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Achieving Sufficient Spectral Bandwidth for Volumetric ^1H Echo-Planar Spectroscopic Imaging at 4 Tesla

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Abstract

Complete coverage of the in vivo proton metabolite spectrum, including downfield resonances, requires a spectral bandwidth of approximately 9 ppm. Spectral bandwidth of in vivo echo-planar spectroscopic imaging (EPSI) is primarily limited by gradient strength of the oscillating readout gradient, gradient slew rate, and limits on peripheral nerve stimulation for human subjects. Furthermore, conventional EPSI reconstruction, which utilizes even and odd readout echoes separately, makes use of only half the spectral bandwidth. In order to regain full spectral bandwidth in EPSI, it has previously been suggested to apply an interlaced Fourier transform (iFT), which uses even and odd echoes simultaneously. However, this method has not been thoroughly analyzed regarding its usefulness for in vivo 3D EPSI. In this Note, limitations of the iFT method are discussed and an alternative, cyclic spectral unwrapping, is proposed, which is based on prior knowledge of typical in vivo spectral patterns.

Keywords

in vivo MR spectroscopic imaging; brain; spectral bandwidth; interlaced Fourier transform

INTRODUCTION

Complete coverage of the in vivo proton metabolite spectrum, including downfield resonances, requires a spectral bandwidth of approximately 9 ppm. Unlike in other MR spectroscopic imaging methods, spectral bandwidth of in vivo ^1H echo-planar spectroscopic imaging (EPSI) is primarily limited by gradient strength of the oscillating readout gradient and gradient slew rate, which must be kept below a certain threshold to avoid peripheral nerve stimulation. While the spectral bandwidth limitation of EPSI is usually not a problem for in vivo proton spectroscopy at a medium magnetic field strength ($\leq 3\text{T}$), aliasing becomes a problem as chemical shift dispersion increases at higher magnetic fields. Several approaches have been suggested to overcome the problem of limited spectral bandwidth for EPSI. Multiple acquisitions with a slight shift in echo time (TE) were proposed (1); however, this approach prolongs minimum acquisition time, which may not be permissible for volumetric EPSI applications. Frequency selective excitation was proposed to restrict the bandwidth of the excited signal (2); however, this method is difficult to apply effectively if large frequency

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variations induced by regional magnetic susceptibility differences occur. This method may also be impractical to use when the repetition time is not long enough to accommodate all sub-bands of the desired full spectral bandwidth. Conventional EPSI reconstruction methods utilize even and odd readout echoes separately, which further aggravates the bandwidth problem as only half the spectral bandwidth is used. To regain the full spectral bandwidth while using even and odd echoes simultaneously, interlaced Fourier transform (iFT) was proposed for reconstruction (3). While the principle of iFT has been shown for 1D EPSI data of a phantom, to our knowledge, its use has not been demonstrated for in vivo applications. Initial results of iFT obtained on a phantom (3) could not completely verify the robustness of this approach. For example, even though the results of ref. 3 verified a considerable reduction in the relative intensity of aliasing with iFT, the extent of residual aliasing was not discussed in detail. In this Note, we further investigate limitations of the iFT method for 3D EPSI. As an alternative to iFT, we explore cyclic spectral unwrapping, which is based on prior knowledge of typical in vivo spectral patterns.

METHODS

All measurements were carried out on a 4 Tesla Bruker MedSpec system (Bruker BioSpin, Ettlingen, Germany) equipped with a Siemens Trio console (Siemens Medical Solutions, Erlangen, Germany) and a Siemens Sonata 40 mT/m gradient system with a maximum slew rate of 200 T/m/s. A TEM head coil (MR Instruments Inc., Minneapolis, MN) was used for radio-frequency (RF) transmission and signal reception. The 3D EPSI pulse sequence used was described earlier (4). Data were acquired in a normal human brain with repetition time $TR = 1780$ ms, $TE = 45$ ms, and global inversion-recovery with inversion time $TI = 280$ ms was used for lipid suppression. The interval between metabolite and water reference excitation pulses was $TR_{wr} = 550$ ms. The readout gradient, applied along the anterior-posterior direction, consisted of 800 lobes of alternating polarity, each having sinusoidal ramps of 100 μ s duration and a constant plateau of 400 μ s duration allowing a full spectral bandwidth of 9.9 ppm to be sampled. After obtaining written informed consent in compliance with institutional policies, brain MRSI data were acquired from a healthy volunteer (35 years old) using a field-of-view (FOV) of 280 mm $\times$ 280 mm $\times$ 180 mm (x, y, z) and a spatial matrix of dimensions $N_x \times N_y \times N_z = 50 \times 50 \times 18$, at a maximum gradient strength of 8.0 mT/m. Oversampling by a factor 2 was used in the readout direction to allow cubic spline resampling onto a Cartesian grid. The iFT algorithm as described in detail in (3) was integrated into the data processing software described earlier (5). This included Gaussian apodization, leading to an effective voxel size of approximately 2 cm³.

