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Parallel reconstruction in accelerated multi voxel MR Spectroscopy

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Abstract

Purpose—To develop the simultaneous acquisition of multiple voxels in localized MR spectroscopy using sensitivity encoding, allowing reduced total scan time compared to conventional sequential single voxel acquisition methods.

Methods—Dual volume localization was used to simultaneously excite voxels in both hemispheres. Receiver coil sensitivity profiles were used to unfold the data. To demonstrate the method, MRS voxels in the left and right hippocampus were measured at 3T, and left and right motor cortex at 7T. Spectra were compared to conventional single voxel acquisitions. Spectra were also recorded from the lesion and contralateral hemisphere of a patient with a low grade oligodendroglioma at 7T.

Results—It was possible to generate signal in two voxels simultaneously and separate the signal originating from the different locations, with spectral results almost identical to those observed using conventional single voxel methods. The method results in an increased chemical shift displacement artifact, which might be improved by advanced pulse designs, and a noise increase due to the unfolding ‘g-factor’, which was larger at 3T than 7T.

Conclusion—The simultaneous acquisition of voxels for MR spectroscopy is possible by using modulated slice selective pulses and receive coil sensitivity profiles to unfold the resulting signals.

Keywords

MR spectroscopy; multi voxel; multi band; high field

Introduction

Single voxel MR spectroscopy (MRS) is commonly used to obtain metabolic information from selected regions within the human body. For both research and clinical studies the

regional distribution of these metabolites is very important, and it is not uncommon for several voxel locations to be acquired in a single examination. For example it is often common practice to acquire information both from a lesion and from a mirror-image contralateral brain region for comparison, or to acquire multiple brain regions (e.g. gray matter, white matter). However, since each acquisition is typically on the order of 5 minutes long, the sequential acquisition of multiple voxels rapidly becomes very time consuming, and so most clinical studies are generally limited to two or three voxels only. As an alternative to scanning multiple locations sequentially, MR spectroscopic imaging (MRSI; (1)) techniques can be employed to simultaneously acquire multiple voxels at the same time. However, MRSI may involve long scans since multiple phase-encoding steps have to be acquired (particularly for 3-dimensional coverage), and also suffers from effects associated with the point spread function due to limited k-space sampling and ghosting (e.g. due to subject motion or other instabilities). Slice-selective localization as used in single voxel (SV) spectroscopy offers the advantage of a better voxel definition since it does not suffer from such artifacts resulting from Fourier transformation of phase-encoded data.

To record multiple-voxels while still using slice-selective based excitation, several approaches have been proposed. One approach to acquiring multiple voxels within the same scan time makes use of the fact that the TR in single voxel MRS is generally much longer than the duration of the pulse sequence and readout window. When this is the case, acquisitions of two locations can be interleaved, so long as care is taken to avoid overlap of the slice selective pulses between the 2 regions (2). In this approach, dynamic shimming can even be used, so that the same line widths can be achieved as if the voxels were acquired separately (3). However, the acquisition of the two voxels is not simultaneous, but rather interleaved, which may for instance pose limitations in functional studies where dynamic responses to a stimulus are studied. Furthermore, by interleaving two acquisitions, the radiofrequency power deposition (specific absorption rate, 'SAR') of the sequence is doubled which might lead to an increased scan time if the power deposition would exceeds the maximum allowed value.

Another approach is based on the Image-Selected in Vivo Spectroscopy (ISIS) (4) or Hadamard (5) encoding. Here the longitudinal magnetization of the different voxels is prepared by additional inversion pulses, and alternates between measurements, so that an add/subtract scheme can be used to separate the voxels. This approach does result in simultaneously acquired data, but relies on a subtraction scheme that requires high stability of both the MR system and the subject. Also, the additional RF pulses may cause signal loss (if they do not fully invert the magnetization) and may again increase the SAR and duration of the scan.

