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Original contributions

Phased array 3D MR spectroscopic imaging of the brain at 7 T☆

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Abstract

Ultra-high-field 7 T magnetic resonance (MR) scanners offer the potential for greatly improved MR spectroscopic imaging due to increased sensitivity and spectral resolution. Prior 7 T human single-voxel MR Spectroscopy (MRS) studies have shown significant increases in signal-to-noise ratio (SNR) and spectral resolution as compared to lower magnetic fields but have not demonstrated the increase in spatial resolution and multivoxel coverage possible with 7 T MR spectroscopic imaging. The goal of this study was to develop specialized radiofrequency (RF) pulses and sequences for three-dimensional (3D) MR spectroscopic imaging (MRSI) at 7 T to address the challenges of increased chemical shift misregistration, B1 power limitations, and increased spectral bandwidth. The new 7 T MRSI sequence was tested in volunteer studies and demonstrated the feasibility of obtaining high-SNR phased-array 3D MRSI from the human brain.

Keywords: MRSI; Brain; Phased array; 7 T

1. Introduction

Whole-body 7 T MR systems for research applications have become commercially available over the past few years from the major magnetic resonance imaging (MRI) manufacturers, and the imaging benefits provided by these ultra-high-field scanners are currently being investigated in several laboratories around the world. The benefits in blood oxygen level dependent (BOLD) contrast at 7 T for functional MRI (fMRI) have been clearly shown in a number studies [1,2]. The improvement in signal-to-noise ratio (SNR) at 7 T has also been shown for volume coils between 7 T and 4 T [3]. Recently, phased-array coils at 7 T have provided more uniform reception and increased sensitivity to visualize small anatomic structures not previously detected [4]. Single-voxel MR Spectroscopy (MRS) studies have demonstrated increased SNR and improved spectral separation at 7 T, which has provided better detection of more metabolites than at lower fields [5–7]. However, three-dimensional (3D) MR spectroscopic imaging (MRSI) at high fields with its much larger volume excitation presents additional challenges such as increased B1 inhomogeneity over the selected region, chemical shift misregistration artifacts, pulse profile and peak power concerns. The goal of this study was to develop and apply customized RF pulses and a specialized sequence for acquiring high spatial resolution 3D MRSI from the human brain at 7 T.

2. Methods

Nine healthy volunteers aged 26 to 46 were scanned on a GE EXCITE 7T (General Electric Healthcare Technologies, Waukesha, WI, USA) scanners. All studies were performed with informed consent following a protocol approved by

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the Committee on Human Research at our institution. A commercial 8-channel array and a volume transmit head coil (NOVA Medical, Wilmington, MA, USA) was used to provide whole brain coverage. Volume transmit was provided by a shielded, high-pass birdcage coil; the receive array consists of eight gapped elements of 12 by 5 cm, tuned to 298 MHz with multiple distributed capacitors [8].

2.1. Imaging

A series of anatomic imaging sequences were performed, followed by a second-order automatic shimming routine and 3D MRSI sequence. A three-plane localizer with low resolution, followed by a high-resolution axial T_2/T_2* weighted gradient recalled echo (GRE) with TE/TR 11.4/250 ms with FOV of 18 cm and 512×512 matrix at 2 mm thickness, and 3D inversion recovery spoiled gradient echo with inversion time of 500 ms, FOV of 24 cm, 256×160 matrix and 3 mm thickness were acquired. Axial slices were prescribed through both the supra- and infratentorial brain. A low-resolution GRE image set was also collected for summing the spectroscopic data. Second-order shimming was performed using the default routine provided by the scanner using the method described by Kim et al. [9].

