Fast Spectroscopic Imaging Using Online Optimal Sparse k-Space Acquisition and Projections Onto Convex Sets Reconstruction

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Long acquisition times, low resolution, and voxel contamination are major difficulties in the application of magnetic resonance spectroscopic imaging (MRSI). To overcome these difficulties, an online-optimized acquisition of k-space, termed sequential forward array selection (SFAS), was developed to reduce acquisition time without sacrificing spatial resolution. A 2D proton MRSI region of interest (ROI) was defined from a scout image and used to create a region of support (ROS) image. The ROS was then used to optimize and obtain a subset of k-space (i.e., a subset of nonuniform phase encodings) and hence reduce the acquisition time for MRSI. Reconstruction and processing software was developed in-house to process and reconstruct MRSI using the projections onto convex sets method. Phantom and in vivo studies showed that good-quality MRS images are obtainable with an approximately 80% reduction of data acquisition time. The reduction of the acquisition time depends on the area ratio of ROS to FOV (i.e., the smaller the ratio, the greater the time reduction). It is also possible to obtain higher-resolution MRS images within a reasonable time using this approach. MRSI with a resolution of 64 × 64 is possible with the acquisition time of the same as 24 × 24 using the traditional full k-space method. Magn Reson Med 55:1265–1271, 2006. © 2006 Wiley-Liss, Inc.

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Magnetic resonance spectroscopy (MRS) was first introduced in the early 1970s to measure in vivo tissue metabolism in intact biological structures (1,2). Since then, MRS has been utilized to measure the metabolic status of almost every organ system in the body, and in particular is an established tool for studying neurochemical and metabolic abnormalities in the human brain. However, because they require relatively long acquisition times and have a low sensitivity (particularly on low-field MRI systems), MRS studies are frequently limited to single-voxel acquisitions, which may not capture information from the most important pathologic regions. MRS imaging (MRSI), also known as chemical shift imaging (CSI), is a combination of MRS and MR imaging (MRI). It is a completely noninvasive, multivoxel technique that can acquire information that is representative of both anatomy and regional metabolic states. In addition, MRSI often provides higher-spatial-resolution in vivo biochemical information than the single-voxel approach. MRSI has been used for basic physiological research and clinical imaging of metabolites (3). Proton (1H) MRSI studies have identified both focal and global neuronal metabolic changes in a variety of diseases, including brain tumor (4), subacute and acute cerebral infarction (5), multiple sclerosis (6), AIDS dementia (7), Alzheimer’s disease (8), degenerative ataxia (9), epilepsy (10), and psychiatric disorders (11). Most of these diseases present challenges to neuronal viability, which particularly relate to a reduction in the N-acetyl-L-aspartic acid (NAA) concentration. Proton MRSI is also capable of revealing the accumulation of lipids (12) and lactate (13) in ischemic myocardium. In addition, applications of phosphorus MRS and MRSI have focused on energy metabolism in the human brain, skeletal muscle, and cardiac muscle (10,14).

Despite its potential, MRSI has been used largely for preclinical research because it requires a relatively long acquisition time to obtain images with sufficient spatial information. Consequently, it is difficult to use on human subjects. Furthermore, physicians are interested in using multiple approaches in order to make accurate, timely diagnoses. These approaches might require MRSI data in addition to other imaging information, such as that obtained by diffusion tensor imaging (DTI), perfusion, and functional MRI (fMRI). In one study session so that more information is available. In order for MRSI to reach its full potential for clinical applications, the acquisition time must be reduced.

A few methods have been proposed to reduce MRSI acquisition time (15). These include echo-planar spectroscopic imaging (EPSI) (16–19), spiral spectroscopic imaging (20,21), parallel spectroscopic imaging (22,23), chemical shift encoding (24,25), and partial k-space sampling (26–35). EPSI and spiral spectroscopic imaging use a single-shot technique in which the polarity of the gradients is rapidly switched during data acquisition. Although this
approach can remarkably reduce data acquisition time, it is sensitive to motion artifacts because the gradient read-out time required to traverse \((k,t)\)-space in EPSI and spiral spectroscopic imaging is longer than that required to traverse only \(k\)-space in EPI and spiral imaging. It is also bound by physiological and instrumentation limits on the gradient switching rate and gradient strength. In addition, spiral spectroscopic imaging requires the acquired data to be reorganized for spectroscopic image reconstruction, which may introduce sophisticated data processing and interpolation artifacts. Parallel spectroscopic imaging requires a special set of RF coils for data acquisition, and prior knowledge of the spatial sensitivity of the RF coils for data reconstruction. Chemical shift encoding spectroscopic imaging requires highly efficient gradient and RF amplifiers, which may be unavailable on many MR systems, particularly high-field systems.

