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Dual-Band Water and Lipid Suppression for MR Spectroscopic Imaging at 3 Tesla

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Abstract

A dual-band water and lipid suppression sequence was developed for multislice sensitivity-encoded proton MR spectroscopic imaging of the human brain. The presaturation scheme consisted of five dual-band frequency-modulated radiofrequency pulses based on hypergeometric functions integrated with eight outer volume suppression (OVS) pulses. The flip angles of the dual-band pulses were optimized through computer simulations to maximize suppression factors over a range of transmitter amplitude of radiofrequency field and water and lipid T_1 values. The resulting hypergeometric dual band with OVS (HGDB + OVS) sequence was implemented at 3 T in a multislice sensitivity-encoded proton MR spectroscopic imaging experiment and compared to a conventional water suppression scheme (variable pulse power and optimized relaxation delays (VAPOR)) with OVS. The HGDB sequence was significantly shorter than the VAPOR sequence (230 versus 728 msec). Both HGDB + OVS and VAPOR + OVS produced good water suppression, while lipid suppression with the HGDB + OVS sequence was far superior. In sensitivity-encoded proton MR spectroscopic imaging data, artifacts from extracranial lipid signals were significantly lower with HGDB + OVS. The shorter duration of HGDB compared to VAPOR also allows reduced pulse repetition time values in the multislice acquisition.

Keywords

water suppression; lipid suppression; brain; magnetic resonance spectroscopic imaging; sensitivity-encoding

Proton MR spectroscopic imaging (MRSI) of the human brain continues to be an active area of both clinical and research investigation (1). The metabolic information provided by MRSI often complements the anatomic information available from conventional MRI and may either provide insights into the pathophysiology of disease conditions or provide useful clinical information in individual patients (2). Since the brain metabolite signals are at least two to three orders of magnitude smaller than the brain water signal, it is traditional to use water suppression presaturation techniques to decrease the amplitude of the water signal in the spectrum, which makes visualization and quantification of the metabolite signals easier

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(1). In addition, although the brain itself does not contain large signals from mobile lipids, the pericranial scalp tissues do contain intense lipid resonances. These signals can interfere with proton brain spectra because of the extended point spread function associated with relatively low spatial resolution MRSI data and the blurring effect of any head motion. Therefore, MRSI is also traditionally performed with lipid suppression (3–6).

Increasingly, proton MRSI is being performed with phased-array receive coils because of their high sensitivity and the ability to use parallel-encoding techniques such as sensitivity encoding (SENSE) (7) or “Generalized Autocalibrating Partially Parallel Acquisition (GRAPPA)” (8) to reduce scan time. This is particularly important since conventional MRSI scan times with two-dimensional or three-dimensional phase-encoding can be extremely long when high spatial resolution and coverage are required. However, lipid suppression is a problem for techniques such as SENSE-MRSI since the phased-array coils have very high sensitivity at the periphery, and also because any imperfections in the parallel reconstruction algorithm will leave residual lipid signals folded over into the brain (7,9). Lipid suppression is particularly a problem for two-dimensional multislice or three-dimensional MRSI acquisitions that are not based on the “point resolved spectroscopy sequence (PRESS)” sequence, which restricts excitation to rectangular volumes within the brain and attempts to avoid excitation of lipids in the scalp, but which therefore has limited ability to cover cortical brain regions.

Numerous methods of water and lipid suppression have been developed for both single-voxel spectroscopy and MRSI of the brain. One of the simplest methods of water suppression is a single chemical shift-selective saturation pulse (“CHESS”) applied at the water frequency, followed by a crusher gradient (10). Such an approach only gives good suppression for a very narrow range of water T_1 values and amplitude of radiofrequency field (B_1) strengths, so alternative approaches were developed to improve suppression factors over a range of T_1 values and B_1 values by using multiple pulses with optimized flip angles and delays, such as “water suppression enhanced through T1 effects (WET)” (11) or “VAPOR” (12). For lipid suppression, various approaches have been developed, including the use of inversion recovery sequences (utilizing the difference in T_1 between water and metabolites (13)), or using spatial outer volume suppression (OVS) pulses (3,14,15). It is common to add OVS to water suppression schemes such as WET or VAPOR in order to provide combined water and lipid suppression. Frequency-selective pulses can also be used for lipid suppression, applied either alone or in combination with frequency-selective water-suppression pulses to create dual-band suppression schemes (5,16).