Proper function of the reconstruction was verified using simulated 2D EPSI data. A data set of dimensions 512 $\times$ 50 $\times$ 50 for the time-, x-, and y-dimensions, respectively, was generated with a readout oversampling factor of 2. The same spectral bandwidth, FOV, and k -space trajectory used for the in vivo experiments were used in the simulations. A homogeneous circular object of approximately 130 mm diameter was generated for resonances representing water (4.7 ppm), NAA (2.0 ppm), and the doublet of Lactate (1.3 ppm) at 4T, and resonances were simulated with 5 Hz linewidth and Lorentzian line shape. The reconstruction was carried out as it was done for the in vivo data with the exception of lipid extrapolation and local B_0 shift correction (5).

The readout gradient design is subject to a number of constraints limiting the spectral bandwidth. Hardware constraints require the duration of each gradient lobe, T , as well as the ramp time to be an integer multiple of 10 μ s, and the readout sampling interval, T/N_x , must be an integer multiple of 1 μ s. Combined with the restrictions due to maximum gradient slew rate and gradient amplitude, only a limited number of value pairs (T, N_x) can be realized for a given FOV. For example, for FOV = 280 mm, the points in the (T, N_x) plane that represent feasible

gradient designs are shown in Fig. 1. The point representing the design used in our experiments, accomplishing simultaneously high resolution while avoiding risk of peripheral nerve stimulation because of excessive gradient slew rate, is circled. Separation of even and odd readout echoes for data processing will reduce the spectral bandwidth achieved with this design to 4.95 ppm. In principle, gradient designs with smaller values of T are feasible; however, these would imply the risk of causing peripheral nerve stimulation in the subject. A reduction in N_x would lower the maximum gradient strength and would reduce the risk of peripheral nerve stimulation, though at the expense of lower spatial resolution.

Prior knowledge about the distribution of resonances in the proton spectrum can be used to alleviate the spectral bandwidth limitation. Downfield resonances, which derive from low concentration metabolites, are usually not detected with EPSI because EPSI data are typically acquired with a relatively small voxel size (high spatial resolution) and relatively long TE (given the strong reduction in the effective transverse relaxation time, T_2 , at higher field). Therefore, only the upfield region is usually of interest, and the spectral bandwidth requirement can be relaxed to 4.5 ppm, which is adequately covered by the spectral sampling used in this study. The data can then be acquired with a frequency offset such that the limited bandwidth available is centered in the upfield region rather than on water. This concept was implicitly used before for 2D EPSI on a 4.7 Tesla animal system (6), as well as for 3D EPSI on a 4 Tesla whole-body system (7); however, it has never been explicitly rationalized. Alternatively, in this study, the data were acquired without the frequency offset and shifted in the spectral domain by the same frequency value during post-processing to unwrap the spectral aliasing. To maintain symmetry of the spectral bandwidth around the on-resonant water peak, the spectral bandwidth was zero-filled appropriately in the down-field region. This facilitated subsequent processing, especially the application of a FIR filter to remove residual water signal from metabolite data (5). The procedure is illustrated in Fig. 2. Note that the spectral bandwidth available in the data separated into even and odd components, SW , must be at least half the width of the band-limited region.

