-scan and intra-scan analyses (p>0.07).

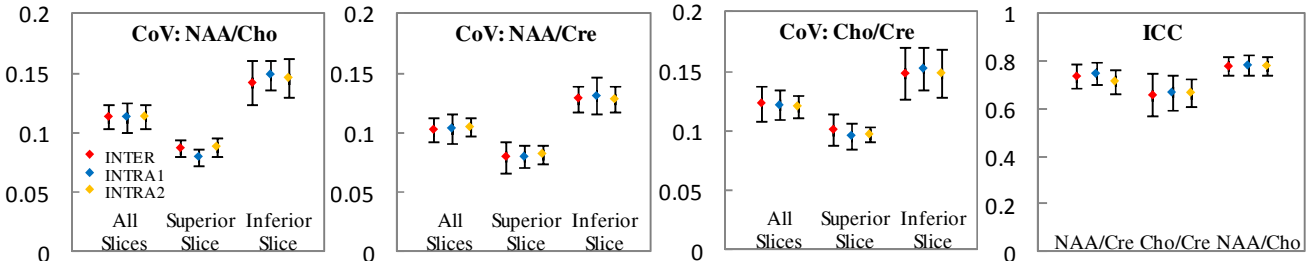

Fig 2. The CoVs and ICCs of metabolite ratios, which are represented as mean ± standard deviation

Discussion: The high percentage of PRESS box overlap and minimal size shift between serial scans indicated the excellent repeatability of the automated positioning method. The fact that no significant difference was found for the CoV or ICC in intra- and inter-scan analysis further validated its robustness. When compared to a previous automated prospective MRSI positioning approach[5], the method here achieved a higher volume overlap percentage (98% vs. 95%) and slightly lower CoV (roughly by 0.02). The CoVs were lower than the values reported for absolute metabolite concentrations in a 3D MRSI reproducibility study[6] that applied manual repositioning by roughly 0.03~0.08. Another difference was that, only 73% of total voxels were examined in the prior study, while 90% of the voxels were used here. Including voxels in lower regions of the brain, where imaging suffers from reduced coil sensitivity and poor shimming, decreased the overall reproducibility as indicated by the lower CoVs obtained for the most inferior slice compared to the most superior slice. The technique evaluated here integrates image registration and positioning (saturation bands as well as PRESS box) into a fully automated pipeline. A further advantage of this technique is its ability to compare results back to the atlas used for registration, which standardizes inter- as well as intra-subject reproducibility study. This will be the focus for future studies.

References: 1. Yung, et. al., Magn Reson Med. 2011,66:911-922; 2. Ozhinsky, et. al., Magn Reson Med. 2013,69:920-930; 3. Li, et. al., Magn Reson Imaging. 2006;24:1295-302; 4. Nelson, et. al., Magn Reson Med. 2001; 46:228–23; 5. Ratai, et. al., JMRI 2008,27:1188-1193; 6. Li, et al., MRM 2002,47:439-446.

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