This paper describes the development of a new hybrid dual-band/OVS water and lipid suppression scheme for proton MRSI of the human brain. The sequence is particularly optimized for lipid suppression and is therefore well suited for application in SENSE-MRSI. The basic building block is the hypergeometric (HG) function (17,18). Two HG functions (with different frequency offsets) were added together to form a dual-band pulse, and then suppression factors were optimized by iterative, numerical simulation for a range of B_1 and water and lipid T_1 values. The (lipid) frequency-selective pulses only suppress the methyl and methylene resonances (0.8–1.4 ppm), so eight OVS pulses for spatially selective suppression of the scalp are also included since frequency-selective suppression cannot eliminate lipid resonances that overlap with metabolites (e.g., the allylic, diallylic, or α -methylene to carboxyl moieties, which resonate between 2.0 and 3.1 ppm).

The performance of the new hypergeometric dual band (HGDB) suppression sequence was compared to VAPOR with OVS pulses in multislice SENSE-MRSI scans.

MATERIALS AND METHODS

Pulse Sequence Design

The HG pulse is closely related to the widely used hyperbolic secant pulses (17–19). When their amplitude is large enough relative to the sweep rate, both HG and hyperbolic secant pulses act as 180° adiabatic pulses, with excellent inversion profiles determined by the range over which their frequency is swept. As the amplitude is reduced, the pulse becomes nonadiabatic and the flip angle decreases, but the pulse retains its excellent frequency profile (5). Like the hyperbolic secant pulses, the HG pulses are derived from an analytic solution to the Bloch equation (20). The hyperbolic secant functions are a particular case of these HG expressions, but unlike hyperbolic secant pulses that feature a symmetric amplitude waveform, the HG expressions include a parameter that controls the asymmetry of the pulse and its resulting frequency profile. The asymmetry of the HG frequency profile, with one sharp edge and one broad, makes it an excellent candidate for both water and lipid suppression, where a sharp cutoff is usually required on only one side of the resonance to be saturated (e.g., upfield from water, or downfield from lipid). Dual-band suppression pulses can be created by summing two HG waveforms in time-reversed direction (21). Setting the peak amplitude of the fat suppression band near the end of the dual-band pulse reduces the relaxation time between the last fat suppression and subsequent pulses and partly accommodates for the shorter T_1 value of lipids. In the summation of the pulses, the amplitude of individual HG pulse components for water and lipid protons can be controlled separately, allowing their flip angles to be individually optimized for the different T_1 values of water and lipid.

All computations were performed in Matlab (Mathworks, Natick, MA). The frequency modulations of the individual bands were adjusted to create a passband between 1.8 and 4.2 ppm with $M_z/M_{eq} > 0.99$. First, the exact band profiles of the individual pulses were determined by numerical simulation of the Bloch equations at a B_1 value corresponding to a 120° flip angle. The sharp edge of the HG pulses varies only slightly with flip angles between 90° and 180° , so 120° was chosen as a starting point to ensure the desired frequency profile even at the highest flip angles encountered in the final sequence. The passband characteristics of the summed pulses were also verified by numerical simulations.

The aim of the optimizations was to find the best combination between spatially selective suppression of fat signals through OVS pulses and five chemical shift selective suppression of water and fat simultaneously (Fig. 1). The delay between the 3rd and 4th suppression pulses was reserved for eight OVS pulses for spatial selective suppression of lipid signals to complement the frequency-selective suppression. The flip angles for the fat suppression pulses were optimized for the shorter T_1 s found in in vivo fat signals. For each intermediary set of parameters, the analytic response was calculated with and without one OVS pulse. The optimization was toward a solution that yielded the best result in both cases. The flip angles for the water suppression pulses were optimized for the longer T_1 s of water, and with no effect from the OVS pulses.

