

# Towards $^1\text{H}$ -MRSI of the human brain at 7T with slice-selective adiabatic refocusing pulses

Tom W. J. Scheenen · Arend Heerschap ·  
Dennis W. J. Klomp

Received: 13 July 2007 / Revised: 14 November 2007 / Accepted: 15 November 2007 / Published online: 22 January 2008  
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## Abstract

**Objective** To explore the possibilities of proton spectroscopic imaging ( $^1\text{H}$ -MRSI) of the human brain at 7 Tesla with adiabatic refocusing pulses.

**Materials and methods** A combination of conventional slice selective excitation and two pairs of slice selective adiabatic refocusing pulses (semi-LASER) results in the formation of an echo from a localized volume. Depending on the used radio frequency (rf) coil efficiency and available rf power, the duration of the adiabatic full passage pulses (AFPs) is adapted to enable echo times down to 50 ms (head coil) or 30 ms (local surface coil).

**Results** An AFP duration of 5 ms with a corresponding bandwidth of 5.1 kHz resulted in a chemical shift displacement error of 23% over 3.8 ppm at 7T. Using a local surface coil and an echo time down to 30 ms, we detected not only the three main metabolites (NAA, Cr and Cho), but also coupled signals from myo-inositol and glutamate/glutamine in spectra from 0.14 cc voxels with linewidths down to 10 Hz in 10 min measurement time.

**Conclusions** The semi-LASER pulse sequence enables  $^1\text{H}$ -MRSI of the human brain at 7T for larger parts of the brain as well as small localized areas with both a high spectral and spatial resolution.

**Keywords** Spectroscopic imaging · Chemical shift displacement error · Adiabatic pulses

## Introduction

Proton MR spectroscopic imaging (MRSI) [1] is the method of choice to detect the spatial distribution of metabolites in the human brain. As both the signal-to-noise ratio (SNR) and chemical shift dispersion are proportional to the main magnetic field strength, the highest available field strength should be used for best performance. 7 Tesla (T) MR systems for human applications are becoming available to the scientific community, with most of the initial research efforts focusing on studies of the brain. Apart from the advantages, some known limitations of human studies at this field strength need to be addressed.

First of all, the linear increase in chemical shift dispersion (in Hz) with field strength forces the bandwidth of excitation and refocusing pulses to increase with field strength, too, maintaining an acceptable chemical shift displacement error (CSDE). This CSDE can be defined as the difference in location of the centre of the excitation or refocusing slices of two resonances with a different chemical shift, proportional to their slice thickness. The combination of radio frequency (rf) power and rf coil-efficiency dictate the duration (and obviously amplitude) of excitation and refocusing pulses, and thereby their corresponding bandwidths. Already at 3T, rf peak powers of up to 35 kW are insufficient to obtain an acceptably low CSDE for refocusing pulses (like MAO optimized 180 degree pulses [2]) using a body rf coil for transmitting. When assuming an equal rf setup for 7T (which is not even common), the conventional rf pulse durations need to increase, leading to smaller instead of larger bandwidths, causing an unacceptably large CSDE. The CSDE of a

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Part of this work has been presented at the ISMRM-ESMRMB joint meeting in 2007 in Berlin, Germany, abstract number 43.

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T. W. J. Scheenen (✉) · A. Heerschap · D. W. J. Klomp  
Department of Radiology (667), University Medical Center,  
Nijmegen Geert Grooteplein 10, 6525 GA,  
Nijmegen, The Netherlands  
e-mail: T.Scheenen@rad.umcn.nl

Mao-optimized  $180^\circ$  pulse [2] with a hypothetical duration of 10 ms (already challenging duration at 7T) and corresponding bandwidth of 0.52 kHz would be larger than 217% over 3.8 ppm, the spectral range of interest in proton spectroscopy from water at 4.7 ppm to lipid  $\text{CH}_3$  at 0.9 ppm.