2.2. Three-dimensional MRSI

Three sets of 3D Point Resolved Spectroscopy (PRESS) acquisitions were performed on volunteers in 3 groups (3 volunteers in each) to investigate the range of the MRSI parameters and RF pulses employed (Table 1). In group one, the standard long TE (144 ms) MRSI was acquired with the custom designed spectral-spatial RF (SSRF) with improved B1 insensitivity and the enlarged chemical shift artifact. In group two, spectra of similar resolution were acquired using routine Shinar-LeRoux (SLR)-designed linear-phase pulses and with short TE (35 ms) to allow visualization of short T_2 metabolites. In group three, regular SLR pulses were employed to achieve short TE (35 ms) for acquisition of high spatial resolution spectra. See Table 2 for list of acquisition parameters. Three Chemical Shift Selective (CHESS) water suppression pulses of 120°, 105°, and 155° with a bandwidth of 200 Hz were used. In all acquisitions, the superior/inferior (S/I) dimensions were selected to be 3 voxels or greater. In the 1 cc acquisition, the bottom slice was at the level of the basal ganglia, and the top slice was located above the ventricles. For the high spatial resolution acquisition, the PRESS selection was chosen near the posterior aspect of the brain in the occipital region. For 1 cc studies, elliptical k-space sampling was employed to minimize scan time, in which 50% of the corner points in k-space were not collected. For the high-resolution 0.35 cc studies, all k-space points were collected. The collected spectra were apodized with 4 Hz Lorentzian filter and processed using custom routines as previously described [10], in which spectra from individual channels were summed using weighted empirical coil profiles generated by low-resolution GRE images. The reported linewidths were calculated before apodization, and SNR values were measured after apodization. SNR is given as peak height over the standard deviation from the far right of spectra (approximately −1 to −2 ppm), where no resonances were observed. A total of 879 voxels from three volunteers were used.

Table 1
MRSI parameters

Parameters	Group 1	Group 2	Group 3
Selection pulse	SSRF	SLR	SLR
TE	144 ms	35 ms	35 ms
TR	2s	2s	2s
Elliptical k-space sampling	Yes	Yes	No
Total imaging time	17.5min	17.5min	17.5min
Spatial resolution	1 cm^3	1 cm^3	0.35 cm^3
Matrix size	12×12×8	12×12×8	8×8×8
OVERPRESS	40%	40%	40%

Table 2
Linewidth for 1 cc acquisitions in Hz

	Cho		Cr		NAA	
	144 ms	35 ms	144 ms	35 ms	144 ms	35 ms
Slice 1	17.2±3.8	15.3±9.4	17.5±4.7	19.1±8.7	21.0±5.6	23.7±10.3
Slice 2	17.4±4.2	20.1±9.7	17.9±4.4	22.3±6.9	21.4±5.4	27.6±11.3
Slice 3	19.5±7.5	22.8±9.3	21.7±5.6	26.8±7.7	25.5±8.8	32.1±16.0

2.3. Spectral-spatial RF

For high-field MR systems, the RF power required to obtain the desired flip angle during excitation increases. For the 7 T scanner, even with an efficient transmit coil, specially designed RF pulses with low peak power and sufficient bandwidth to include all metabolites of interest are required. In addition, to address the nonuniform B1 excitation at 7 T due to dielectric and wavelength effects, the SSRF was designed with adiabatic characteristics, allowing the proper PRESS selection as shown in Fig. 1. SSRF pulses with a sweep width of 712 Hz, duration of 30 ms and peak power of 0.18G were created using the methodology proposed by Cunningham et al. [11]. The spectral envelop of the RF was a hyperbolic-secant, and the spatial subpulses are of Gaussian shape, which has a time bandwidth product of 3.5. The spectral window was centered between Creatine (CR) and N-Acetyl Aspartate (NAA), which is wide enough to cover metabolites of current clinical interest from Choline (Cho) to NAA. The increased power deposition demanded the increase of TR to 2 s in order to stay within FDA limits. Although this caused a lengthening of scan time, it was necessary not only to stay within Specific Absorption Rate (SAR) limit but also to avoid saturation as the T_1 of metabolites lengthen with increased field strength.