The individual HG pulse shapes were calculated with the following parameters for Eq. 1 in Rosenfeld et al. (22): $a = 2$, $b = 0.6$, $c = -3$, $d = +1.5$, $\Omega_0 = 4.7$ ($\omega_{1max} = 0.2$ kHz) for the water band and $a = 4$, $b = 0.5$, $c = -4$, $d = +2$, $\Omega_0 = 4.7$ ($\omega_{1max} = 0.2$ kHz) for that fat band, both truncated at 1% of the maximum amplitude.

$$\begin{aligned}
\omega_x &= \omega_1 = \Omega_0 \frac{\sqrt{z(1-z)}}{az+b} & t &= \ln \left(\frac{z^b}{(1-z)^{a+b}} \right) \\
\omega_y &= 0 & z &\in [0, 1], t \in [-\infty, \infty] \\
\omega_z &= \omega - \omega_0 = \frac{cz+d}{az+b} - \omega_0
\end{aligned} \tag{1}$$

A Matlab script for generating these pulses is available on request. With a pulse width of 30 msec, the transition width on the “sharp” side of the water pulse profile (as calculated from Eq. 10 of Rosenfeld et al. (22)) was less than 36 Hz, and the predicted suppression bandwidth (measured at the 1% residual $|M_z|/M_{eq}$ level) was 490 Hz. For the fat suppression pulse, after rescaling to 30-ms duration, the calculated transition was 30 Hz and the nominal bandwidth, 1 kHz. The relative amplitudes of the water and fat suppression bands were determined from amplitude scaling factors (C_k) determined by optimization for individual HG pulses. The error function for the Levenberg-Marquardt optimization was the minimization of the absolute residual magnetization of a multipulse sequence, with given delays analytically calculated over 200 B_1 values covering an up to 4-fold variation. The response $M_{ZN}(B_1, T_1)$ of an N pulse sequence was calculated analytically as described previously (21), with T_1 weighting during interpulse delays.

It was assumed that the response of the HGDB pulses can be treated as the sum of the response of the individual HG pulses, which is a reasonable assumption for the low B_1 values used here, and was also verified by numerical simulations. The T_1 values of water and lipid were assumed to range from 500 to 3000 msec and 250–450 msec, respectively, at 3 T (23,24). The OVS pulses were assumed to have no effect on the water resonance. The cost function (Eq. 2) of the numerical simulation was defined to cover a range of $N T_1$ values and $M B_1$ values.

$$\begin{aligned}
\varepsilon &= \sum_{j=1}^N \sum_{i=1}^M \frac{w_i}{NM} \frac{|M_z(C_1, \dots, C_K, T_{1j}, B_{1i})|}{M_{eq}} + 0.1 \times \frac{STD(C)}{\bar{C}} \\
&\text{where } w_i = \exp[\log(.01) \cdot x_i^{40}], x_i \in [-1, +1] \text{ and} \\
&B_{1i} \in [B_{1\min}, B_{1\max}]
\end{aligned} \tag{2}$$

where $K = 5$ in the current optimization, for water and lipid. The weighting function w_i was designed to emphasize midrange B_1 values over extreme values. The inclusion of the second term in Eq. 2 avoids excessively high or low flip angles.

An 100-msec delay was inserted between pulses 3 and 4 to accommodate the eight OVS pulses. These OVS pulses (2.09-kHz bandwidth, 110° flip angle, each of 4-msec duration followed by a 1.5-msec crusher gradient of 10 mT/m amplitude) were arranged in an octagonal pattern around the brain. The center of this OVS section was set at 121 msec prior to signal excitation. The total length of the HGDB sequence was 230 msec.

MRSI Experiments

All experiments were performed on a 3-T system (Achieva; Philips Healthcare, Best, The Netherlands), equipped with an eight-channel phased-array receiver coil. Phantom experiments to measure the passband profile were performed on a NiCl_2 -doped water phantom with a T_1 of 0.35 sec.

Five normal subjects (three males and two females; age 41 ± 8 years) were studied after written institutional review board-approved consent was obtained. The HGDB suppression pulses were used as prepulses for a slice-selective spin echo MRSI sequence. The spin echo

sequence used frequency-modulated excitation and refocusing pulses, with peak B_1 of 13.5 μ T and bandwidths of 4.26 kHz and 2.15 kHz, respectively. Three 13.2mm thick axial slices with 2.2mm gaps were recorded. A field of view of 190×230 mm was sampled with a matrix size of 27×33 and a SENSE factor of 2 in anterior-posterior and 1.5 in right-left directions (total SENSE factor = 3), giving a resultant nominal in-plane resolution of 7×7 mm and voxel size of 0.65 cm^3 .