With the increasing use of higher field strengths and large arrays of multiple receiver coils, it has been demonstrated that spatial localization information can be encoded by using the spatial variation of the receive coil sensitivity profiles. This approach has been used extensively for parallel imaging (e.g. (6,7)) in MRI and MRSI (e.g. (8–13)), and can result in high acceleration factors, particularly in high magnetic field systems (14). This principle has not only been applied to reduce scanning time for phase encoded MRI, but also to separate signal from multiple slices which are simultaneously excited (15,16) and for multiple

localized regions excited simultaneously (17). Considerable work has gone into designing ‘multiband’ RF pulses that can simultaneously excite 2 or more slices (18,19). These approaches however, have not been applied in MR spectroscopy, and the reduction in bandwidth of multiband RF pulses is not considered problematic for imaging of water. For MR spectroscopic localization however, reduced RF bandwidth results in increased chemical shift displacement artifacts, particularly at the high magnetic field strength of 7 tesla. For localized single voxel MR spectroscopy, it is desirable that the chemical shift displacement artifact be kept to a minimum in all three directions.

In this work, it was hypothesized that receive coil sensitivity spatial profiles can be used for the separation of multiple MRS voxels that are excited simultaneously. To demonstrate the general applicability of the method, it was implemented with three different localization techniques (chosen as a function of available B_0 and B_1 field strength), 2 different field strengths (3 and 7T, also using body and brain transmit coils, respectively), and 2 different brain regions (hippocampus, and motor cortex) in healthy volunteers. In addition, the clinical applicability of the method at 7T was tested in a patient with a right hemispheric low grade oligodendroglioma. Experiments were performed at 7T since high field is expected to be particularly beneficial for parallel encoding techniques (20). However, it also important to verify that multiband MRS is also feasible at the commonly available clinical field strength of 3T.

Methods

Theory

To demonstrate the proposed MRS technique, the initial pulse of the SV localization sequence was replaced with a multiband excitation pulse, that will excite two parallel voxels. This was chosen to be applied in the sagittal plane so that voxels were simultaneously excited in the left and right hemispheres. The spatial separation of the simultaneously excited signals from both voxels was accomplished by using the SENSitivity Encoding (SENSE) formalism (6,17). The sensitivity profiles were averaged over each spectroscopy voxel and concatenated in a sensitivity matrix S , which has dimensions of $R \times N$, where R is the number of voxels to be unfolded (here 2), and N is the total number of receiver coils (here 32). The unfolding matrix was calculated according to (6):

$$U = (S^H \Psi^{-1} S)^{-1} S^H \Psi^{-1},$$

where Ψ represents the receiver noise matrix and H indicates the transpose complex conjugate. With the unfolding matrix, the time-domain domain signals from each voxel can be separated by multiplying the acquired multi-channel signal with the matrix U for every point in the acquisition. The SENSE unfolding inherently results in phase and sensitivity weighted receiver coil combination for maximizing SNR from the array coil. The discrimination between different spatial locations is dependent on the difference of the receiver sensitivity profiles in the two voxels, which can be expressed by the (geometry) g -factor. Unfolding locations with a high g -factor leads to increased noise in the spectra. The

g-factor was calculated to assess possible noise increase in the brain locations that were studied according to (6):

$$g_p = \sqrt{[(S^H \Psi^{-1} S)^{-1}]_{p,p} (S^H \Psi^{-1} S)_{p,p}}$$

Where the p indicates the p -th voxel. Note that for two voxel unfolding as performed here, the g -factors for both voxels are equal. Spatial maps of the g -factor were generated by calculating the unfolding matrix and g -factor for all locations in the sensitivity map, using a fixed location in the right hemisphere as the second location. In this way a spatial map was generated to assess the ability of the two MRS voxels to be unfolded, and the minimal spacing between voxels can be assessed.

Unlike SENSE-encoded MRI or MRSI, where SNR is decreased compared to the unaccelerated acquisition by a factor of $g \times R$, where R is the acceleration factor (i.e. scan time reduction), in the multiband MRS application described here, the SNR reduction only depends on the g -factor, since the scan time per acquisition is unchanged.