Secondly, the transmit  $B_1$  field is inhomogeneous, leading to poor slice selection profiles when using conventional rf pulses. Accurate volume selection using slice selective rf pulses is a prerequisite for  $^1\text{H}$ -MRSI of the brain in order to exclude contamination with large lipid signals from the skull, or water signals from poorly shimmed regions outside the selected volume. Conventional slice selective rf pulses are optimized for the desired flip angles within the slice and negligible flip angles outside the slice using the non-linear Bloch equations [3]. Large deviations from the intended flip angle due to inhomogeneous transmit  $B_1$  fields not only cause signal attenuation, but may also increase the side lobes of the slice profile, leading to unwanted non-zero flip angles outside the selected volume [4,5]. In addition, when strongly coupled spin systems are observed in spin echo experiments, the spectral shape of the corresponding signals can vary, depending on the local flip angle of the refocusing pulses [6].

Thirdly, rf pulses at higher frequencies deposit more rf power. All pulse sequences need to be designed in such a way that the head or body absorbs no more than the corresponding limit in specific absorption rate (SAR) of electromagnetic energy. This limits both the amount of rf pulses per unit time, and the amplitudes and durations of these rf pulses.

Two of the afore-mentioned limitations can be handled by the use of adiabatic pulses. These pulses have relatively high bandwidths and their flip angles are insensitive to transmit  $B_1$ -inhomogeneities. In addition, adiabatic refocusing pulses have sharp slice selection profiles to produce a localized spin echo. With the semi-LASER pulse sequence [7]—a hybrid of conventional excitation and full localization by adiabatic selective refocusing [8]—the volume of interest (VOI) of the MRSI experiment is defined with conventional slice-selective excitation and two orthogonal pairs of slice-selective adiabatic refocusing pulses. After a sharp definition of the VOI, accurate localization of metabolite signals is performed with a combination of elliptical k-space sampling and apodization of k-space before Fourier transformation, reducing voxel bleed to a minimum, while sensitivity is maintained [9].

In this work, we explore the possibilities of the semi-LASER pulse sequence for 3D  $^1\text{H}$ -MRSI of the human brain at 7T with a volume head-coil and with a local surface coil. Localization and excitation profiles of the pulse sequence were tested with phantoms. By adapting adiabatic rf pulse durations to an efficient local transmit receive coil, one can perform 3D  $^1\text{H}$ -MRSI of a small part of the brain with an echo

time of 30 ms with an acceptable CSDE, remaining within SAR limits.

## Materials and methods

### Subjects and instrumental set-up

Two healthy, fully informed and aware volunteers were examined on a 7T whole body MR system (Siemens Medical Solutions, Erlangen, Germany): one with a transmit receive circularly polarized (CP) head coil (Invivo corporation, Orlando, USA), and the other with a home-built transmit receive surface coil with a diameter of 6 cm.

### Pulse sequence

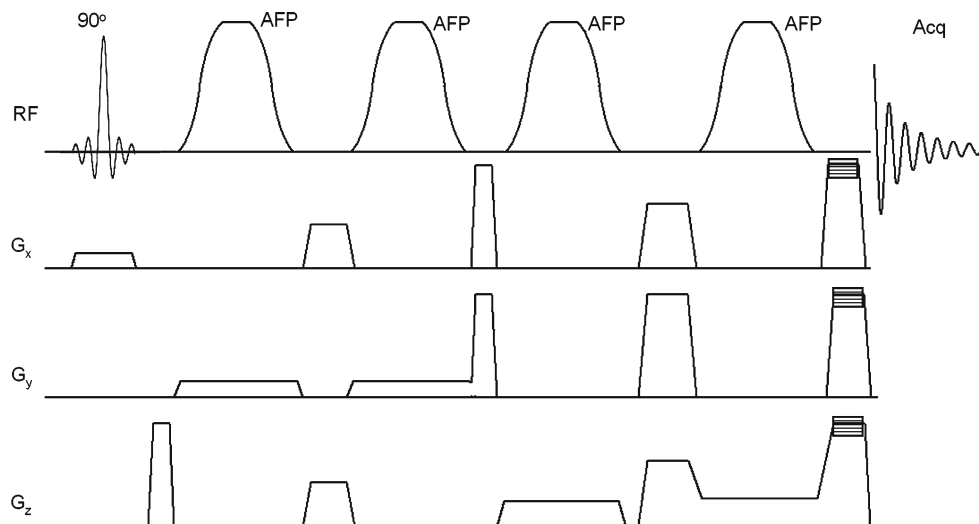
The rf core of the semi-LASER pulse sequence [7] consists of slice-selective excitation of the spins with a Shinnar–Le-Roux optimized  $90^\circ$  pulse and perpendicular slice selective refocusing of the spins by two pairs of adiabatic full passage (AFP)  $180^\circ$  pulses. The amplitude and frequency modulations ( $\gamma B_1(t)$  and  $\Delta\omega(t)$ ) of the second-order hyperbolic secant adiabatic pulses with duration  $T_p$  were created with the following equations using a time bandwidth product of 26 (10):