Partial \(k\)-space sampling approaches employ a conventional phase-encoding method that is familiar to most MR investigators and requires no hardware modification. There are two strategies for this approach: heuristic central \(k\)-space sampling (also known as keyhole sampling) (29,33–35) and optimized sparse \(k\)-space sampling with a limited region of support (ROS) (31–33). Although central \(k\)-space sampling is an easy and commonly used method to reduce scanning time, it causes ringing artifacts due to data truncation, and it worsens the spatial resolution because of a broader point spread function (PSF). A number of investigators have considered the \(k\)-space optimization method for imaging data sampling with a limited ROI and a prior knowledge of ROS (26–28,30–33). These methods have various drawbacks, including hard-to-interpret optimization criteria in some cases and in all cases the inability to select the \(k\)-space sample locations in real time.

However, a few investigators have considered a new approach in which data sampling is performed using a set of repeated rectangular arrays whose locations are spaced at sub-Nyquist density (36–38). It has been proven theoretically that this strategy can markedly reduce the MRSI data acquisition time, and it does not have the above-mentioned drawbacks. In a preliminary study we recently demonstrated that this technique can be practically instituted on a MRI scanner despite its unique and unusual data sampling scheme, which would require sophisticated software (39). In this report we describe in detail how we made optimal data sampling with a limited ROS approach possible and practical. We developed and implemented this technique on a 4T whole-body system with a Varian INOVA console.

**MATERIALS AND METHODS**

Our approach consists of three basic steps: First, we define the MRSI ROI from a scout image. The ROI is used to create an ROS as a basis for optimizing the data acquisition. Second, we use an online (i.e., real-time) sequential forward array selection (SFAS) algorithm to determine which \(k\)-space data are to be acquired based on the selected ROI. Third, we use the projections onto convex sets reconstruction method for the MRSI data processing. The procedure is described in detail below.

**Localization of the ROI and ROS**

The fundamental assumption underlying this approach is that only partial data are required if only a partial region of the entire image (i.e., the FOV) is of interest and has nonzero signal intensity. This can be accomplished by providing a priori knowledge (i.e., the ROS) before acquiring data. Before the MRSI acquisition, a specific ROI is planned on scout images, which can be acquired using a \(T_1\)-weighted imaging sequence. The signal outside the ROI can be suppressed during MRSI acquisition by using the localization by adiabatic selective refocusing (LASER) sequence with two dimensions of phase encoding (41). This sequence provides 3D localization, and each dimension is selected with a pair of adiabatic full-passage pulses. The ROI parameters are used to create an ROS as the basis for optimizing a subset of the necessary phase-encoding arrays using the SFAS algorithm to reduce acquisition time. With this approach, we performed 2D \(^3\)H-MRSI using a modified 2D spin-echo sequence with adiabatic selective refocusing to localize metabolic signal in the ROI. This was incorporated with a specific, required phase-encoding array determining by the SFAS.

**SFAS Theory**

The SFAS theory was described in detail by Gao and Reeves (38). We briefly summarize it here. Uniform sampling of \(k\)-space at a Nyquist rate within a known ROS is not time-efficient due to its redundant sampling if the ROS does not fill the entire FOV. Conversely, nonuniform sampling can break the Nyquist barrier. In principle, the minimum number of samples required is equal to the number of voxels in the ROS (i.e., the localized ROI)—not the total number of voxels of the image in a given FOV. However, the sampling array must be chosen carefully to avoid significant noise amplification and/or a singularity.

SFAS was developed to optimize sparse \(k\)-space samples for arbitrary sparse ROS by minimizing noise amplification and the sum of squared errors in reconstructed MRS images. To demonstrate how this algorithm works, we consider a sampling geometry in which the individual samples are laid out on a rectangular grid pattern, as shown in Fig. 1. The black circles represent the original full \(k\)-space locations. The green circles in Fig. 1a represent the data samplings of the initial selected array in its
original position, which can be arbitrarily chosen. A non-uniform sampling pattern is formed by moving the initial selected array sequentially to different locations, as shown in Fig. 1b–d with circles in blue, red, and yellow, respectively, according to the SFAS algorithm. This is essential to minimize the sum of squared errors and the noise amplification of the reconstructed image until the desired number of samples is reached based on the ROS.

