Reconstruction of randomly under-sampled spectra for *in vivo* ^{13}C magnetic resonance spectroscopy

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ABSTRACT

Purpose: Over the past decade, many techniques have been developed to reduce radiofrequency (RF) power deposition associated with proton decoupling in *in vivo* Carbon-13 (^{13}C) magnetic resonance spectroscopy (MRS). In this work we propose a new strategy that uses data under-sampling to achieve reduction in RF power deposition.
Materials and methods: Essentially, proton decoupling is required only during randomly selected segments of data acquisition. By taking advantage of the sparse spectral pattern of the carboxylic/amide region of *in vivo* ^{13}C spectra of brain, we developed an iterative algorithm to reconstruct spectra from randomly under-sampled data. Fully sampled data were used as references. Reconstructed spectra were compared with the fully sampled references and evaluated using residuals and relative signal intensity errors.
Results: Numerical simulations and *in vivo* experiments at 7 Tesla demonstrated that this novel decoupling and data processing strategy can effectively reduce decoupling power deposition by greater than 30%.
Conclusion: This study proposes and evaluates a novel approach to acquire ^{13}C data with reduced proton decoupling power deposition and reconstruct *in vivo* ^{13}C spectra of carboxylic/amide metabolite signals using randomly under-sampled data. Because proton decoupling is not needed over a significant portion of data acquisition, this novel approach can effectively reduce the required decoupling power and thus SAR. It opens the possibility of performing *in vivo* ^{13}C experiments of human brain at very high magnetic fields.

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1. Introduction

Carbon-13 (^{13}C) magnetic resonance spectroscopy (MRS) has evolved into a powerful tool for studying brain metabolism and neurotransmission [1–5]. One major limitation in the clinical applications of *in vivo* ^{13}C MRS is the required high RF power for decoupling the large one-bond ^{1}H—^{13}C scalar couplings ($^1J_{CH}$ = 125–145 Hz). Specifically, the required RF strength for coherent decoupling has to be much greater than $^1J_{CH}$ [6]. The local and average specific absorption rate (SAR) accumulates linearly with the duration of decoupling and increases quadratically with field strength [6]. To prevent tissue overheating, *in vivo* ^{13}C MRS of human brain has been traditionally limited to relatively lower field strengths (≤4 Tesla).

To overcome the abovementioned problems, numerous strategies have been proposed to reduce RF power deposition associated with proton decoupling, such as using shaped or adiabatic RF pulses [7–10], shortening sampling time, or employing frequency-domain windowed stochastic decoupling [11]. In particular, Li et al. have developed

carboxylic/amide ^{13}C MRS using low RF power broadband stochastic proton decoupling [12–14]. Recently, they have demonstrated that the low RF power carboxylic/amide ^{13}C MRS technique can be safely applied to occipital lobe human brain studies at 7 Tesla [14].

In contrast to the crowded short-TE proton spectra of brain, the corresponding ^{13}C spectra are sparsely populated. This is especially so in the carboxylic/amide region of *in vivo* ^{13}C spectrum of brain. Since the sparsity of the frequency domain translates into redundancy of information in the time domain, various time-domain under-sampling schemes for the indirect dimensions have been devised to accelerate multidimensional data acquisition in magnetic resonance imaging and high resolution nuclear magnetic resonance (NMR) spectroscopy [15,16].

The purpose of the present study is to propose and demonstrate a new strategy for further reducing RF power deposition of proton decoupling by under-sampling during data acquisition of one-dimensional *in vivo* ^{13}C MRS. This new strategy uses a windowed decoupling scheme in the time domain in which decoupling is only required during randomly selected segments of data sampling. The spectra are iteratively reconstructed using those randomly selected segments of data only. Because the proton decoupling is not needed over a significant portion of data acquisition, this novel approach can effectively reduce the required decoupling power and thus SAR.

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2. Materials and methods

The carboxylic/amide region of ^{13}C spectrum is sparsely distributed and the spectral baseline in the carboxylic/amide region remains fairly constant. By taking advantage of this information, an iterative algorithm was developed to reconstruct spectra from random under-sampled datasets. The random under-sampling scheme begins with a fully sampled core followed by random sampled data segments throughout the dataset [17]. The under-sampling rate is defined as the percentage of under-sampled data over the full data length.

All frequency domain data points of *in vivo* ^{13}C spectrum are classified into two groups: 1) the signal group P where all data points are part of signal peaks; and 2) the empty frequency group Z where all data points have zero amplitude after baseline removal. In order to restore information from non-sampled data points, the reconstruction algorithm iteratively forces the under-sampled spectrum $f(k)$ to zero amplitude at known frequency intervals. The under-sampled spectrum $f(k)$ is the Fourier transformed of the under-sampled time domain data $x(s)$, where k refers to frequencies and s refers to under-sampled data locations.