For comparison to HGDB, a VAPOR water suppression sequence with eight OVS pulses was used. The VAPOR (12) sequence was adapted for application at 3 T with eight pulses and the following flip angles and delay times: 90° , 150 msec; 90° , 100 msec; 160.2° , 122 msec; 90° , 105 msec; 160.2° , 102 msec; 90° , 61 msec; 160.2° , 67 msec; and 160.2° , 30 msec. Gradient crushers following pulses 1 through 7 were 10 msec in duration in all directions. The crushers following the last pulse were 5 msec in duration. Gradient strengths in mT/m along x, y, and z directions were (10,0,0), (0,10,0), (0,0,10), (9,0,0), (0,8,0), (0,0,7), (8,0,0), (0,10,10). Eight OVS pulses (flip angle 120°) were inserted between the 5th and the 6th VAPOR water suppression pulses. The flip angles of the OVS pulses in VAPOR were limited by scanner software. The center of the OVS pulses in the VAPOR sequence was 215 msec preceding signal excitation, and the total length of the VAPOR sequence with these parameters was 728 msec.

Echo time/pulse repetition time was 144 msec/2.5 sec for HGDB and 144 msec/3.5 sec for VAPOR since the longer VAPOR sequence required a longer pulse repetition time. Specific adsorption rate (SAR) for three slices was 2.6 W/kg for HGDB and 1.9 W/kg for VAPOR, both within the US Food and Drug Agency limit of 3.0 W/kg for neuroimaging. Total scan time was 10 min 37 for HGDB and 14 min 51 sec for the VAPOR sequence. Prior to data acquisition, a rapid combined amplitude of static field and B_1 mapping technique was used to optimize amplitude of static field homogeneity with up to 2nd-order shim correction and to determine the optimal average transmit B_1 level over the volume of the MRSI slices.

For quantitative comparison of water and lipid suppression factors over the whole volume of the brain used for MRSI, phase-encoding gradients were turned off and spectra were measured from the whole slab excited for MRSI using the spin echo pulse sequence, as described above.

Spectral data processing was performed using in-house software (25). Metabolic images were generated by peak integration and linear interpolation after voxel-by-voxel susceptibility corrections and application of a high-pass filter with 50-Hz bandwidth to remove the residual water signal (26). Metabolic images were masked using a “skull-strip” method to remove any signals outside the brain, based on coregistered MR images.

RESULTS

Simulation Results

The optimized sequence is graphically illustrated in Fig. 1. Figure 2 shows the calculated residual Z-magnetization for the optimized dual-band sequence as a function of frequency offset and B_1 field strength for the T_1 values of (a) lipid and (b) water. The nominal B_1 was fixed at $\gamma B_{1\text{nom}}/2\phi = 75$ Hz (1.758 μ T). When $\gamma B_1/2\phi$ is within the range of 75–150 Hz, the suppression scheme works well, with residual water and lipid signals in the 0–5% range and a greater than 98% efficiency (for long T_1 compounds) within the desired spectral passband. At $\gamma B_1/2\phi$ values over 150 Hz, the water and lipid suppression factors are still excellent; however, magnetization within the passband starts to become saturated. At $\gamma B_1/2\phi$ values less than 50 Hz, the water and lipid suppression factors decrease rapidly.

Experimental Results

The experimental spectral profile of the HGDB sequence in the doped water phantom is plotted in Fig. 3 and shows good general agreement with the simulations in Fig. 2b. The water signal is fully suppressed at 4.7 ppm, while the passband magnetization is nearly 100% at 4.2 ppm (i.e., width of transition = 0.5 ppm, or approximately 64 Hz). Similarly, on the other edge of the passband, the magnetization goes from 100% at around 1.8 ppm to ~5% at 1.3 ppm.