RF Pulse Design

Dual band 90° degree slice-selective pulses were calculated for each experiment by point-by-point summation of the two individual RF pulses used to excite voxels in the left and right hemispheres. Typically, the resulting dual band pulse had twice the amplitude, and would have exceeded the maximum transmit B_1 of the system. Therefore the amplitude was reduced and the duration of the pulse lengthened accordingly to maintain the correct flip angle. This caused an increase in the minimum sequence TE and also lowered the bandwidth of the excitation pulse. The slice profile of the dual band pulses were both simulated with the Bloch equations and measured in a homogeneous phantom at 7T to confirm that no unexpected out-of-voxel excitation occurred due to this modification of the RF pulse.

For experiments at 3T, a standard PRESS (point-resolved spectroscopy; (21)) sequence was used with an asymmetric sinc excitation pulse (15 uT, 6,4 ms). A decrease in bandwidth from 1 kHz to 0.5 kHz occurred for this pulse when converted to dualband excitation, resulting in an proportional increase in the CSDE in the left-right dimension, to 66% voxel shift between 1.3 (Lactate) and 3.9 ppm (Creatine).

For experiments at 7T, because of the greater chemical shift dispersion, either the sLASER (semi-localized by adiabatic selective refocusing; (22,23)) or STEAM (stimulated echo acquisition mode; (24)) pulse sequences were used, with high-bandwidth frequency modulated ‘fremex05’ excitation pulses (25) (bandwidth 3.1 kHz, peak B_1 20 μ T, duration 6.5 ms) (Figure 1). For the dualband implementation of this pulse, the duration increased to 13 ms and the bandwidth decreased to 1.5 kHz (i.e. 51% chemical shift displacement left-right between 1.3 and 3.9 ppm). Despite the longer duration, excitation profiles measured in a phantom were virtually identical to those recorded using individual voxel excitation (Figure 1). The sLASER pulse sequence was used in supratentorial brain locations where sufficiently high transmit B_1 allowed the use of high bandwidth (>12 kHz) adiabatic gradient modulated refocusing pulses (23). The STEAM pulse sequence was used in the

temporal lobe, where the peak B_1 was not sufficient to allow use of the sLASER adiabatic pulses. In all scans a 4 kHz acquisition bandwidth and 2048 sampling points were used.

Since multiband excitation pulses typically have either higher amplitude (and/or duration) compared to conventional slice selective RF pulses, pulse sequence SAR will usually be higher than that corresponding to single voxel excitation. In some instances, particularly at 7T, this increased the minimum pulse sequence repetition time (TR) that could be used, but in most cases the increase in TR was below 1%.

Experimental

Experiments were performed on Philips 'Achieva' scanners operating at both 3T and 7T (Philips, Best, The Netherlands) equipped with dual transmit capabilities (body coil at 3T, volume head coil (Nova Medical, Inc, Burlington, MA, USA) at 7T) and a 32 channel receive coils (Nova Medical, Inc, Burlington, MA, USA). The study was approved by the local Institutional Review Board and written informed consent was given by all volunteers prior to the exam.

The receive coil complex sensitivity profiles were mapped with a low-flip angle gradient echo sequence, with images collected both from each element of the receive phased-array, as well as the larger transmit coil (body coil at 3T, head transmit coil at 7T). B_0 shimming (second order at both field strengths) was performed with an image-based shimming algorithm (26) that minimized B_0 distortions in both voxels simultaneously. Since B_0 shimming in general performs poorer when using larger regions of interest, the impact on the water line width of simultaneous shimming was compared with shimming of the two voxels separately.

