UNSUPERVISED BRAIN TUMOR TISSUE DIFFERENTIATION BASED ON MRSI WITH CORRECTION FOR THE CHEMICAL SHIFT DISPLACEMENT ARTIFACT

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Target audience: MRS scientists and neuroradiologists with an interest in postprocessing methods and classification of brain MRSI data

Purpose: To account for the Chemical Shift Displacement (CSD) artifact in the framework of unsupervised brain tumor tissue differentiation methods based on 2D magnetic resonance spectroscopic imaging (MRSI) data. The CSD artifact is specific to the localization protocol used for selecting a certain volume of interest inside the brain. For vendor-provided point-resolved spectroscopy (PRESS) localization of MRSI on 3T clinical scanners, the CSD artifact implies that spectra corresponding to voxels within ~2cm of the borders of the selected volume are distorted, in the sense that peaks at peripheral spectral regions are (heavily) suppressed. This effect may be wrongly interpreted as lower concentration or lack of some metabolites in the outer regions of the localized volume and may also hinder the methods for unsupervised tissue differentiation (e.g., non-negative matrix factorization [1,2]). These methods can disentangle mixed tissue voxels in MRSI data acquired from brain tumors, and thus extract representative, tissue-specific spectra (called spectral sources), as well as their spatial mixing coefficients in the selected volume, as long as the spectra in the MRSI matrix can be assumed to be an approximate linear mixture of a few spectral sources. Here, we propose an approach to take the CSD artifact into account when evaluating the spatial distribution of tissue-specific spectral sources obtained from hierarchical non-negative matrix factorization [2].

Methods: ***Data***. MRSI data from glioma patients were acquired on a 3T MR scanner (Achieva, Philips, Best, the Netherlands). The MRSI protocol had the following imaging parameters: 2D PRESS, TR/TE = 2000/35ms, field of view: 16cm*16cm, volume of interest (VOI): maximally 8cm*8cm, slice thickness: 1cm, acquisition voxel size: 1cm*1cm, reconstruction voxels: 0.5cm*0.5 cm, receiver bandwidth: 2000Hz, carrier frequency of the water suppressed measurement set to 2ppm, samples: 2048, number of signal averages: 1, water suppression method: MOIST, shimming: pencil beam second order, parallel imaging with SENSE factor: left-right: 2 anterior-posterior: 1.8, 10 circular saturation bands in order to avoid lipid contamination from the skull. The acquisition time was 3 minutes, 30 seconds. ***Preprocessing***. The MRSI signals were preprocessed by the Philips system: 2D FFT from k-space to normal space, phase and eddy current correction. Further, water filtering was performed in MATLAB with HLSVD-PRO [3]. The matrix of voxels within the VOI (of maximal size 16*16) was initially cropped by removing the outer three rows and columns at each side, since in this case the inner matrix did not suffer from CSD artifacts. After Fourier transformation of the time-domain signals, the real part of the obtained spectra was truncated to the frequency region 0–4.5 ppm, the negative values were set to 0 and the obtained real-valued spectra were set as columns of a matrix X. ***Spectral sources estimation***. X is approximately factorized as the product X = WH using a hierarchical non-negative matrix factorization algorithm [2]. The k columns of W (k=2 or 3) are called spectral sources and represent the most distinct tissue-specific spectra within the considered MRSI dataset. The k rows of H encode the linear mixing weights of each spectral source for each spatial location in the cropped MRSI matrix. ***Spatial re-estimation with CSD correction***. Spatial weights for each spectral source are computed from all voxels in the non-cropped MRSI matrix as follows: a non-negative least squares (NNLS) problem is solved for each voxel, in order to express each spectrum as a linear combination of the already computed k spectral sources in W. However, the columns of W are first filtered in a location-dependent way, in order to approximate the effect of the CSD artifact at each location. To this aim, for each frequency ω in the frequency interval of interest, a simulated PRESS profile excitation image is shifted along the spatial coordinates of the MRSI volume, where the spatial shift is directly proportional to the frequency offset from ω to the carrier frequency, and then is used to compute correction factors for each voxel at each frequency offset (see Figure 1).