Spectra for the whole MRSI slab used to test different suppression schemes are shown in Fig. 4. VAPOR gave very good water suppression results, but VAPOR combined with OVS only gave modest lipid suppression. The HGDB + OVS sequence gave water suppression factors a factor of 2 better than VAPOR, and lipid suppression was nearly 10 times better than VAPOR + OVS. Numerical integration gave residual water and lipid signals (percentages of unsuppressed) as follows: VAPOR: water $2.3 \pm 0.1\%$, lipid $99 \pm 4\%$, VAPOR + OVS: water $2.3 \pm 0.1\%$, lipid $46 \pm 5\%$, HGDB (without OVS): water $1.0 \pm 0.3\%$, lipid $10 \pm 6\%$, HGDB + OVS: water $1.0 \pm 0.4\%$, lipid $5 \pm 3\%$.

Figure 5 and Fig. 6 show the result of a multislice SENSE-MRSI scan on a volunteer with the HGDB + OVS sequence (Fig. 1). None of the masked metabolite images (Fig. 5) have visible contamination of subcutaneous lipid signals within brain parenchyma, which can also be seen in the spectra shown in Fig. 6, which compare the performance of the HGDB + OVS and VAPOR + OVS sequences. Spectra are plotted from nine selected voxels from the central MRSI slice to illustrate the relative lipid suppression performance of both sequences. The high-pass filter function of the spectral processing software successfully eliminated the residual water peaks for both HGDB + OVS and VAPOR + OVS spectra in all nine voxels, so that water signal is absent from both sequences. However, the HGDB + OVS sequence produced far superior lipid suppression at all nine locations.

Finally, Fig. 7 shows a comparison of lipid metabolic images (displayed without skull-strip masking) for the HGDB + OVS and VAPOR + OVS suppression schemes. The much-improved lipid suppression of the HGDB sequence can be seen both in the scalp, as well as throughout the brain, confirming the globally lower lipid contamination in SENSE-MRSI using the HGDB + OVS sequence.

DISCUSSION

Sufficient water and lipid suppression is crucial for successful MRSI studies of the brain. Lipid suppression is particularly important for MRSI studies with limited spatial resolution, where the extended point-spread function can result in appreciable contamination of brain voxels with signal from pericranial lipid. The problem is compounded when using phased-array coils (which have very high sensitivity in the pericranial regions) and parallel encoding techniques, which may result in lipid foldover into the brain if parallel reconstruction is not perfect. Traditionally, lipid suppression in multislice MRSI is performed using OVS (3); however, the suppression factors obtained by this technique are modest because only a single OVS sequence is used, making it very sensitive to variations in flip angle (B_1 field strength) and lipid T_1 values. An attractive alternative is to use frequency-selective lipid pulses and to combine them in a multiple (as in the “WET” sequence), dual-band approach (together with water suppression) that can be used to compensate for both variations in B_1 and T_1 ; this approach has recently been demonstrated for brain MRSI (16). The current study extends this work further in the following ways; (a) it builds the basic dual-band pulses using an HG function, which has sharper unilateral transition bands; (b) it allows the effective flip angles of water and lipid to be optimized separately; and (c) it builds in an

OVS component, which is critical for saturating the nonmethyl/methylene lipid resonances, as well as improving overall lipid suppression.

In experimental data, lipid suppression using this HGDB + OVS scheme proved superior to the conventional approach of VAPOR + OVS, which had excellent water suppression but much worse lipid suppression. The VAPOR sequence is also considerably longer, with eight radiofrequency pulses and delays; this can be a problem for multislice MRSI experiments where minimization of the presaturation sequence is important when incorporating as many slices as possible into one pulse repetition time period. The HGDB sequence gave quite adequate water suppression without the need to incorporate more radiofrequency pulses and longer sequences.

A significant limitation of all frequency-selective lipid suppression schemes is that they cannot be used to detect resonances that coresonate in the same regions of the spectrum; this also applies for the HGDB sequence. Therefore, if the detection of compounds such as lactate, alanine, or the branched-chain amino acids valine, leucine, or isoleucine, is required, other suppression schemes must be considered.