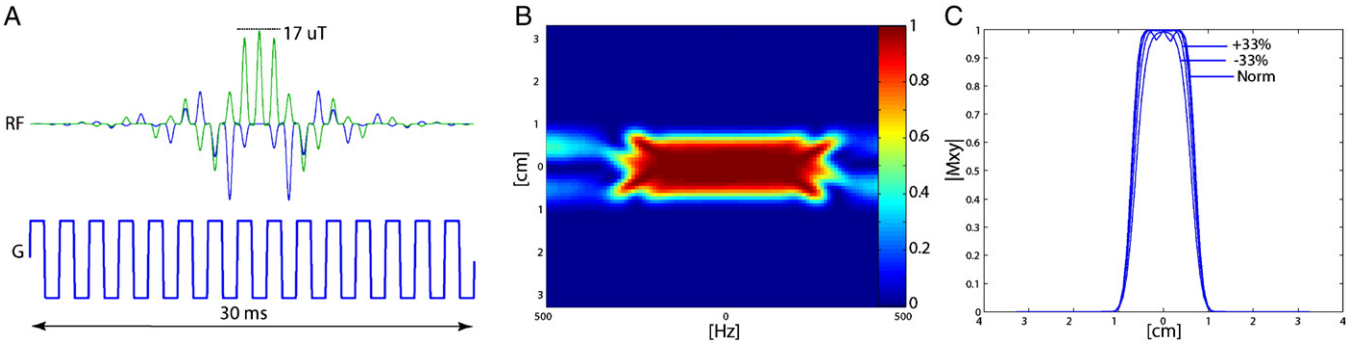

Fig. 1. (A) A partially adiabatic SSRF pulse for 7T acquisitions. Blue and green lines are the real and imaginary components, respectively. (B) Simulated spectral vs spatial profile (180° flip angles) shows an absence of chemical shift misregistration. (C) Spatial profile for RF amplitude of ±33% showing adiabatic behavior showing only slight changes in profile. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.4. Very selective saturation pulses

Due to peak B1 and SAR requirements of the high field system, the very selective suppression pulses [12] had to be specially designed for this 7 T MRSI study as well as the SSRF pulses. Six, fixed 40mm wide very selective saturation (VSS) bands with 0.12G peak B1 and bandwidth of 5868 Hz were placed around PRESS box for approximately 1000-fold out-of-volume suppression and to sharpen the edges and reduce chemical shift misregistration for the PRESS-selected volume. It has much higher bandwidth than Le Roux's original design [13], thus providing spatial profile with higher selectivity.

3. Results

Excellent-quality 3D MRSI data were acquired from normal volunteers utilizing the specialized 7 T PRESS MRSI sequence incorporating the novel RF pulses described above. The MRSI data from a total volume of 168 cm^3 in Fig. 2 demonstrates the uniformity, high SNR and minimal chemical shift misregistration provided by the new SSRF and VSS pulses designed for this study. Similar to MRSI acquisitions at lower fields, the employment of VSS pulses were important for obtaining PRESS selection with sharp edges. The SNR and linewidth numbers are reported in Tables 2 and 3 by axial slice.