RESULTS

The problem of residual aliasing with iFT reconstruction is illustrated in Fig. 3, showing in (a) a typical proton spectrum from a normal human brain for the full spectral bandwidth and in (b) and (c) for a reduced width to emphasize details in the metabolite region. The data shown in Figs. 3b and c have been phased to present the upfield and downfield region, respectively, in absorption mode. The phase difference between both representations is approximately 90° . Major metabolite resonances have been assigned as NAA (N-acetyl-aspartate, 2.01 ppm), Cr (Creatine, 3.03 ppm and 3.93 ppm), and Cho (Choline, 3.19 ppm). A strong Nyquist artifact is visible at the edges of the spectral width in Fig. 3a. Residual aliasing occurs in the downfield region in Figs. 3b and c with aliased peaks assigned as “NAA” (6.96 ppm), “Cr” (7.97 ppm), and “Cho” (8.17 ppm). As expected, the chemical shift difference between true and aliased peaks is approximately 4.95 ppm. In general, we found that the majority of voxels is affected by these artifacts to a variable extent. While in the example shown in Fig. 3 the relative area of the aliased NAA peak is on the order of 10% of that of the true NAA peak, phantom studies have shown that the relative area of the aliased peaks can reach up to 25% of the corresponding true peaks (data not shown). Simulations of 2D EPSI data verified that the iFT algorithm was properly implemented (data not shown). Furthermore, these simulations indicated that negligible differences in spectral aliasing resulted from the use of the theoretical k -space trajectory as compared to the measured one, from the use of different readout oversampling factors, and from the inclusion of simulated eddy current effects, respectively. Significant spectral aliasing resulted from simulated phase errors between even and odd readout echoes.

In Fig. 4 is shown the spectrum from the same voxel as in Fig. 3; however, it is reconstructed with cyclic unwrapping of aliased spectral components. Note that the spectrum is shown over the entire spectral bandwidth of 9.1 ppm and that spectral zero filling in the downfield region effectively extended the spectral bandwidth by 4.16 ppm. The horizontal bar indicates the zero-filled region (5.1–9.3 ppm). All spectral components are retrieved, and aliasing and Nyquist artifacts are avoided. Near the transition between the original spectrum and the region filled with zeros, a distortion of the baseline is visible. This distortion can be worse in cases of broad residual water peaks; however, the baseline varies smoothly across the spectrum and will therefore not affect spectral analysis performed as suggested in (8), which includes a non-parametric baseline fit.

In Fig. 5 are shown images obtained by peak integration over the NAA peak at 2.01 ppm (a), the aliased NAA peak at 6.96 ppm (b), and the Nyquist artifact (c), as well as the corresponding structural images (d). The Nyquist artifact was integrated symmetrically. The peak integral display was chosen since our software did not allow fitting of the aliased metabolite peaks due to their inherently low signal-to-noise ratio (SNR). In Figs. 5a and b, image scaling was chosen to emphasize the NAA signal, causing signals of residual lipid and water to appear saturated. In addition, baseline estimation and subtraction was performed using a 4th-degree polynomial fit prior to spectral integration in (b) in order to separate the relatively small aliased signal from the dominant baseline contribution due to the Nyquist artifact.

DISCUSSION

We attribute the relatively large residual aliasing and Nyquist artifacts in our data to instrumental imperfections causing the phase relationship between even and odd data to be disturbed. It should be noted that while results from both conventional and iFT reconstructions in (3) are shown over a chemical shift range of 9 ppm, the graphs did not include regions beyond this spectral range to fully assess the Nyquist artifact. In Eqs. [1] and [2] are shown the expressions for the spectral functions G and H describing the true and aliased spectral components, respectively.

$$G(\omega) = \frac{\exp(-i\omega\tau)}{1 - \exp(a2\pi i\xi)} F^e(\omega) - \frac{\exp(a2\pi i\xi)}{1 - \exp(a2\pi i\xi)} F^o(\omega), \quad [1]$$

$$H(\omega) = \frac{-\exp(-i\omega\tau)}{1 - \exp(a2\pi i\xi)} F^e(\omega) + \frac{1}{1 - \exp(a2\pi i\xi)} F^o(\omega). \quad [2]$$

In these equations, i represents the imaginary unit, F^e and F^o are the Fourier transforms of the even and odd time series, respectively, for a given k -space location in the readout dimension, τ is the time between adjacent even and odd samples at this location, and $\xi = \tau/T$. The frequency ω runs from $-SW/2$ to $+SW/2$ with $SW = 2\pi/2T$, and the sign α is positive for negative frequencies and vice versa. Apart from some changes and a few corrections of notation, Eqs. [1] and [2] are equivalent to Eq. [1] in [3], which provides further details of the implementation. According to Eqs. [1] and [2], parameters τ and ξ from even and odd echo acquisitions must be accurate, and even and odd data, F^e and F^o , respectively, from the same k -space location along readout must match to obtain proper spectral reconstruction with iFT. In practice, however, this level of accuracy may be difficult to obtain.