To demonstrate the effectiveness of the method under a variety of conditions and brain locations, experiments were performed in (experiment a) left and right hippocampi at 3T (normal volunteer), (experiment b) left and right motor cortex at 7T (normal volunteer), and (experiment c) left and right temporal lobes at 7T (in a patient with a right temporal oligodendroglioma). Details of the pulse sequence parameters are given in Table 1. For the hippocampal experiment at 3T (experiment a), voxel positioning was performed on a 3D-T1 weighted scan, and additional outer-volume suppression was achieved with two sagittal saturation bands placed over the scalp adjacent to the left and right temporal bones. For the 7T experiment in a patient diagnosed with a right temporal oligodendroglioma (experiment c), voxel positioning was performed based on both 3D-T1 weighted and 3D-FLAIR (fluid attenuated inversion recovery) images (27). The second voxel was positioned in the mirror image location in the contralateral hemisphere to the tumor.

Dual voxel MR spectroscopy was performed on both water suppressed and unsuppressed acquisitions. Water suppression in all cases was performed with the VAPOR sequence (28). SNR was calculated as the ratio between the maximum signal in the frequency domain of the unsuppressed acquisitions and the standard deviation of the last 256 points in the time domain of the water suppressed spectra. A leakage factor was calculated to assess the spillover of signal from one location into the other due to both the unfolding reconstruction and imperfect RF pulses. The leakage factor was calculated from the water signal from

separate excitations of both voxels. The leakage factor was defined as the percentage of the signal that was observed in the second location if only the first voxel was excited and vice versa (see for example the residual peak in Figure 3a, right).

Results

Calculated g-factor maps at both 3T and 7T are shown in Figure 2. For unfolding the left and right motor cortex at 7T the g-factor was 1.00 (Figure 2a), indicating a negligible overlap of the receiver profiles, and therefore allowing unfolding of the 2 voxels with virtually no noise amplification. Unfolding of the left and right hippocampus at 7T (spectra not shown) also resulted in a g-factor of 1.00 (Figure 2b). For unfolding of the left and right hippocampus at 3T, the g-factor was 1.14 (Figure 2c), indicating a modest reduction in SNR due to the unfolding algorithm.

Due to simultaneous B_0 shimming of the two voxels, the B_0 field homogeneity was expected to be slightly lower as compared to shimming of the voxels individually. However, the water line width as measured in one volunteer increased by only 1% (11.2 Hz to 11.3 Hz) on average for the two voxels in the motor cortex at 7T, indicating a negligible shimming penalty for these locations (experiment b).

The unfolding results at 3T (experiment a, Figure 3) showed a leakage factor for the right and left hippocampus of 1.2%. The simultaneous excitation resulted in similar spectra, albeit at reduced SNR due to a less favorable g-factor (1.14), and the right voxel showed an increased lipid signal likely due to differences in chemical shift displacement. The mean SNR of the unfolded spectra was 85% of the SNR in the separate acquisitions, in good agreement with the g-factor calculation.

A separate excitation of the right (experiment b, Figure 4) and left motor cortex at 7T showed 0.4% leakage from one voxel to the other, as seen from the separate water acquisitions. The simultaneous excitation and separation of both voxels resulted in similar spectra as obtained with the separate excitations (Figure 4c,f) with a g-factor of 1.00. The mean SNR in the unfolded spectra was 103% of the SNR in the separate acquisitions (i.e. most likely identical, within the measurement error).

Dual voxel acquisition (experiment c) was performed in a patient with a clinically stable and untreated right hemispheric oligodendroglioma diagnosed 5 years earlier by excisional biopsy. T1-weighted and FLAIR images were used to plan a voxel in the T2 hyperintense region of the lesion above the resection cavity in the right temporal lobe and a second voxel in the contralateral hemisphere (Figure 5a). Individual spectra obtained from the tumor (Figure 5b) show an increased level of choline, reduced N-acetylaspartate and increased levels of lipids or lactate at 1.3 ppm and increased levels of lipid or macromolecules at 0.9 ppm compared with the contralateral region of interest (Figure 5c), consistent with prior studies (29). Simultaneous acquisition of the same voxels (Figure 5d,e) resulted in very similar spectra, although some difference in residual water signal were observed, likely due to differences in chemical shift displacement. A leakage factor of 1.0% was observed. The

mean SNR of the unfolded spectra was 99% of the separate acquisitions. The calculated g-factor for these two locations was 1.00.