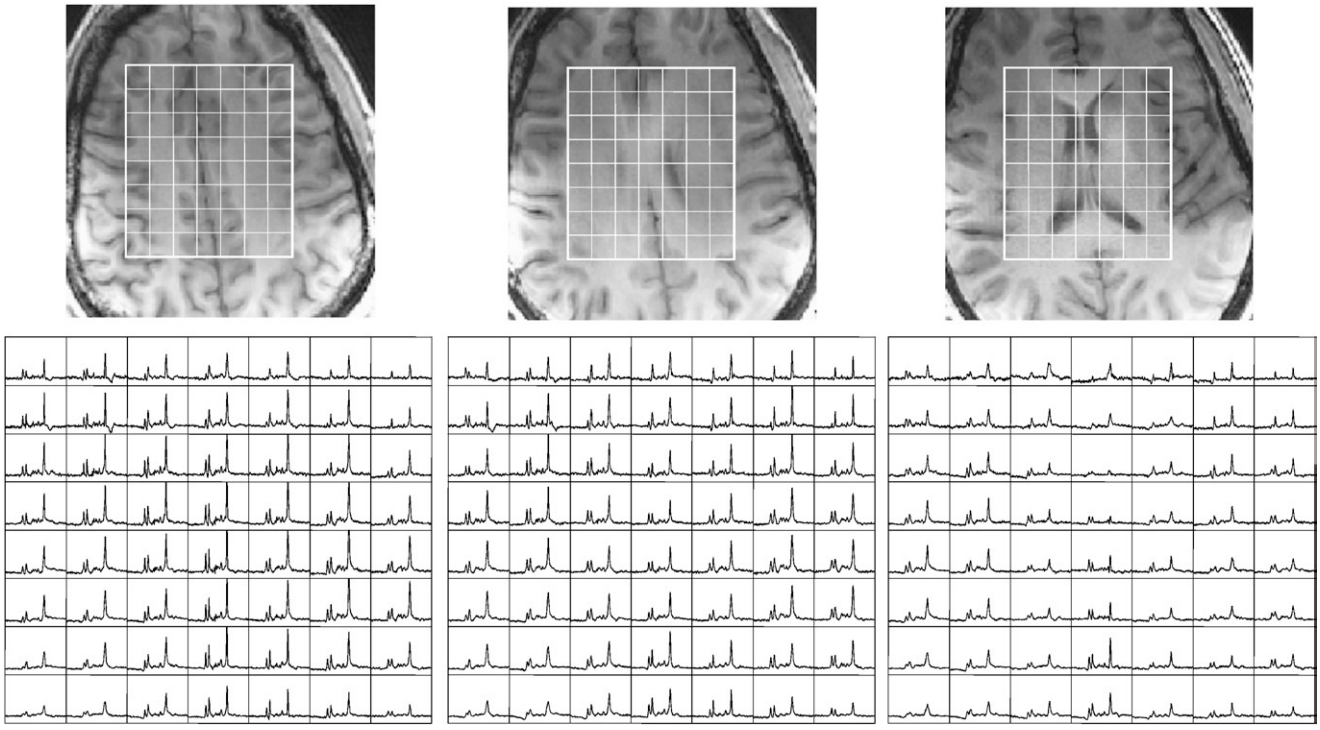

Fig. 2. 1cc 3D MRSI of the brain using SSRF with VSS. It demonstrates good quality spectra but variable linewidth due to residual B0 inhomogeneity.

Table 3
SNR for 1 cc acquisitions

	Cho		Cr		NAA	
	144 ms	35 ms	144 ms	35 ms	144 ms	35 ms
Slice 1	54.7±20.5	103.0±27.4	69.7±17.8	167.1±43.2	164.1±30.3	278.5±71.3
Slice 2	57.3±29.2	92.9±30.5	74.5±28.4	141.0±53.2	154.3±50.5	202.1±69.6
Slice 3	34.2±19.1	61.3±26.0	43.9±22.0	94.5±45.0	89.5±39.7	127.8±65.0

Although only longer echo times are achievable with the 30 ms SSRF pulses, Fig. 3A demonstrates the Glx peak at long TE, in comparison with the short TE acquisition shown in Fig. 3B.

Acquisitions of high spatial resolution 3D-MRSI (7 mm per size, 0.34 cm^3) at short TE were also shown to be feasible at 7 T. A selected voxel is demonstrated in Fig. 4A. The following SNR and linewidth numbers are for the short TE acquisitions. Choline had a linewidth of 9.6±4.5 Hz and an SNR of 15.9±6.4; creatine had a linewidth of 14.3±3.2 Hz and an SNR of 34.8±12.8; NAA had a linewidth of 17.9± 5.3 Hz and an SNR of 54.9±19.0.

4. Discussion

With the recent nonsignificant risk classification of 7 T MRI scanners by the US Food and Drug Administration, ultra-high-field in vivo MR images and functional data with improved SNR and susceptibility contrast have been demonstrated at various institutions [14–16]. However, hardware and acquisition changes are necessary to accommodate the increased field strength [17,18]. For MR spectroscopic acquisitions at high field, enhanced sensitivity to magnetic susceptibility and uniformed excitation are two major fundamental challenges. Peak and average RF power requirements and coil performance issues also compound the acquisition process. Due to these challenges, prior 7 T MRS studies have focused single voxel acquisitions of relatively large 8-cm^3 voxel sizes [5–7,19] or 2D acquisitions [20,21]. This approach has limited value for many applications due to the small spatial coverage across the brain and large voxel size. In this article, we demonstrated the feasibility of acquiring 3D MRSI of the human brain at 7 T using SSRF and regular SLR with respective advantages and disadvantages.