$$\gamma B_1(t) = \gamma B_1^{\max} \operatorname{sech}(\beta\tau^2) \quad (1)$$

$$\Delta\omega(t) = \frac{26\pi}{T_p} \int \operatorname{sech}^2(\beta\tau^2) d\tau \quad (2)$$

with  $\tau = 2t/T_p$  defined in the interval  $-1 \leq \tau \leq 1$ , and  $\operatorname{sech}(\beta) = 0.01$ . When used in pairs the coherent phase evolution during the first adiabatic pulse is exactly restored with the second pulse, resulting in in-phase refocusing [8]. The rephasing gradient compensating the dephasing second half of the slice-selection gradient during excitation is merged with the third crusher gradient in the corresponding direction. Positioning the crusher gradients, which suppress spurious echoes and unwanted FIDs, is done symmetrically around every AFP in one direction. Around the final AFP pulse large crusher gradients are applied in all directions. Phase-encoding gradients in 2 or 3Ds are superimposed on the final crusher gradient before signal reception (Fig. 1).

The water signal is suppressed by a slightly modified WET (water suppression enhanced through  $T_1$  effects) scheme [11]. With the transmit receive surface coil, the maximum available rf transmit power easily allowed an AFP pulse duration of 5.0 ms, with a resulting bandwidth of 5.1 kHz and a minimum pulse sequence echo time of 30 ms. Shorter pulse durations with corresponding higher amplitudes would cause large experimental repetition times to remain within SAR



**Fig. 1** The core of the semi-LASER spectroscopic imaging pulse sequence. Crusher gradients are positioned around every adiabatic full passage (AFP) pulse, with the largest pair around the final AFP pulse. Phase-encoding gradients in 2 or 3Ds are superimposed on the final crusher gradient

limits. The AFP pulse duration for the CP head coil was 10 ms, limited by maximum rf transmit power, resulting in a bandwidth of 2.5 kHz and an echo time down to 50 ms.

