



Highly-accelerated quantitative 2D and 3D localized spectroscopy with linear algebraic modeling (SLAM) and sensitivity encoding



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ARTICLE INFO

Article history:

Received 5 April 2013

Revised 27 September 2013

Available online 18 October 2013

Keywords:

Localized spectroscopy

Chemical shift imaging (CSI)

SLAM

Brain

Cancer

Heart

ABSTRACT

Noninvasive magnetic resonance spectroscopy (MRS) with chemical shift imaging (CSI) provides valuable metabolic information for research and clinical studies, but is often limited by long scan times. Recently, spectroscopy with linear algebraic modeling (SLAM) was shown to provide compartment-averaged spectra resolved in one spatial dimension with many-fold reductions in scan-time. This was achieved using a small subset of the CSI phase-encoding steps from central image *k*-space that maximized the signal-to-noise ratio. Here, SLAM is extended to two- and three-dimensions (2D, 3D). In addition, SLAM is combined with sensitivity-encoded (SENSE) parallel imaging techniques, enabling the replacement of even more CSI phase-encoding steps to further accelerate scan-speed. A modified SLAM reconstruction algorithm is introduced that significantly reduces the effects of signal nonuniformity within compartments. Finally, main-field inhomogeneity corrections are provided, analogous to CSI. These methods are all tested on brain proton MRS data from a total of 24 patients with brain tumors, and in a human cardiac phosphorus 3D SLAM study at 3T. Acceleration factors of up to 120-fold versus CSI are demonstrated, including speed-up factors of 5-fold relative to already-accelerated SENSE CSI. Brain metabolites are quantified in SLAM and SENSE SLAM spectra and found to be indistinguishable from CSI measures from the same compartments. The modified reconstruction algorithm demonstrated immunity to maladjusted segmentation and errors from signal heterogeneity in brain data. In conclusion, SLAM demonstrates the potential to supplant CSI in studies requiring compartment-average spectra or large volume coverage, by dramatically reducing scan-time while providing essentially the same quantitative results.

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1. Introduction

Spatially localized magnetic resonance spectroscopy (MRS) has provided valuable insight into many normal and diseased human conditions [1–11]. Compared to single voxel MRS techniques, such as PRESS [12], STEAM [13] and ISIS [14], the standard multi-voxel chemical shift imaging (CSI) method [15] has the advantages of accessing multiple regions simultaneously with higher signal-to-noise ratio (SNR) per unit scan-time. However, the clinical application of CSI is limited by the long scan time required to apply a complete set of phase-encoded acquisitions before the individual voxel spectra can be reconstructed. In addition, due to the way that SNR adds in magnetic resonance imaging (MRI) and MRS, SNR lost

by setting the voxel size smaller than needed during acquisition, cannot be entirely restored post-acquisition [16,17].

Many methods have been proposed to speed-up CSI acquisitions. These include methods that combine spectral and spatial encoding [18,19]; and those that actually reduce the amount of image *k*-space sampled by gradient-encoding [17,20–33]. In general, the latter fall into three categories: (a) methods employing parallel imaging [20–23]; (b) those incorporating prior knowledge based on scout MRI [17,24–29]; and (c) those using compressed sensing and sparse reconstruction [30–33]. Of these, only Category (a) methods are currently in widespread use in clinical MRI/MRS scanners. Of Category (b), SLIM [24], GSLIM [25] and SLOOP [26] are strictly speaking, non-CSI methods that in theory offer superior resolution to CSI by eliminating Fourier bleeding. Indeed, this has been the focus of their *in vivo* applications to date, which have been limited to retroactively acquired CSI data [34–39]. Thus, although SLIM and SLOOP could provide faster scanning than CSI [24,26,29], to our knowledge no speed advantage has been

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demonstrated proactively *in vivo* or in humans. Category (c) methods are relatively new, and have seen even less use, perhaps reflecting the low SNR of most non-hyperpolarized MRS applications, which is not ideal for compressed sensing.