Projections Onto Convex Sets Reconstruction

Because of this unique sampling scheme, the raw data cannot be processed by 2D fast Fourier transform (FFT), the traditional method for MRI and MRSI data processing. Instead, the raw data obtained by this method are processed with an image reconstruction algorithm specifically designed for this case. Free induction decay (FID) signals are first processed by performing a DC correction, 6 Hz Gaussian line-broadening, and 50 Hz convolution difference before reconstruction. The resulting data are processed by 1D FFT in the time domain and are placed in the appropriate corresponding k-space coordinate. The spatial-domain spectra are then reconstructed iteratively with the projections onto convex sets algorithm which can be shown in this case to yield the least-squares solution (38). We will now describe the rationale for this approach.

Consider a uniform \( m \times n \) grid of k-space samples for a given MR spectral slice arranged in a column vector \( y \). Let \( x \) represent the unknown spatial image slice at a particular k-space coordinate. The spatial-domain spectra are then reconstructed iteratively with the projections onto convex sets algorithm which can be shown in this case to yield the least-squares solution (38).

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\[
y = Fx + u
\]

Denote by \( y \), the optimized collection of the sparse k-space data set that is irregularly distributed in a uniform \( m \times n \) data matrix with the remaining samples filled with zeros and arranged in a column vector. Also, define a diagonal matrix \( R \) with diagonal elements set to one in the locations that multiply a vector. Let \( u \) be zero-mean, independent, identically distributed noise. Then the observed signal at a given spectral slice can be expressed as

\[
y = R Fx + u
\]

This sets all rows from Eq. [1], in which data are not actually collected, equal to zero. Define a diagonal matrix \( S \) with diagonal elements set to one in the locations that correspond to the ROS, and zero elsewhere, such that \( x = Sx \). In other words, since the ROS is defined as the region with nonzero intensities, \( x \) is actually equivalent to \( Sx \), with diagonal matrix \( S \) representing the ROS mask. Then \( Sx \) defines the projection onto the ROS. This projection works by setting all non-ROS values equal to zero and leaving the others as they are. The mapping \( x + F^H R (y - Fx) = x + F^H (y - RFx) \) defines the projection onto a space defined such that all acquired values at the optimal k-space locations are equal to \( y \). This projection works by setting the k-space values at the acquired locations equal to \( y \) and leaving the other k-space values as they are. The matrix \( F^H \) represents the complex conjugate of \( F \), and \( F^H F = I \) since \( F \) represents the unitary FFT. The solution of \( x \) after \( k \) iterations, denoted as \( \hat{x}_k \), can be solved by iteratively using projections onto convex sets as described in Eq. [3] by combining the two projections into a single iteration:

\[
\hat{x}_k = S \hat{x}_{k-1} + SF^H (y - RF \hat{x}_{k-1}) = SF^H (y + (I - R) F \hat{x}_{k-1})
\]

where \( I \) is an identity matrix, and \( x_0 = 0 \). When the distance of the solutions at the last two iterations is less than a preset tolerance, the solution has converged. This algorithm finds the solution within the ROS that best matches the acquired sparse k-space data in a least-squares sense. Our experience indicates that the solution converges within 100 iterations, which is what we used in our reconstruction. Each spatial slice of the MR spectrum is reconstructed using this algorithm, and then spectroscopic images of different metabolites are obtained following the spatial reconstruction.

Protocol

All MRI and \(^1\)H MRSI studies were conducted on a 4T Varian whole-body imaging system (Palo Alto, CA). Multiple-slice scout images with 256mm×256mm FOV and 256 x 256 matrix size were acquired using a T1-weighted gradient-echo imaging sequence. An ROI was selected on the desired scout image. Shimming was performed on the selected ROI. The ROI parameters were transferred to the 2D MRSI experiments to localize and obtain metabolic signals using a spin-echo 2D MRSI sequence. Water suppression was achieved by using a broadband semiselective excitation pulse along with a frequency-selective delays alternating with nutation for tailored excitation (DANTE) pulse applied to the water resonance. Water residual magnetization due to insufficient crushing gradients that normally appear at the center of the image was further moved to the corner by phase alternating at the receiver or transmitter. We used the same ROI parameters and the isolated corner pixel to generate the ROS for the online-optimized acquisition of k-space locations using our online SFAS algorithm. By including the corner pixel in the ROS, SFAS is capable of eliminating the aliasing due to the imperfection of water suppression.