#### Phantom measurements

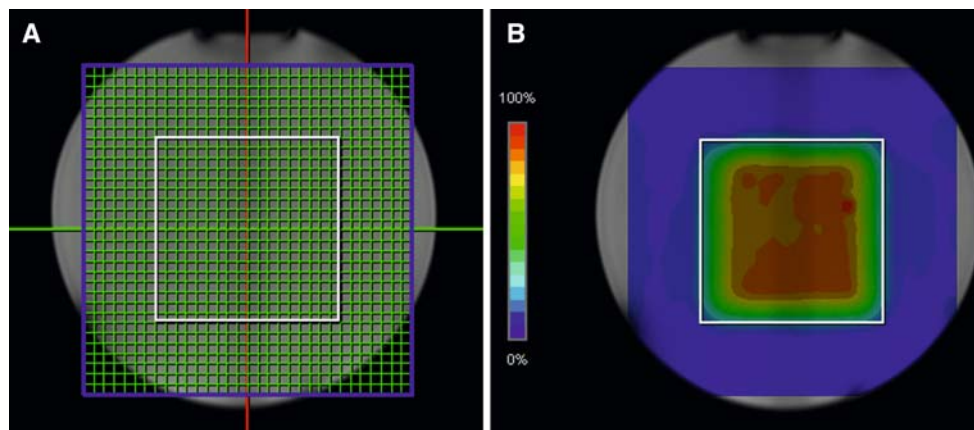
A spherical phantom (diameter 17 cm) containing BAYOL-oil (Siemens Medical Solutions) with a single resonant signal was measured with the CP head coil. Three perpendicular localizing gradient echo images (repetition time (TR) 20 ms, echo time (TE) 5 ms, voxel size  $1.1 \times 1.1 \times 10$  mm, field of view (FOV)  $280 \times 280$  mm) were sufficient to serve as background images to localize the MRSI matrix. The 2D semi-LASER experiment had the following parameters: carrier frequency at the oil singlet signal, FOV  $144 \times 144$  mm, matrix size  $20 \times 20$ , volume of interest (VOI)  $80 \times 80$  mm, slice thickness 10 mm (selected with the excitation pulse), acquisition bandwidth 2,000 Hz, 512 spectral data points, 1 average with an elliptical k-space sampling, TR 1.89 s, TE 51 ms, total measurement time 8 min. After Hamming filtering and zero-filling to a  $32 \times 32$  k-space matrix, Fourier transformation of spatial and spectral dimensions was done with the Siemens Syngo software. The oil singlet was fitted with a Lorentzian line shape.

#### Volunteer measurements

For an anatomical overview of the brain of the volunteer we acquired axial high resolution  $T_2$ -weighted turbo spin echo (TSE) images (effective TE 89 ms, TR 4.05 s, field of view FOV  $220 \times 197$  mm, matrix size  $448 \times 322$ , resolution  $0.49 \times 0.61$  mm, 11 slices, thickness 3 mm) with the CP head coil. Hyperechoes were used to reduce rf power depo-

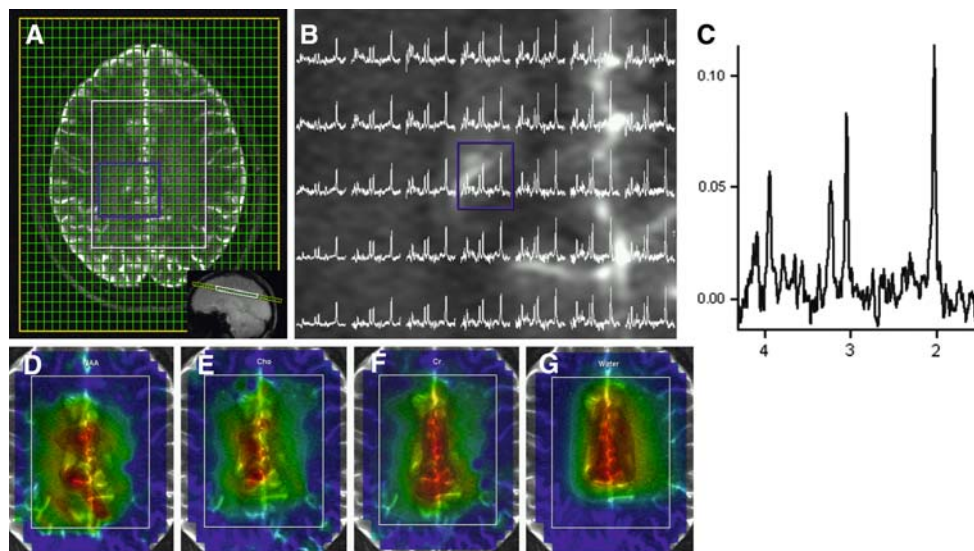
sition [12]. The subsequent 2D MRSI data set was acquired with these axial  $T_2$ -weighted images as background images. Slice selection of the axial plane was done with the excitation pulse. Parameters for the MRSI experiment: carrier frequency at 3.0 ppm, TR 1.75 s, TE 50 ms, FOV  $192 \times 160$  mm, matrix size  $24 \times 20$ , VOI  $90 \times 70$  mm, slice thickness 8 mm, acquisition bandwidth 2,000 Hz, 1,024 spectral data points, 1 average with an elliptical k-space sampling, total measurement time 9 min. An unsuppressed water reference data set was also acquired to illustrate the CSDE of the water signal. After an automated map shim of the VOI, the linear shim values were further adjusted manually towards the smallest linewidth of the VOI. With the TR of 1.75 s these measurements were done at the system calculated SAR limit for the head of 3.2 W/kg.