Recently, we introduced another Category (b) MRS localization method, “spectroscopy with linear algebraic modeling” or SLAM [17], wherein compartmental-average spectra are acquired using a greatly reduced CSI phase-encoding gradient set selected from central k -space where SNR is highest. The spectra are reconstructed from C compartments segmented from scout MRI, which are incorporated into the standard CSI model using an auxiliary “b” matrix [17]. SLAM was demonstrated on both retroactively and proactively acquired one-dimensional (1D) phosphorus (^{31}P) human cardiac CSI data, yielding either a 4 to 8-fold acceleration in scan-time with the same quantitative results, or a $\sim 40\%$ SNR improvement for the same scan-time, as compared to our standard protocol [2,4,5].

In the present work, SLAM is extended to two- (2D) and three dimensions (3D), and in addition, combined with parallel imaging techniques, specifically SENSE [20], to achieve dramatic speedup factors of 5–120 compared to CSI and SENSE CSI [21]. A modified SLAM reconstruction algorithm is introduced that improves accuracy by reducing the method’s sensitivity to signal inhomogeneity within compartments. Additional improvements are provided to incorporate spatial and temporal main (B_0) and RF (B_1) field inhomogeneity terms, including eddy-current correction. These advances are implemented on 2D and multi-slice proton (^1H) MRS studies of the brains of healthy subjects and patients with tumors, both retroactively and proactively. Brain compartmental average metabolite levels and ratios from CSI and SENSE CSI are determined and quantitatively compared with those from corresponding high-speed SLAM spectra. Finally, 3D SLAM is applied to ^{31}P MRS in a phantom and in human heart, with speedup factors of 100 and 7, respectively.

2. Theory

The conventional CSI [15] reconstruction can be cast as a linear equation:

$$\mathbf{s}_{M^*N} = \mathbf{PE}_{M^*M} \times \mathbf{p}_{M^*N}, \quad (1)$$

where \mathbf{s} is the known vectorized signal matrix, \mathbf{PE} is the phase-encoding operator, and \mathbf{p} is the unknown vectorized spectral matrix. For 1D CSI, \mathbf{PE} is simply a discrete Fourier transform (DFT) operator. For 2D or 3D CSI, \mathbf{PE} is the Kronecker product [40] of double or triple serial DFT operators, respectively. M is the total number of phase-encoding steps or spatial voxels, and N is the number of chemical shift domain data points.

When sensitivity encoding [20,21,41] is used, Eq. (1) is rewritten as:

$$\mathbf{s}_{M^*N} = \mathbf{E}_{M^*M} \times \mathbf{p}_{M^*N}, \quad (2)$$

where \mathbf{E} is the combined phase-encoding and sensitivity-encoding operator, and M' denotes the product of the number of coil elements, N_c , and the (reduced) number of phase-encoding steps, M_R ($=M/R$, where R as the SENSE acceleration factor). While defined in Ref. [41], \mathbf{E} can be constructed by stacking the product of \mathbf{PE} with the sensitivity encoding matrix, \mathbf{SE} , of each coil element, as

$$\mathbf{E} = \begin{bmatrix} \mathbf{PE}_{M^*M} \times \mathbf{SE}_{M^*M}^1 \\ \mathbf{PE}_{M^*M} \times \mathbf{SE}_{M^*M}^2 \\ \vdots \\ \mathbf{PE}_{M^*M} \times \mathbf{SE}_{M^*M}^{N_c} \end{bmatrix}, \quad (3)$$

where $1, 2, \dots, N_c$ index each coil element. Furthermore, as described in Ref. [41] for SNR optimization, “pre-whitening” can be done to both sides of Eq. (2) by multiplying $(\mathbf{L}^{-1} \otimes \mathbf{I})_{M^*M'}$, where $\mathbf{L}_{N_c N_c}$ is obtained from a Cholesky decomposition of the noise covariance matrix [41]; $\mathbf{I}_{M_R M_R}$ is an identity matrix; and \otimes is the Kronecker operator [40].