For a small phase error, ε , in F^e , which can be written as $F^e \cdot \exp(i\varepsilon)$ in Eqs. [1] and [2], $\exp(i\varepsilon)$ can be approximated by a Taylor expansion, yielding

$$F^e \approx F^e \cdot \left(1 + i\varepsilon - \frac{1}{2}\varepsilon^2\right) = F^e \cdot \left(1 - \frac{1}{2}\varepsilon^2\right) + \varepsilon F^e \exp\left(i\frac{\pi}{2}\right), \quad [3]$$

for terms up to second order. The first order error term is therefore 90° out of phase with respect to the true term even for the slightest deviation. This result is consistent with the observed

phase relationship between the data shown in Figs. 3b and c. Additionally, the second order error term leads to a loss of signal amplitude. It should also be noted that the iFT algorithm leads to loss in signal-to-noise ratio due to division by small numbers (9).

The spatial distribution of the aliased NAA signal (“NAA”) shown in Fig. 5b is difficult to interpret since the spectral integral of this signal is affected by baseline distortions due to residual water and by noise. The low SNR is visible particularly in the lower slices, which usually show reduced SNR due to the decline in the B_1 profile toward the front edge of the TEM coil used. Because of these factors, the spatial distribution of “NAA” appears much less homogeneous than that of NAA. Phantom studies showed no significant differences between the spatial distributions of the two peaks (data not shown). The Nyquist artifact shown in Fig. 5c exhibits a concentric modulation pattern with high intensities in the image center followed by alternating regions of low and high intensities. This pattern was verified also in phantom studies (data not shown), and the low spatial frequency of the signal modulation indicates that a relatively small volume in k -space near the k -space center is affected most by the phase errors that give rise to the artifact. This may simply reflect the fact that the iFT method is most sensitive to phase errors in regions of k -space where maximum signal occurs and where phase errors do not tend to be dominated by either phase-encoding or noise.

Another method of increasing spectral bandwidth for 3D EPSI without significant increase of the readout gradient amplitude (and slew rate) would be to choose the readout direction along the inferior-superior direction. Since in this direction the spatial resolution is only 10 mm (as opposed to 5.6 mm in the other two directions), the readout gradient strength would be lower at a given spectral bandwidth, and peripheral nerve stimulation could be avoided. However, in general, unlike in the other two directions, the excited volume and FOV need to be positioned in the inferior-superior direction, and an off-center position of the readout FOV would be impossible to realize. The sign of the required frequency offset, applied during data acquisition, would have to be alternated between even and odd echoes, which would require frequency switching rates that exceed the hardware limitations. In addition, with the readout gradient along the inferior-superior direction, more phase-encoding steps would be needed to maintain the in-plane resolution, which would lead to a significant increase in measurement time.

CONCLUSIONS

In this Note, we have demonstrated that the interlaced Fourier transform, iFT, is extremely dependent on phase stability and may therefore fail in practice to sufficiently eliminate spectral aliasing in many voxels of in vivo proton 3D EPSI data. Instrumental instabilities leading to small but significant phase incompatibility between even and odd readout echoes are the most likely cause of this effect. While in (3) less than 100 voxels were available from a homogeneous phantom, more than 3000 voxels from most regions of the brain were analyzed in this study, allowing a thorough assessment of the spectral quality achievable with iFT. An alternative technique, cyclic spectral unwrapping, was proposed and shown to allow adequate reconstruction of 3D EPSI data, provided the spectral bandwidth after even-odd echo separation is on the order of 4.5 ppm or above. Relaxing the constraint on minimal spectral bandwidth allows the use of longer readout gradient lobes with smaller amplitude. A less demanding gradient design also has the advantage of generating less heating effects in the gradient coil former and passive steel shims, and thus gives rise to smaller frequency drift (4). Another advantage is that the acoustic noise level and pitch are reduced compared to shorter gradient lobes of higher amplitude. The cyclic spectral unwrapping approach requires that downfield resonances do not give rise to detectable signals, which may not be true at very short echo times and, therefore, this method could be of limited use for some applications. However, improvements in RF pulse design to better cope with RF field inhomogeneities at higher

magnetic fields will likely lead to longer adiabatic pulses, preventing significant reduction in TE.