In the examination of the second volunteer we positioned a surface coil over a part of the temporal and parietal lobe of the brain, approximately 5 cm behind and above the left ear. The volunteer was measured in right lateral position in the magnet. The examination consisted of a dual echo time fast spin echo imaging series (TE 11 and 95 ms, TR 2 s), followed by 3D MRSI with the semi-LASER sequence with the following parameters: carrier frequency at 2.7 ppm, TR 2.4 s, TE 30 ms, FOV  $36^3$  mm<sup>3</sup>, matrix size  $10^3$ , VOI  $20^3$  mm<sup>3</sup>, acquisition bandwidth 2,000 Hz, 1,024 spectral data points, 1 average with an elliptical k-space sampling, total measurement time 10:22 min. The  $90^\circ$  pulse was chosen to selectively excite the plane parallel to the coil conductors; the refocusing pulses were slice selective in the other two directions. Concurrent temperature measurements at the skin closest to the capacitors of the coil with two fiber-optic thermometers guaranteed a safe use of this coil. The measured temperature increase was never more than 0.5°C.



**Fig. 2** Localization and excitation profile of semi-LASER  $^1\text{H}$ -MRSI in an oil phantom at 7T. The white box in **a** represents the VOI of the MRSI experiment, the blue box is the size of the FOV. The gradient

echo image is overlaid with a color-coded image of the integral of a Lorentzian fit to the oil resonance, showing an exact match of excited signal and VOI



**Fig. 3** 2D  $^1\text{H}$ -MRSI of the brain of a healthy volunteer at 7T. In **a** the 2D FOV of the MRSI matrix is outlined in yellow (VOI in white) and overlaid on a transverse  $T_2$ -weighted TSE image. In the sagittal image inset, the position of this slice in the brain is indicated. The spectra from voxels inside the blue box are overlaid onto the  $T_2$ -weighted image in

a spectral map **b** with range 1.5–4.3 ppm. The spectrum of the centre voxel of the spectral map (blue voxel) is enlarged in **c**. Color-coded overlays of the integral of Lorentzian fits to *n*-acetylaspartate (NAA), choline (Cho), creatine/phosphocreatine (Cr) and water are shown in **d** to **g**

From all MRSI measurements the spatial dimensions were filtered with a Hamming filter and zero-filled to the nearest power of two before Fourier transformation. Lorentzian line fitting to either the unsuppressed water signal or metabolite signals in the spectra was performed with the Siemens Syngo software.

## Results

As the oil phantom did not contain electrolytes, it did not disturb  $B_1$  homogeneity. The accurate localization and slice

selection of the semi-LASER sequence in this situation is illustrated by an overlay of the integral of the Lorentzian line fit to the oil resonance of every voxel over the gradient echo localizer images (Fig. 2b).

The AFP pulse duration attainable with the CP head coil was 10 ms (corresponding to  $\gamma B_1 = 650$  Hz), the corresponding bandwidth of the pulse was 2.5 kHz, resulting in a CSDE of 45% over 3.8 ppm. The water signal slice locations (offset 1.7 ppm from carrier frequency) were displaced by 20% of their thickness (Fig. 3g). Although the non-uniform reception profile of the coil resulted in increased signal intensities in the centre of the head (Fig. 3b, d, g), the  $^1\text{H}$ -range of

interest from the lactate signal at 1.3 ppm to the myo-inositol signal at 4.1 ppm was equally excited in 67% of the voxels in both directions of the 2D matrix (Fig. 3b). The linewidth at half maximum of the magnitude spectrum of the total VOI was 29 Hz, phased spectra of individual voxels had varying linewidths down to approximately 9 Hz (voxels in centre of the head, Fig. 3c).