Discussion

In this work, a method for simultaneous excitation and separate reconstruction of signals from dual voxels in the left and right hemispheres of the brain is demonstrated to accelerate MRS studies. Dual volume acquisition was achieved by incorporating a dual-band excitation pulse into a conventional single voxel localization technique. With this approach, two parallel voxels have to be prescribed, limiting the degrees of freedom for placement somewhat as compared to single voxel acquisition where both voxels can be rotated arbitrarily. The receiver coil sensitivity patterns were then used to unfold the two voxels in post-processing. The technique worked well, provided that the g-factor for the two regions to be unfolded was low. The advantage of the technique is that scan time is halved compared to two conventional single voxel acquisitions. The potential disadvantages of the technique are the longer duration and lower bandwidth of the dual-band pulses, leading to increased chemical shift displacement artifacts, increased SAR, and longer minimum TE.

Dual band excitation and unfolding with the coil sensitivities is only possible if enough separation is available between the voxels of interest. The method was demonstrated to work well in two different locations of normal brain at 3T (hippocampi) and 7T (motor cortex), and at 7T in a patient with a temporal lobe oligodendroglioma, where the tumor spectrum was compared with that from a simultaneously acquired voxel from the contralateral brain tissue (a comparison very commonly performed in clinical MRS). The examination of spectra from the left and right hippocampi is also often performed for the evaluation of patients with temporal lobe epilepsy, for instance by Connelly et al (30). Use of the simultaneous excitation method with unfolding would allow for these commonly used clinical protocols to be done in half the time compared to conventional sequential acquisitions.

A clear B_0 field dependence could be seen in the added noise from the unfolding algorithm. For bilateral voxels in the motor cortex and hippocampus (data not shown) at 7T with a 32-channel receiver coil, there was no significant noise amplification. At 3T, also with a 32-channel coil, in the hippocampus the unfolding did lead to modest noise increase. The improved performance at higher field (7T) is expected due to the increased interaction of the RF field to tissue and therefore increased spatial variance in the RF field as compared to 3T (14). The method is also expected to work better the more receiver coils that are available; a limitation is that voxels adjacent to one another are likely to suffer from high g-factors, particularly at lower field strengths and with fewer than 32-channel receiver coils. It should be noted that 'leakage' of signal from one voxel to another can also occur because of imperfect RF pulse excitation; in practice it is difficult to separate recon-associated leakage from this effect. Computer simulations of RF pulses and dualband experiments will be required to further investigate the relative magnitudes of these two effects. In voxels that are close together, a combination with conventional phase-encoded spectroscopic imaging techniques is likely to be superior to only methods based only on variations in the receiver sensitivity profiles.

In principle, the method could also be extended to more voxel locations in multiple directions (15) if appropriate high bandwidth multiband RF pulses are available, and the voxel locations can be unfolded with low g-factors. To excite in multiple directions, additional slice selective pulses (other than the initial excitation pulse) will need to be converted to dual- or multi-band excitation, for instance as demonstrated in the fMRI experiments performed in reference (15). Note that experiments of this type are more likely to be feasible with STEAM or PRESS, than with sLASER, since the implementation of dualband adiabatic pulses would most likely require longer echo times, and involve high RF power deposition, resulting in prolongation of the TR.

There are several possible approaches to improving multiband pulse design for application to MRS. Combining asymmetric RF pulses with time shifted B_1 maxima (31), or by applying the VERSE principle (32) may overcome some of the limitations associated with reduced pulse bandwidth. While it has been reported that MR systems can suffer from degraded slice profiles due to unwanted deviations in the RF transmit chain, and that such artifacts are even more pronounced with multi-band RF pulses (33), the slice profile measurements (figure 1) did not show any significant differences between single and multi-voxel excitations. However this may be scanner dependent, and care must be taken that the generated RF pulses do indeed generate the desired slice profiles.