REFERENCES

1. Matsui S, Sekihara K, Kohno H. High-speed spatially resolved NMR spectroscopy using phase-modulated spin-echo trains. Expansion of the spectral bandwidth by combined use of delayed spin-echo trains. *J Magn Reson* 1985;64:167–171.
2. Hirata S, Bito Y, Yamamoto E. Expansion of the spectral bandwidth by spatial and chemical shift selective saturation in high-speed magnetic resonance spectroscopic imaging. *Magn Reson Med* 1996;35:611–616. [PubMed: 8992214]
3. Metzger G, Hu X. Application of interlaced Fourier transform to echo-planar spectroscopic imaging. *J Magn Reson* 1997;125:166–170. [PubMed: 9245375]
4. Ebel A, Maudsley AA. Detection and correction of frequency instabilities for volumetric 1H echo-planar spectroscopic imaging. *Magn Reson Med* 2005;53:465–469. [PubMed: 15678549]
5. Ebel A, Maudsley AA. Improved spectral quality for 3D MR spectroscopic imaging using a high spatial resolution acquisition strategy. *Magn Reson Imaging* 2003;21:113–120. [PubMed: 12670597]
6. Bito Y, Ebisu T, Hirata S, Takegami T, Yamamoto Y, Tanaka C, Naruse S. Lactate discrimination incorporated into echo-planar spectroscopic imaging. *Magn Reson Med* 2001;45:568–574. [PubMed: 11283983]
7. Posse, S.; Alger, JR. Proton echo-planar spectroscopic imaging (PEPSI) in human brain at 1.5, 3 and 4 Tesla; Proceedings of the 12th Scientific Meeting of ISMRM; Kyoto. 2004; p. 2286
8. Soher BJ, Young K, Govindaraju V, Maudsley AA. Automated spectral analysis III: Application to in vivo proton MR spectroscopy and spectroscopic imaging. *Magn Reson Med* 1998;40:822–831. [PubMed: 9840826]
9. Yan H, Mao JT. Noise-reduction in MR echo planar image-reconstruction. *IEEE Trans Med Imaging* 1991;10:148–153.

FIG. 1. Distribution of feasible combinations of readout gradient lobe duration, T , and number of readout samples per lobe, N_x , for $\text{FOV} = 280$ mm and the hardware constraints given in the text. The point representing the design parameters used for this study, $T = 600$ μs and $N_x = 50$, is circled.

FIG. 2.

Schematic illustration of the cyclic unwrapping method. The spectral distribution, $S(\omega)$, shown in (a) is band-limited in the upfield region and partially aliased into the downfield region due to insufficient spectral bandwidth, SW . Shaded areas are not sampled and shown only to illustrate the periodicity of the Fourier transform. The modified spectral distribution, $S'(\omega)$, shown in (b) is obtained by cyclically shifting the aliased portion of the spectrum shown in (a) and filling the downfield region with zeros to maintain a symmetric spectral bandwidth, SW' .

FIG. 3.

Typical spectrum from normal human brain obtained at TE = 45 ms. The full spectral bandwidth is shown in (a), while a reduced width is shown in (b) and (c) with zero-order phase correction applied to present the upfield and downfield region, respectively, in absorption mode. Resonance assignments in quotes indicate aliased peaks.

FIG. 4. Spectrum from the same voxel shown in Fig. 3 reconstructed with the cyclic spectral unwrapping method. The horizontal bar indicates the zero-filled region (5.1–9.3 ppm).

FIG. 5. Images obtained by peak integration over the NAA peak at 2.01 ppm (**a**), the aliased NAA peak at 6.96 ppm (**b**), and the Nyquist artifact (**c**), as well as the corresponding structural images (**d**).