Imaging with conventional pulse sequences with the local surface coil is a challenge. As none of the used rf pulses are adiabatic, only a narrow band at a specific distance from the coil conductors of the surface coil experiences the desired flip angle for the pulses in the used spin echo sequence (Fig. 4b, c). With this coil, AFP pulse durations of the semi-LASER spectroscopic imaging sequence could be reduced to 5 ms (corresponding to  $\gamma B_1 = 1,300$  Hz), resulting in bandwidths of 5 kHz, and a CSDE of 23% over 3.8 ppm. Although excitation with semi-LASER was non-adiabatic, we still managed to collect spatially resolved spectra from small voxels down to  $3.6 \times 3.6 \times 3.6 \text{ mm}^3$  (before apodization) from a box close to this coil (Fig. 4d, e). The true resolution of this measurement including a broadening factor of 1.78 is best approximated by a sphere with a volume of 0.14 cc. Spectral quality is excellent, common signals from *n*-acetylaspartate (NAA), choline (Cho) and creatine/phosphocreatine (Cr/PCr) are present throughout the VOI, but also myo-inositol (Ins) and glutamate/glutamine (Glu/Gln) signals can be discerned in these small voxels (Fig. 4f). Residual lipid signals were present in some voxels, but were small enough not to interfere with the NAA signal at 2.04 ppm. The linewidth at half maximum of the magnitude spectrum of the total VOI was 28 Hz, phased spectra of individual voxels had varying linewidths down to approximately 10 Hz (Fig. 4f).