In summary, a method is presented to simultaneously excite multiple MRS voxels, which are then unfolded using the SENSE algorithm and the measured receive coil sensitivity profiles. The method has the potential to significantly reduce scan time, for instance when scanning a lesion as well as a comparison contralateral region of interest. The method works best greater numbers of receiver coils which have different coil sensitivities, which tend to be more localized at 7T, but is feasible at 3T with 32-channel receiver coils.

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Figure 1.

Amplitude modulation (AM) and frequency modulation (FM) of the high bandwidth 'fremex05' single band (a) and dual band (b) RF pulses that were used at 7T. (c) The voxel profile in the direction of the excitation pulse was measured in a phantom at 7T. The top line displays a whole-slice readout through the phantom, and depicts the overall flip angle and receive sensitivity. The lower three lines show projections with 'fremex05' slice selection. The single volume measurements show comparable slice profiles those with dual band excitation (c).

Figure 2.

Noise amplification (g-factor maps) for unfolding a target voxel in the right hemisphere. The g-factor maps (color maps) were generated throughout the brain by pairing all voxels in the 3D reference scan with the target voxels (red boxes). In the contralateral locations that were used in subsequent experiments (yellow boxes), the g-factor was low. For the motor cortex (a,b) and hippocampus (c,d) at 7T no noise amplification was observed ($g=1.00$). For the hippocampus at 3T (e,f), because of the more slowly varying receive coil B_1 profiles, some noise amplification is observed ($g=1.14$).

Figure 3.

Dual voxel MRS of the hippocampus at 3T (experiment a). In the top row (a,d) only the right voxel is excited and the data is subsequently unfolded. In the second row (b,e) only the left voxel is excited, and in the bottom row (c,f) both voxels are excited and subsequently separated. From the water spectra 1.2% leakage was seen from one voxel into the other. The right voxel of the simultaneously excited voxels shows an increased lipid artifact. Due to the lower g-factor the SNR was lower, with 85% of the SNR of the separate acquisitions.

Figure 4.

Water signal (left) and metabolite signal (right) of a dual voxel MRS of the motor cortex at 7T (experiment b). In the top row (a,d) only the right voxel is excited and the data is subsequently unfolded. In the second row (b,e) only the left voxel is excited, and in the bottom row (c,f) both voxels are excited and subsequently separated. From the water spectra 0.4% leakage was seen from one voxel into the other. The spectral quality of the simultaneously excited voxels was similar with 103% of the SNR of the separate acquisitions.

Figure 5.

Dual voxel acquisition in a patient with a stable, post-operative right temporal oligodendroglioma at 7T (experiment c). T1 weighted and FLAIR images (a) were used to plan the voxel location in the right temporal lobe. Spectra in the tumor (b) show an increased level of choline (Cho), reduced N-acetylaspartate (NAA) and increased levels of lipids or lactate at 1.3 ppm and increased levels of lipid or macromolecules (MM) at 0.9 ppm compared with the contralateral grey matter tissue (c). Simultaneous acquisition of the same voxels (d,e) results in virtually identical results, although some difference in residual water signal are observable.

Pulse sequence acquisition details, brain location, and calculated g-factors. For all locations the experiment was performed three times, once for the left-only, once for the right-only and once for the simultaneous excitation and acquisition.

Table 1

Experiment	Field Strength	Location	Pulse Sequence	TR/TE/TM (ms)	VOI (mm ³)	Averages	g-factor	Acquisition time (min)
(a)	3T	Hippocampus	PRESS	2000/31	30×15×15	64	1.14	2:08
(b)	7T	Motor Cortex	sLASER	5000/43	20×20×20	32	1.00	2:40
(c)	7T	Temporal Lobe (tumor)	STEAM	3000/19/34	20×20×20	64	1.00	3:12