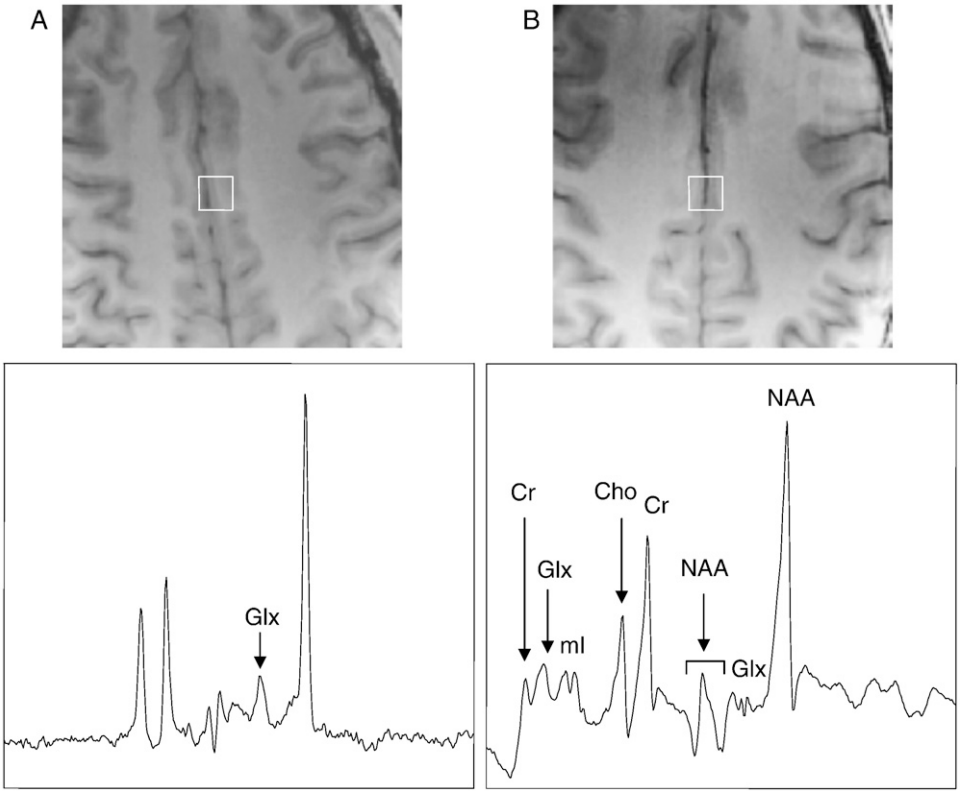

Fig. 3. Spectra obtained using SSRF with TE 144 ms (A) and SLR with TE 35 ms (B) at 1 cc resolution and TR 2 s. 8×8×8 with elliptical k-space sampling. Total time of 17.5 min.

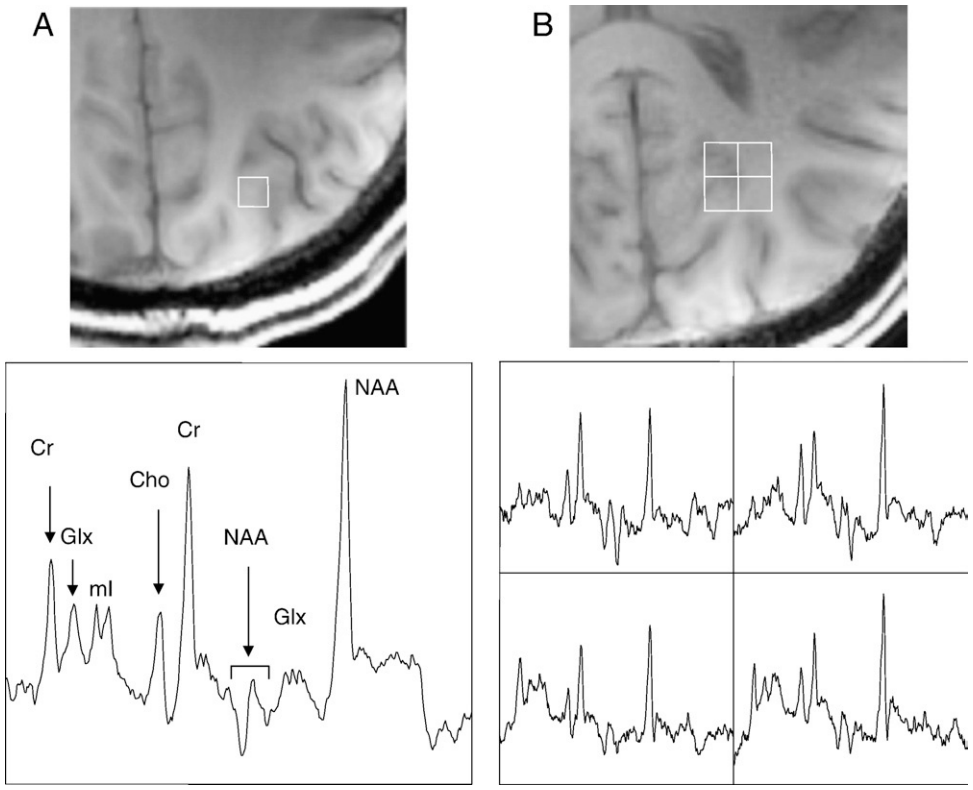

Fig. 4. 0.35 cc spectra with TE of 35 ms and TR 2 s. 8×8×8 phase encoding for a total acquisition time of 17.5 min. The array (B) demonstrates the gray and white matter metabolite concentration differences, in which choline is higher in white matter.