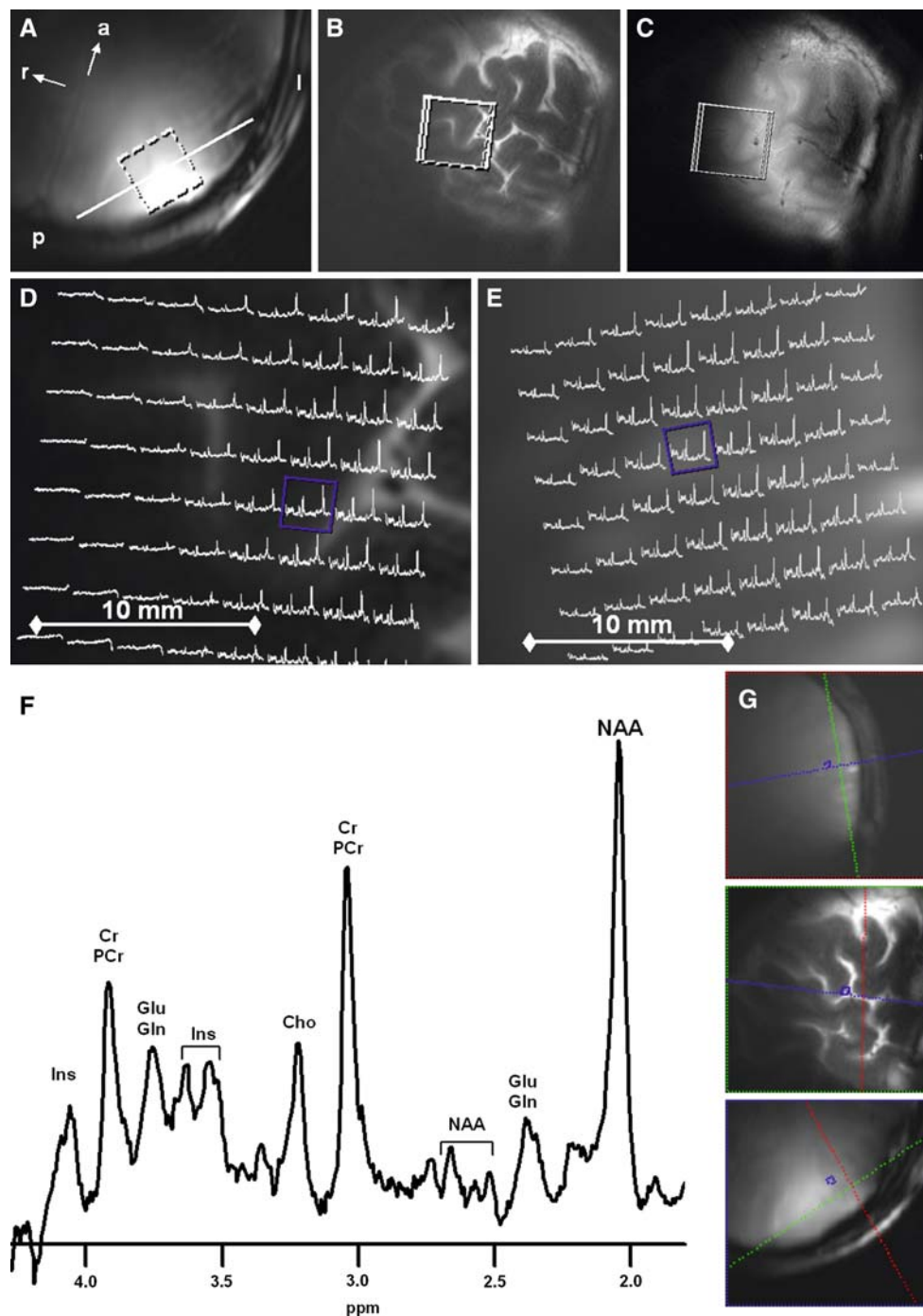
## Discussion

In this study, we present the first results of  $^1\text{H}$ -MRSI of the human brain with adiabatic refocusing pulses at 7T. VOI selection with the semi-LASER sequence keeps the chemical shift displacement error to an acceptable size. Due to the available rf power and increased chemical shift dispersion at 7T, slice selection with conventional rf pulses would cause enormous CSDEs (>217% over 3.8 ppm). The semi-LASER sequence produces very useful spectra at an echo time of 50 ms over larger regions of the brain with a CP coil, or from a small part of the brain at TE 30 ms with a surface coil. Currently, differences in SNR exist over the VOI due to non-uniform detection as well as non-adiabatic excitation with an inhomogeneous transmit  $B_1$  field. The available RF power, but even more so the SAR limit for the head in combination with the need for an acceptable TR and total acquisition time dictate AFP pulse durations of 10 ms and thereby a minimal echo time of 50 ms with the CP head coil. Measurements with

a small surface coil with shorter pulse durations decrease the CSDE and illustrate that some of the current limitations can be overcome with excitation with a multi-channel transmit–receive head coil with small coil elements and normalization for sensitivity. Having multiple channels available for transmission would open possibilities for  $B_1$  shimming, reducing the amount of deposited rf power for acceptable  $B_1$  transmit profiles. The size of the part of the brain that can reliably be measured and quantified currently depends on the non-adiabatic slice-selective excitation pulse. For full brain applications adiabatic excitation and 3D adiabatic refocusing could be considered (LASER [8]), but the addition of another two adiabatic pulses would have two important implications. The minimal echo time would be prolonged, in the presented experiments from 30 to at least 40 ms for the surface coil, and from 50 to 70 ms or more for the CP head coil. Furthermore, it would also further increase rf power deposition, prolonging the TR to remain within SAR limits. If adiabatic excitation is performed at half the power of a single adiabatic refocusing pulse (i.e., adiabatic half passage) and another pair of AFP pulses is added for full 3D localization, the amount of deposited rf power with LASER would exceed semi-LASER by 58%, demanding an increase in TR of 58% to remain within SAR-limits. RF power deposition of a single adiabatic refocusing pulse is ninefold higher than the conventional slice selective excitation pulse used in this work.