Of note is that the optimization used in the current simulations relied on analytical solutions of the residual Z-magnetization. When optimizing for lipid suppression, it is important to consider that lipid resonances, in addition to experiencing the HGDB pulses (if there are methyl or methylene groups), may also experience zero, one, or two OVS pulses, depending on their spatial location. Therefore, the simulations should be constrained to provide adequate lipid suppression simultaneously for lipids experiencing different numbers (including zero) of OVS pulses.

Some limitations of this study are the constraints on the OVS flip angle and the relatively high SAR of the proposed HGDB sequence. Further optimization efforts might address these issues by including HG pulse bandwidth and OVS flip angle as parameters to be optimized, as well as cost functions that include factors such as pulse sequence length and SAR, in addition to water and lipid suppression factors. Reducing the number of pulses will also address most of these problems, but this will limit the ranges of B_1 and T_1 over which the suppression sequence is effective and it will be harder to optimize for good lipid suppression both with and without the OVS pulses.

In summary, a dual-band water and lipid suppression method was developed for multislice SENSE MRSI based on the HG waveform. OVS pulses were integrated in the sequence to further enhance lipid suppression. This method is shorter than VAPOR water suppression with integrated OVS, resulting in a reduced scan time for multislice MRSI, as well as improved water- and lipid-suppression performance. The method appears well suited for use with phased-array coils and parallel-encoding techniques such as SENSE-MRSI.

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FIG. 1. Schematic depiction (amplitude and frequency) of the HGDB suppression scheme with integrated OVS pulses. For clarity, slice-selective and crusher field gradient pulses are not included.

FIG. 2.

Simulations of residual Z-magnetization for (a) lipid ($T_1 = 0.25$ – 0.45 sec) and (b) water ($T_1 = 0.5$ – 3.0 sec) after the HGDB + OVS sequence (Fig. 1) as a function of the B_1 strength. Contour plots show the spectral frequency dependence (X-axis) of the residual Z-magnetization for lipid ($T_1 = 0.35$ sec) and brain water ($T_1 = 0.75$ sec) as a function of B_1 (Y axis). Red corresponds to zero suppression (i.e., full signal detected), while green corresponds to full suppression (no signal detected). The dashed vertical line indicates the position of the lipid resonance in (a) and the water resonance in (b).

FIG. 3.

Experimental passband/suppression profile measured in a phantom containing NiCl_2 -doped water phantom, obtained by measuring the phantom water signal as the scanner center frequency was incremented across the spectrum.

FIG. 4.

Whole-slab spin-echo brain magnitude spectra recorded with various suppression schemes: no water or lipid suppression (black line), the VAPOR water suppression sequence only (red), combined VAPOR and OVS (blue), HGDB without OVS (green), and HGDB with OVS (purple). VAPOR gives good water suppression, but VAPOR + OVS only gives modest lipid suppression (50%). In contrast, HGDB has both good water and lipid suppression, with the best lipid suppression obtained with the HGDB plus OVS sequence. The improvement using OVS is particularly evident where the residual lipid signal resonates above 1.6 ppm (and is therefore less well suppressed by HGDB without OVS (green line)). The water and lipid suppression factors for each sequence are given in the text. Note that the “ringing” observed in the spectrum without any suppression is due to the limited data acquisition time that causes some truncation of the strong water signal. The Y-axis is plotted on a linear scale.

FIG. 5.

Metabolic images (choline, Cho; creatine, Cr; N-acetyl aspartate, NAA) in a normal volunteer recorded using multislice SENSE-MRSI with HGDB + OVS. Acquisition details are given in the text. Note the lack of residual water or lipid artifacts in all three slices. T_1 -weighted localizer images are also shown, including voxels chosen for spectral display in Fig. 6.

FIG. 6.

Nine selected voxels from the HGDB + OVS (red lines) dataset in Fig. 5. Black lines show the results of a VAPOR + OVS SENSE-MRSI dataset for comparison from the same subject and voxels. Note the far superior lipid suppression using HGDB + OVS compared to VAPOR + OVS.

FIG. 7. Lipid metabolic images (displayed on same brightness/contrast) for SENSE-MRSI using **(a)** HGDB + OVS and **(b)** VAPOR + OVS. Residual lipid and SENSE foldover artifacts (arrows) are significantly reduced with HGDB + OVS, including the mesial frontal bone marrow lipid signal from the falx cerebri.