Using the SFAS approach, a \( 4 \times 4 \) or \( 8 \times 8 \) array is moved to various locations and throughout the entire \( 32 \times 32 \) k-space to obtain a subset of optimized sampling locations based on the ROS. These sampling locations are obtained by minimizing the sum of squared errors and the noise amplification in reconstructed spatial-domain spectra (i.e., in reconstructed MRSI) as described above. Both high-spatial- and low-spatial-frequency information is covered nonuniformly. MRSI data are acquired with a modified 2D spin-echo MRSI sequence (TR/TE= 2000/75 ms) and with a specific phase-encoding array that is obtained from the SFAS optimization. An FID with 1024 complex data points is acquired for each k-space location of the optimized phase-encoding array. MRSI data are processed and
reconstructed with the use of a locally-developed, userfriendly graphic user interface (GUI) software package using the projections onto convex sets approach. The software package can provide metabolite mappings of the ROI and spectroscopic information for each voxel of the image.

We demonstrated this technique with both a phantom and a human brain on a 4T whole-body MRI scanner. The FOV was set to 256mm x 256mm and the data matrix size was 32 x 32. A small fraction of k-space locations (192 in this case) were selected from full-k-space locations (1024) based on the ROS according to the SFAS algorithm. To compare the MRSI data with those obtained by the conventional and keyhole data acquisition schemes, acquisitions with 1024 full k-space points and 193 central k-space points were conducted. Using our acquisition scheme, another measurement was performed with slightly more data points (256 in this case) to demonstrate the improvement of the signal-to-noise ratio (SNR) by the addition of just a few more acquisition data points. We also demonstrated this technique in a human brain. In addition, using the full k-space data, we retrospectively calculated the SNR values for various acquisition conditions by selecting optimized k-space locations according to the SFAS algorithm.

RESULTS

Figure 2 illustrates the results from a phantom containing 12.5 mM NAA, 10 mM creatine hydrate, 3.0 mM choline chloride, 7.5 mM myo-inositol, 12.5 mM L-glutamic acid (monosodium salt), 50 mM potassium phosphate, and 5 mM DL-lactic acid (lithium salt). Figure 2a shows a $T_1$-weighted scout image of the phantom with the ROI indicated by a white box. Figure 2b shows an ROS image with 133 nonzero voxels created from the ROI given in Fig. 2a, which provides the prior information for optimized acquisition of k-space samplings. The ROS includes a voxel in the upper left corner to account for a lack of water suppression at this location. This ROS (including the isolated point) illustrates that the technique can handle an arbitrarily shaped ROS. Figure 2c shows the NAA image reconstructed from 192 optimized k-space data points, which are shown in Fig. 2k. With less than 19% of full k-space data points, it takes only 6 min for the optimized acquisition, compared to 34 min for acquisition of the full 32 x 32 k-space. However, due to the PSF (shown in Fig. 2l) the spatial resolution (voxel size = 0.6 cm$^3$; thk = 1.0 cm) is identical to that of the full k-space data set shown in Fig. 2d. Figure 2e shows the NAA image reconstructed from the keyhole sampling data set. It shows image blurring and ringing artifacts due to the voxel contamination from the broadened PSF shown in Fig. 2m. Figure 2f exhibits the NAA image reconstructed from 256 optimized k-space data points. Also shown in Fig. 2g–j are spectra located at the center (position at matrix [16, 16]) of the image of Fig. 2c–f, respectively.

Figure 3 shows the SNR of the spectra as the function of the number of optimized k-space sampling locations from the phantom data shown in Fig. 2. The SNR was based on the NAA peak and was averaged from the center 36 pixels of the MRSI data. The open triangle, circle, and square symbols represent the measured SNR from the full k-space sampling (1024 locations), and optimized 256 and 192 locations, respectively. The closed circles connected by a solid line are SNR values calculated retrospectively from the full k-space data. The fact that the measured and the calculated values agree suggests that the technique is effective and the theory is well defined. It demonstrates that SNR increases with the number of data points collected.
which agrees with the conventional wisdom that noise decreases with increased phase-encoding steps (15).

