Constrained Source Space Spectroscopy: Multivoxel Spectroscopy Without a Gradient Readout

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Purpose: Magnetic resonance spectroscopy (MRS) is an established, non-invasive tool that can be used to study metabolic changes in normal as well as diseased tissues. There are two main categories of voxel localization in MRS: single voxel spectroscopy (SVS) and chemical shift imaging (CSI), which measures many voxels simultaneously but has a long acquisition time. SVS offers improved signal to noise (SNR) per unit time, localization and water suppression although it can only measure one voxel at a time. The purpose of this work is to develop an intermediate MRS technique that can quickly measure the spectra from a small number of voxels simultaneously with high SNR per unit time.

Methods: A technique called constrained source space imaging (CSSI)[1] using a modified SVS sequence to excite multiple voxels and SENSE[2] reconstruction was developed for fast fMRI applications. We have refined this approach for MRS to measure the spectra from multiple voxels simultaneously. This technique, referred to as constrained source space spectroscopy (CSSSY), has all the benefits of traditional SVS. Fig 1 is the modified point resolved spectroscopy[3] (PRESS) sequence implemented on a GE MR750 3.0T. The first RF pulse is amplitude modulated by a cosine waveform to excite two voxels instead of one, and the dotted line is an optional gradient echo readout to assist in the placement of the voxels. The two voxels can be placed arbitrarily. The two spectra are then are then reconstructed using SNR optimized SENSE[2], using coil sensitivity measured from two sets of fast gradient echo readout scans (one using the head coil as receive, the other using the body coil). This technique was verified in healthy volunteers and applied to a patient with low-grade glioma *in vivo* to obtain two spectra simultaneously. One voxel was placed inside the tumor in the non-enhancing T2/FLAIR hyperintense, expansile lesion within the right cingulate gyrus, the other in homologous tissue of the contralateral hemisphere. We used AQSES[4] to quantify the metabolites N-Acetylaspartic acid (NAA), choline (Cho) and creatine (Cre), and lactate (Lac), present inside the spectra.

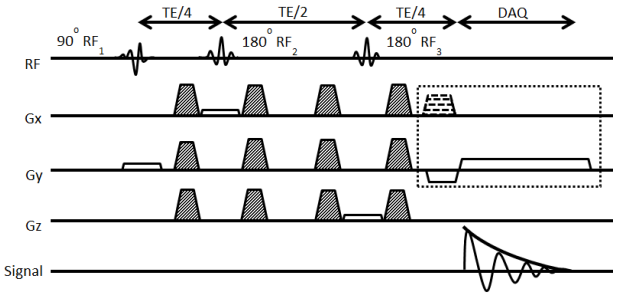

Fig 1: CSSSY pulse sequence.

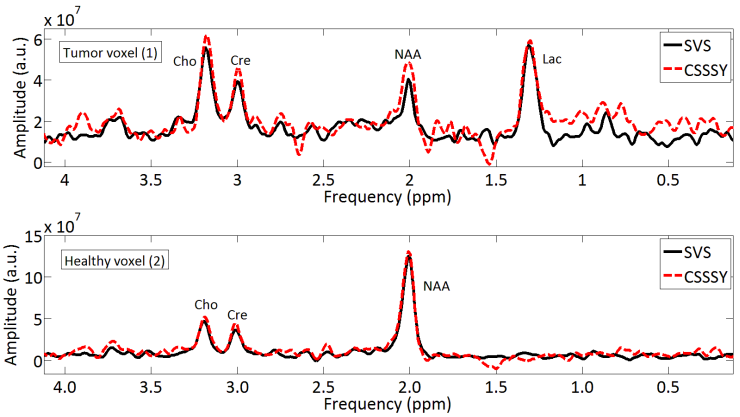

Fig 2: Two spectra obtained from both CSSSY and SVS, for comparison.

Results: Fig 2 is the two voxels spectra measured simultaneously with TR/TE = 1500/288 ms, 128 excitations (total acquisition time of about 3.5 minutes), flip angle = 63°, readout bandwidth = 2500 Hz with 1024 points, voxel size = (20 mm)^3. The spectrum was also measured using stock PRESS with identical positioning and parameters and is used as the gold standard, as it will be free from any artefacts introduced by the reconstruction, and is also plotted in Fig 2. As can be seen from the two voxels the technique produces similar spectra when compared to SVS, although some systematic non-noise discrepancies can be observed. The root mean square (RMS) value of the standardized difference[5] (SD, difference of the two curves divided by the error) for the tumor voxel and the healthy voxel was 1.05 and 1.39, respectively. Table 1 is the quantified metabolites for both spectra. Although there are some significant differences between the quantified metabolites (choline and lactate for voxel 1) the absolute differences are relatively small and the spectra are qualitatively similar. An experiment was done to measure how well the reconstruction performs as distance is varied. The two voxels were placed inside the brain of a healthy volunteer and the position of one was varied. The spectra from the stationary voxel was reconstructed and compared to the SVS spectrum. The RMSD(SD) was calculated at each position and is shown in Table 2. The RMSD(SD) is relatively close to 1 for all positions, which indicates fairly good agreeance between the two techniques, and the reconstruction tends to improve with increased voxel separation, but not in a monotonic way due to the complex dependence of the sensitivity matrix, and thus reconstruction, on position.

	NAA (a.u.)	Cho (a.u.)	Cre (a.u.)	Lac (a.u.)
Voxel 1 SVS	2.18 ± 0.15	1.38 ± 0.05	1.45 ± 0.11	3.23 ± 0.10
Voxel 1 CSSSY	2.30 ± 0.15	1.16 ± 0.05	1.64 ± 0.13	3.63 ± 0.13
Voxel 2 SVS	8.45 ± 0.13	1.01 ± 0.05	2.01 ± 0.13	N/A
Voxel 2 CSSSY	8.36 ± 0.15	1.03 ± 0.05	1.92 ± 0.13	N/A

Table 1: Metabolite quantification

Separation (mm)	20	30	40	50	60	70
RMSD(SD)	1.55	1.39	1.91	1.69	1.21	1.19

Table 2: Quantification of differences between SVS and CSSSY

Conclusions: We have shown that this technique works relatively well at extracting multiple spectra in the absence of a gradient read-out. Future improvements in the estimation of the coil sensitivity and smaller voxels should improve the overall reconstruction. We are going to continue extracting healthy and tumor tissue spectra simultaneously from low-grade glioma patients for validation. This work has potential applications in any *in vivo* spectroscopy experiment where a small (greater than one) number of regions are of interest and lengthy acquisition times of CSI are impractical.

References
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