A method employed by previous MRSI studies at lower fields to minimize the chemical shift artifact is to over prescribe the volume (OVERPRESS) and utilize VSS pulses to sharpen the edges of the PRESS-selected volume and saturate the outside [12]. With the increased field, power of these VSS is becoming an issue as each surface of the box required at least one pulse and additional ones if graphic saturation were prescribed. This required the redesign and implementation of optimized VSS pulses for 7 T MRSI. Using tools offered from the Electrical Engineering Department at Stanford University, a set of 0.12G peak power VSS were designed and implemented for the use at 7 T. Based on visual inspection, it showed excellent spatial profile, yielding sharp edges for the PRESS selection. This is critical because no matter whether SSRF or SLR pulses were employed to select the PRESS volume, the high bandwidth, small transition band VSS pulses were required for out-of-volume suppression, sharpening the selected region and reducing chemical shift misregistration.

The use of SSRF is important due to the larger bandwidth requirement of the pulses to limit chemical shift artifact, which can be used in conjunction of OVERPRESS. The SSRF employed in this study also has adiabatic properties, which allowed the acquisition to be much less sensitive to nonuniform excitation. The symmetric sweep property of the SSRF yielded B1 insensitivity; therefore, spectra remained consistent across the PRESS selection and all voxels were considered in the analyses. The customized low peak power and low SAR VSS pulses were also very important. At lower field, this may not be a concern because the SAR limit would allow multiple VSS to be played. However, at 7 T, under a reasonable TR, only one VSS per band can be played within the SAR limit.

The linewidths in this 3D MR spectroscopic imaging study were higher than previously reported for single voxel 7 T MRS studies [6], due presumably to the much larger spatial coverage and increased B0 inhomogeneities for the MRSI data. The variation in spectral linewidth due to nonuniformity in the field may be improved by future improvements in higher-order shimming hardware and software. Increased linewidths were observed near the edge of PRESS volume due to residual B0 inhomogeneities after higher-order shimming.

The SSRF pulses provided the major advantage of having large bandwidth and adiabatic properties. This allowed high-quality MRSI data to be acquired over a large 3D volume in the brain. However, a limitation to these pulses is the requirement of longer TE acquisitions due to the pulse length of the SSRF pulses. The two SSRF 180° pulses were each 30 ms long compared to the 6.5-ms pulse length of the SLR pulses. The SLR pulses allowed a TE of 35 ms, in which short T_2 metabolites were clearly observed. Due to modulation at higher field and properties of the SSRF, even at long TE, the Glx peak was clearly

detected in the volunteer studies, shown in Fig. 3A. Simulation has shown this peak is primarily Glu at this TE [22]. This may be of clinical interest, as Glu is readily detectable without editing techniques at 7 T. Other short TE metabolites may also be visible, but due to the limited sweep width of the SSRF, they are not seen. Further studies are required to determine the modulation and corresponding modifications to the acquisition, which may further improve the visualization.

These initial 3D MRSI investigations of the human brain at 7 T highlighted the need of optimal higher-order shimming to address B0 variability across the volume. The top slice above the ventricle had the best shim, which can be observed visually and confirmed by the linewidth and SNR computed from the peak heights of the metabolites. The slices near and at the level of the nasal sinus air-tissue interface (moving from slice 2 to slice 3) showed worse SNR and larger linewidth due to high level of magnetic susceptibility. It is especially clear towards the edges of the PRESS box because the higher-order shim region was manually selected, with an ellipsoid covering most of the selection. The most inferior axial slice demonstrated the worst shim as it was the closest to the air–tissue interface and the resultant magnetic susceptibility shifts.

This initial investigation incorporated the design and application of new specialized RF pulse designs for obtaining high-spatial-resolution 3D MRSI at 7 T from large selected volumes with increased B1 insensitivity and reduced chemical shift misregistration. The results of this study demonstrated the feasibility of this method to study metabolite distributions at 7 T and highlighted the benefit of higher-order shimming, low-power very selective suppression pulses and custom designed RF excitation pulses.

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