Figure 4 illustrates an in vivo study of a healthy human subject. Figure 4a shows a $T_1$-weighted scout image with a white box indicating the ROI. Figure 4b shows the NAA image reconstructed from data obtained using the 240 $k$-space locations (shown in Fig. 4e) that were optimized by using the ROS shown in Fig. 4d. Also shown in Fig. 4c is the creatine (Cr) image reconstructed from the same $k$-space locations as in the NAA image. The overlapped white lines in Fig. 4b and c represent the edge information of the $T_1$-weighted brain scout image. With true $32 \times 32$ pixel resolution and 0.6 cm$^3$ nominal voxel size, NAA and Cr images show some differences between tissues (i.e., cerebrospinal fluid (CSF), and gray (GM) and white (WM) matter). As reported previously, NAA and Cr are absent from CSF, and Cr is higher in GM than in WM. The optimized $k$-space acquisition required only 8 min, compared to 34 min for the full $32 \times 32$ matrix. Therefore, the acquisition time was reduced by 76%. Figure 4f displays the PSF function from the 240 optimized $k$-space points located in Fig. 4e, which guarantees the least voxel contamination in the reconstructed NAA and Cr images. Figure 5 shows three spectra from predominantly GM, WM, and CSF. It shows that NAA is approximately the same in GM and WM, while Cr is higher in GM than in WM, and there is no metabolic signal in CSF.

**DISCUSSION**

Both the phantom and in vivo experiments show that good-quality spectroscopic images can be obtained by using the newly developed online SFAS optimized acquisition of $k$-space and projections onto convex sets reconstruction approach. It is possible to obtain the same resolution as that achieved with the full $k$-space acquisition method with an approximately 80% reduction of acquisition time. The required acquisition time using the SFAS approach depends on both the ratio of the ROI size to the FOV dimension and the size of the imaging matrix (i.e., it depends on the ratio of the number of nonzero voxels in the ROS to that of voxels in the whole image). The smaller the ROI-to-FOV ratio, the less acquisition time is required. The larger the imaging matrix chosen, the higher is the resolution of the reconstructed image. The required optimal acquisition time for $24 \times 24$ and $32 \times 32$ images is about 3–5 and 6–8 min vs. 20 and 34 min, respectively, for full $k$-space acquisition with TR = 2 s. The required optimal acquisition time for $64 \times 64$ MRSI using this approach is equivalent to that for full $24 \times 24$ $k$-space acquisition if SNR permits. We foresee that this method will further reduce data acquisition time by enabling interleaved, mul-

**FIG. 3.** Plot demonstrating the relationship between the SNR values and the number of optimized acquisition $k$-space data points. The SNR was calculated based on the NAA resonance. The optimized $k$-space locations were determined by the SFAS algorithm. The open triangles, circles, and squares represent the measured SNR from the full $k$-space sampling (1024 locations), and the optimized 256 and 192 locations, respectively. The closed circles connected by a solid line are SNR values calculated retrospectively from the full $k$-space data.

**FIG. 4.** Human brain data. a: $T_1$-weighted scout image with a selected ROI covering the inner structures of the brain indicated by the rectangular box. b: NAA and c: Cr maps were generated from integration of the NAA and Cr peaks, respectively. d: ROS image determined from the selected ROI. e: The selected sampling locations of $k$-space in the optimized acquisition and f: their corresponding PSFs are also shown. NAA and Cr maps were reconstructed from MRSI data acquired with optimized 240-$k$-space locations. The MRSI data were obtained using a 2D spin-echo MRSI sequence with TR/TE = 2000 ms/75 ms, in-plane resolution = $8.0 \times 8.0$ mm$^2$, and slice thickness = 10 mm.
tislice MRSI if the specific absorption rate (SAR) can be maintained under U.S. FDA regulations. It is also possible to create an ROS with isolated ROS to optimize sparse k-space acquisition if there are sparse isolated targets within the same image slice. One other possible variation of this technique would be to apply 3D MRI and MRSI. For example, 3D 31P MRSI with 13 x 13 x 13 matrix size and TR = 3 s requires about 110 min to acquire full 13 x 13 x 13 k-space data, and 46 min to acquire spherical central k-space with the method reported by Maudsley et al. (35) and Hetherington et al. (40). We estimate that it will take about 36 min or less to acquire a 3D 13 x 13 x 13 MRSI using SFAS algorithm. The only trade-off of this approach is a relatively low SNR compared to that obtained with the full k-space acquisition, even though the noise amplification is minimized in the optimization. The lower SNR of this technique appears to agree with the conventional wisdom that fast MRSI does not provide improved sensitivity (15). Thus, this technique may be limited to high-field MRSI, where sensitivity may not be an issue. It is essential to improve the SNR of this method, and that issue is currently being investigated.

REFERENCES


FIG. 5. Representative in vivo 1H MR spectra from a 0.6-cc voxel are presented for (a) WM, (b) GM, and (c) CSF.