Signals of glutamate, glutamine and myo-inositol were detected in large parts of the VOI, even at the used voxel size of 0.14 cc. The spectral pattern of these strongly coupled spin systems will be different in the semi-LASER sequence compared to conventional PRESS. The four adiabatic RF refocusing pulses can reduce antiphase coherence resulting from J-coupling and therefore improve the spectral shape of coupled spin systems, which has been shown at 3T [13, 14]. As this spectral shape also depends on refocusing pulse angles, the observed constant shape throughout most of the VOI of Glu/Gln and Ins was to be expected, as adiabatic refocusing is insensitive to transmit  $B_1$  inhomogeneities. A detailed analysis of the spectral shape itself of these signals is beyond the scope of this paper. We showed that these signals can be locally detected in 0.14 cc voxels of a 3D MRSI matrix with an acceptable CSDE in approximately 10 min at 7T.

Shimming the main magnetic field in the VOI is extremely important to achieve a high spectral quality. Although in this study only first order shim values were manually optimized after an automatic 3D phase map shim of first and second order, we were able to reach linewidths down to 9 Hz of phased spectra from individual voxels. When moving from 1.5 to 3T, average linewidths from signals of different metabolites and different voxels in an MRSI experiment have been reported to increase from 3.5 to 6.1 Hz [15]. Our preliminary data indicate that this increase in linewidth does not scale linearly with field strength, which has been suggested



**Fig. 4** MRI and 3D  $^1\text{H}$ -MRSI of a small part of the brain of a healthy volunteer with a local surface coil at 7T. In an axial gradient echo localizer image (**a**; r,l,a,p is right, left, anterior, and posterior, respectively) the plane of the spin echo images parallel to the coil conductors (**b**, TE 95 ms and **c**, TE 11 ms) is indicated with the *white line*. The VOI of the 3D MRSI matrix is indicated with the *white box* in **a–c**. In two perpendicular spectral maps of the VOI of the 3D MRSI matrix the spectra are displayed from 1.8 to 4.3 ppm. In a plane perpendicular to the coil **d** the signal decreases with distance to the coil, mainly because

of the  $B_1$  reception profile. In a plane almost parallel to the coil **e**, the intensities of the different signals in the spectra are more homogeneous throughout the VOI. Voxels largely overlap, as the true size of a voxel is approximated by a 3.2 mm-radius sphere. The SNR of a single spectrum of the 3D dataset (location illustrated in **g**) still allows the identification of many different metabolite signals **f**. Spectral postprocessing consisted of apodization (400 ms Hamming window centered at 0 ms), Fourier transformation and manual zero-order phase correction

in literature [15, 16]. The available SNR at 7T within acceptable measurement times enables voxel sizes in MRSI to decrease, which could result in smaller linewidths. Optimized automatic shim algorithms could further improve, or at least speed up, the shimming procedure before the MRSI measurement.

## Conclusions

We presented 2D and 3D  $^1\text{H}$ -MRSI of the human brain at 7T with acceptable chemical shift displacement errors. By moving to smaller coil elements pulse durations can become short enough to enable 3D localized  $^1\text{H}$ -MRSI at an echo time of 30 ms with multiple adiabatic refocusing pulses. With a CSDE of 30% over 5 ppm an uncontaminated spatial resolution of 0.14 cc was attained. This opens up the possibility for detailed spatial metabolic exploration of the human brain at this field strength.

**Acknowledgments** We thank Mark Ladd and David Norris (Erwin L. Hahn Institute for Magnetic Resonance Imaging, Essen, Germany) for the possibility to work on the 7T MR system, and Karsten Wicklow and Ulrich Fontius (Siemens Medical Solutions, Erlangen, Germany) for their help with hardware and imaging pulse sequences. This work was supported by a grant (916.56.036) of The Netherlands Organisation for Health Research and Development (ZonMw).

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