In the first step, the initial $x_1(s)$ is the under-sampled FID obtained directly from the scanner. The algorithm first places zeros into the time intervals $\bar{s}$ when no decoupling is applied:

$$x_1(\bar{s}) = 0. \tag{1}$$

Starting from the second iteration, the algorithm reconstructs the frequency domain data by forward Fourier transform ($\mathcal{F}$) of the under-sampled data, and replaces the Z group data by zero in the frequency domain:

$$f_n(k) = \begin{cases} \mathcal{F}(x_n(s)) & k \in P \\ 0 & k \in Z. \end{cases} \tag{2}$$

Then, inverse Fourier transforms ($\mathcal{F}^{-1}$) were used to transform the updated frequency domain data back into time domain, and the algorithm computes the error term ε_n, which is defined as the absolute norm difference between the updated time domain data and the under-sampled-experimental data [17,19].

$$x_n(s + \bar{s}) = \mathcal{F}^{-1}(f_n(k)); \tag{3}$$

$$\varepsilon_n = abs|x_n(s + \bar{s}) - x_1(s)|. \tag{4}$$

If the error ε_n is larger than a manually set threshold, which is usually a very small number ($<10^{-6}$), the algorithm will replace the time domain data in the sampled segments by experimental data and continue to the next iteration:

$$x_{n+1}(s) = x_1(s); \tag{5}$$

$$f_{n+1}(k) = \begin{cases} \mathcal{F}(x_{n+1}(s + \bar{s})) & k \in P \\ 0 & k \in Z; \end{cases} \tag{6}$$

$$x_{n+1}(s + \bar{s}) = \mathcal{F}^{-1}(f_{n+1}(k)); \tag{7}$$

$$\varepsilon_{n+1} = abs|x_{n+1}(s + \bar{s}) - x_1(s)|. \tag{8}$$

The iteration continues until the error is less than the manually set threshold, which means the calculated time-domain data are consistent with the under-sampled experimental data. A maximum iteration number (>5000) is also set to stop the algorithm when it fails to converge. This occurs when the under-sampling rate is too high.

Numerical simulations were performed to verify and evaluate the iterative reconstruction of under-sampled data. Signals including ϒ-aminobutyric acid (GABA1 182.3 ppm), glutamate (Glu5 182 ppm), *N*-acetylaspartate (NAA1 179.7 ppm), NAA4 (179.5 ppm), glutamine (Gln5 178.5 ppm), aspartate (Asp4 178.4 ppm), Glu1 (175.3 ppm), Asp1 (175.1 ppm), Gln1 (174.8 ppm) and NAA5 (174.3 ppm) were simulated using a global linewidth and individual intensities obtained from fitting *in vivo* ^{13}C datasets [14]. Random noise was added to the simulated data to match the noise level observed *in vivo*. Two under-sampling strategies were compared: a random sampling pattern (A) and a coherent sampling pattern with gradually decreasing under-sampling rate (B). Both strategies began with a fully sampled core. Spectra were iteratively reconstructed using the under-sampled datasets based on Eqs. 2–8. Spectra from fully sampled data were also used to validate the proposed approach. To compare the signal-to-noise ratio (SNR) between full sampling and under-sampling, Monte Carlo simulations were performed with the same noise level but different realizations of random noise. Different core sizes and under-sampling rates were evaluated by comparing the residuals and signal intensity errors between the reconstructed spectra from under- and the corresponding fully sampled datasets. Signal intensities for simulated metabolites were computed using non-linear fitting with Lorentzain-Gaussian lineshape functions. The signal intensity errors were defined as the difference between fitted signal intensities from under- and fully sampled data divided by signal intensities from fully sampled data.

Four sets of *in vivo* ^{13}C human brain data [13,14] acquired using a Siemens Magnetom 7 T scanner (Siemens Healthcare, Erlangen, Germany) were analyzed to validate the iterative fitting technique. Detailed experiment settings could be found in Refs. [13,14] and are briefly summarized here. RF power in the proton channel and RF power of the ^{13}C coil were both calibrated before the experiments [13,14]. Each subjects were infused with [2-^{13}C] D-glucose and the *in vivo* data were acquired after 60–90 min of infusion, when the signal achieved a relative steady state. Product localizer and shimming sequence was first applied to properly position each subject and provided relatively homogeneous B_0 field within a $6 \times 6 \times 6$ cm^3 selected cubical voxel from each subject. *In vivo* ^{13}C spectra were acquired from the selected voxel using a modified Siemens FID sequence that uses low power broadband stochastic proton decoupling. Specific acquisition parameters were: hard pulse length = 500 μs, spectral width (SW) = 5 kHz, data points = 1024 and TR = 6 s. A total of 48 averages were acquired with acquisition time = 205 ms for each average [13,14]. Since the carboxylic/amide ^{13}C spectral region is free from lipid contamination (the lipid carboxyls do not overlap with metabolite carboxyls), the experimentally observed spectral structures of ^{13}C baseline are fairly simple and remain unchanged in all datasets [14]. We used an in-house developed non-linear fitting algorithm [18] and generated a ^{13}C baseline model from all *in vivo* data sets. Different under-sampled data were generated by changing the sampling rate randomly but with a predetermined sampling density pattern. Different under-sampling rates were evaluated using the same criteria as in numerical simulations. The relatively small lipid signal appeared around 178 ppm from *in vivo* data was fitted using a group of Lorentzain-Gaussian functions. All algorithms were programmed in MATLAB (R2015b).

3. Results

Fig. 1 shows the sampling pattern of two under-sampling strategies and the corresponding reconstructed spectra. Spectra from fully sampled dataset are also displayed for visual comparison and residual error calculation. The random sampling strategy A resulted in very small residuals. In comparison, the coherent under-sampling strategy B shows larger residuals for the same under-sampling rate. The mean signal intensity errors averaged from all metabolites for strategy A and strategy B are 1.28% and 2.50%, respectively. Similar results were obtained for all other under-sampling rates investigated in this study. Therefore, only results from the random under-sampling strategy A are reported below. A 20% fully sampled core size was chosen based on numerical simulations and was used in the following under-sampling rate evaluations. Fig. 2 compares SNR from full sampling with under-