2.1. SLAM localization with prior knowledge

For simplicity, Eq. (2) is used throughout to represent both conventional CSI and the pre-whitened SENSE CSI reconstruction, the latter differentiated by the “SENSE” label. Introducing an auxiliary matrix, \mathbf{b} , containing the spatial information defining the C compartments segmented from MRI, results in:

$$\mathbf{s}_{M^*N} = \mathbf{E}_{M^*M} \times \mathbf{b}_{M^*M}^{-1} \times \mathbf{b}_{M^*M} \times \mathbf{p}_{M^*N}. \quad (4)$$

As described in Ref. [17], \mathbf{b} is composed by adding “−1” elements into C columns of an identity matrix. Note that the first dimension of the \mathbf{p} matrix carries ordered spatial information for all of the voxels. Accordingly, the location of each of the C columns corresponds to the first voxel of each of the C compartments. The “−1” elements are located in each of the C columns after the first voxel, and correspond to all the rest of the voxels in each compartment. These elements are used to eliminate hypothetically identical rows in the \mathbf{p} matrix in accordance with the compartment model [17].

Assuming that the individual CSI spectra in each of the C compartments are identical, dimensional reduction [17] of Eq. (4) then leads to:

$$\mathbf{s}_{M^*N} = \mathbf{E}_{M^*M} \times \mathbf{b}_{M^*C}^r \times \mathbf{p}_{C^*N}^r, \quad (5)$$

where $\mathbf{p}_{C^*N}^r$ is obtained from retaining the C non-eliminated rows in \mathbf{p}_{M^*N} , which correspond to the spectra of the C first voxels in the C compartments, respectively. $\mathbf{b}_{M^*C}^r$ is obtained by retaining the C columns in $\mathbf{b}_{M^*M}^{-1}$ corresponding to the C non-eliminated rows.

2.2. Algorithms for SLAM and SENSE SLAM reconstruction

Two algorithms are used to reconstruct SLAM or SENSE SLAM spectra. The first is the same one described in Ref. [17]:

$$\mathbf{p}_{C^*N}^r = (\mathbf{E}_{M^*M} \times \mathbf{b}_{M^*C}^r)^+ \times \mathbf{s}_{M^*N}, \quad (6)$$

where “+” denotes the Moore–Penrose pseudo-inverse when $M' > C$, or the inverse when $M' = C$. The second, slightly different, algorithm is denoted with asterisks as SLAM* or SENSE SLAM*

$$\mathbf{p}_{C^*N}^r = (\mathbf{b}_{M^*C}^r)^+ \times (\mathbf{E}_{M^*M})^+ \times \mathbf{s}_{M^*N}. \quad (7)$$

Both algorithms require that $M' \geq C$, which is easily fulfilled in practice, e.g., $C = 3$ for cardiac spectroscopy [17], or $C = 4$ or 5 for SLAM MRS of brain, as exemplified later. With conventional (Eq. (6)) SLAM, $M' \leq M$ always, and typically $M' \ll M$, which means that $(\mathbf{E}_{M^*M})^+$ is generally under-determined. Conversely, for SENSE SLAM* (Eq. (7)), $M' = N_c M/R$ could easily exceed M making $(\mathbf{E}_{M^*M})^+$ over-determined (e.g., with a combination of an $N_c = 32$ element coil and an acceleration factor $R = 16$). In any case, numeric regularization is recommended, especially where SENSE reconstruction is involved and SNR is low. Here, a truncated singular value decomposition (TSVD) [42] method is utilized wherein values below, for example 2% of the maximum, are discarded to ensure that the condition number [43] is not greater than 50. In practice, the level of numeric regularization may be optimized for non-ideal/low SNR data, by increasing the level of numeric regularization until the results become stable.

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