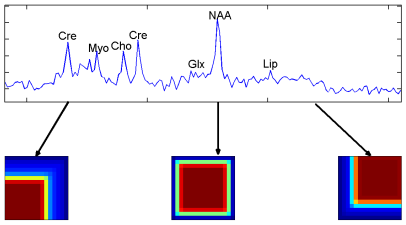

Figure 1: Schematic illustration of CSD, when carrier frequency is set on NAA. Blue spatial regions indicate suppressed spectral components, while red regions indicate full excitation.

Results: The hNMF method recovered two spectral sources for low grade glioma patients, assigned to tumor and normal tissue, while three spectral sources, also including necrosis, were computed for highest grade gliomas (see Figure 2). Unsupervised nosologic images, created by encoding the weighting matrices corresponding to each spectral source as a channel in an RGB image, exhibit black borders if CSD correction is not applied, meaning that all spectral sources have weight close to zero in those regions. This effect practically disappears when CSD correction is applied, although estimated error maps (data not shown) indicate lower reliability at voxels on the outer borders compared to inner voxels.

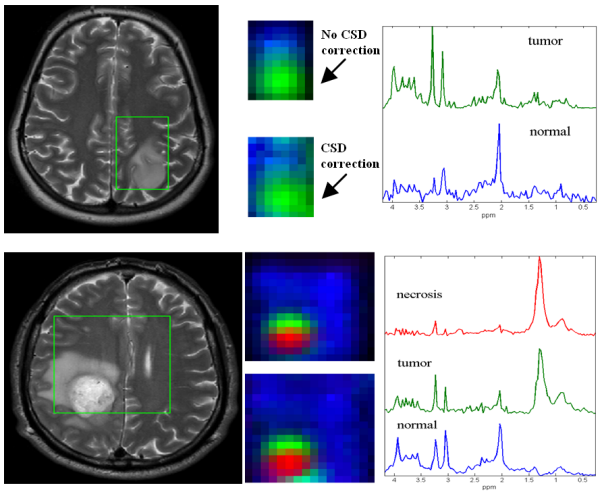

Figure 2: Illustration of unsupervised nosologic imaging without or with CSD correction on a grade II glioma patient (top) and a grade IV glioma patient (bottom).Left: T2-weighted MR image with MRSI VOI in green. Center: unsupervised nosologic images obtained without (top) or with (bottom) correction for CSD. Red, green and blue encode the contribution of the necrosis, active tumor and normal spectral sources, resp., shown on the right.

Discussion: Chemical shift displacement is an inherent drawback of the PRESS volume localization method. Other sequences have been developed, which suffer less from CSD, e.g., sequences based on semi-adiabatic pulses, but these are not yet widely distributed by all scanner vendors. Another PRESS-based approach would be to extend the PRESS volume even outside the head, such that the brain region of interest is in the central part of the grid, not affected by CSD, and to apply inner volume saturation. Still, lipid resonances from the skull might still distort inner voxels, which is not desirable since lipids are an important marker for necrosis in brain tumors. Correction methods for the CSD artifact have also been previously proposed, but were used either prior or after metabolite quantification [4,5]. CSD has typically been ignored till now in (unsupervised) classification-based methods. CSD implies that spectra corresponding to the same tissue type can look significantly different if one is located, for instance, in the middle and the other at the border of the MRSI matrix. If hNMF is applied to spectra from the whole non-cropped MRSI matrix, the computed spectral sources can reflect spectral differences pertaining to the CSD artifact instead of actual tissue type differences [2].

Conclusion: In this study, the chemical shift displacement artifact has been taken into account for re-estimating the spatial distribution of tissue-specific spectral sources extracted from glioma patients using a rapid short echo time 2D MRSI acquisition protocol based on the PRESS volume localization method. This permits recovery of tissue distribution closer to the borders of the PRESS volume.

References: [1] Su et al, *NMR Biomed* 2008, **21**:1099-1492. [2] Li Y et al, *NMR Biomed* 2012, epub ahead of print. [3] Laudadio T et al, *J Magn Reson* 2002, **157**:292-297, [4] Nelson S, *Magn Reson Med* 2001, **46**:228-239, [5] McLean M et al, *Magn Reson Med* 2000, **44**:401-411.