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Author/s:

Ordidge, R;Cleary, J;Glarin, R;Blunck, Y;Farquharson, S;Moffat, B

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Ultra-High Field Magnetic Resonance Imaging using Composite RF (STEP) Pulses

Ordidge R*, Cleary J*, Glarin R*, Blunck Y*, Farquharson S⁺, Moffat B*

*Melbourne Brain Centre Imaging Unit, University of Melbourne, Australia, ⁺

Florey Institute for Neuroscience and Mental Health, Melbourne, Australia

ABSTRACT

Ultra-high field MRI offers many opportunities to expand the applications of MRI. In order for this to be realized, the technical problems associated with MRI at field strengths of 7 Tesla and greater need to be solved or mitigated. This paper explores the use of new variations of composite RF pulses, named Serial Transmit Excitation Pulses (STEP), in contrast to parallel pulse techniques, in order to remove and/or mitigate the effects of non-uniform B_1 excitation fields associated with the subject (e.g. the human brain). Several techniques based on STEP sequences are introduced and their application to human brain imaging is presented and evaluated.

CORRESPONDING AUTHOR

Professor Roger Ordidge, Melbourne Brain Centre Imaging Unit, Kenneth Myer Building, 30, Royal Parade, University of Melbourne, Parkville, Vic 3010, Australia.

Email: roger.ordidge@unimelb.edu.au

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LIST OF ABBREVIATIONS

STEP: Serial Transmit Excitation Pulses

MRS: Magnetic Resonance Spectroscopy

3D-FLAIR: 3 Dimensional Fluid Attenuated Inversion Recovery

SAR: Specific Absorption Rate

DWI: Diffusion-Weighted Imaging

KEYWORDS

RF pulse design; Brain imaging; Ultra-high field; B_1 inhomogeneity correction; B_0 inhomogeneity correction; Other applications.

BACKGROUND

Magnetic Resonance Imaging (MRI) at high magnetic fields (e.g. 7 Tesla (7T) and above) provides unprecedented detail of the human brain but there is a need to deal with the challenges posed by fundamental physics when moving to ultra-high magnetic fields (1,2). The main difficulties arise from the wide variation in the strength of the exciting B_1 field at these higher resonant frequencies. Despite many already promising clinical imaging applications on 7T systems, additional work is likely to help widen the scope of clinically available applications at 7T. The biggest problem encountered at higher magnetic fields, other than cost, is the non-uniform RF fields used for excitation that exist at 7T and above, caused by the electrical properties of the body at the higher RF frequencies associated with the higher fields (3). Non-uniformity is also inherent when using surface RF coils for transmission of the excitation pulse at lower field strengths (4). Ideally, the RF excitation pulse should typically deliver a 90° , 180° or other desired rotation (“flip”) of the nuclear magnetization vector to provide the maximum signal strength over the dimensions of the sample (e.g. the human head). In practice the RF field might

typically vary at 7T by a factor of three or more, causing loss of both signal strength and alteration of image contrast by producing magnetization rotations typically that are far from ideal (usually much less than the ideal excitation). This reduces signal amplitude, produces non-uniform spatially dependent image contrast that is difficult to interpret, and distorts physiological measurements derived from MRI and MRS (5).

One approach to the correction of B_1 non-uniformity has been the implementation of parallel RF transmission through multiple RF coils that surround the object, each of which has a different spatial excitation pattern (6). Computer optimization can then be used to calculate a corrected RF pulse shape for each coil, that when applied simultaneously (in-parallel) counteract this non-uniformity (7, 8). Specialized RF pulse designs such as the multiband Spokes pulses design (9), which uses RF excitation with bi-directional gradient waveforms (10), have shown some promise at resolving this problem. Another approach is to apply volumes of dielectric material that seek to balance the distribution of tissue non-uniformity (particularly tissue voids) within the RF coil so as to generate a more uniform dielectric sample that has properties designed to avoid the generation of non-uniform B_1 fields (11). The use of SERIAL-transmit, parallel-receive MR imaging, where multiple surface coils are used for RF transmission, has also been shown to provide improvements at 9.4T (12). Each of these approaches have disadvantages in terms of complexity and Specific Absorption Rate (SAR) concerns.

Composite RF pulses were proposed for MRS to counteract the effect of these RF non-uniformities by the replacement of a single RF pulse by a series of pulses with multiple excitation angles and optimized phases compared with the on-resonance signal. One original application in NMR spectroscopy was to gain greater signal from the edges of a test tube sitting within a saddle-type RF coil. However, the requirement in MRS to produce signals with phase coherence across the entire sample, required complicated sequences with high RF power requirements and significant sensitivity to off-resonance signals compared to the main operating frequency. An early example of such a sequence for MRS was published by Levitt (13) and uses a 90° - 180° composite pulse, with a phase

shift of greater than 90° between the pulses, ideally 135° . This approach is similar, at least in the ratio of pulse amplitudes to the work currently described. The higher RF power requirements for this and similar sequences, renders such RF sequences difficult to apply to the human brain due to RF heating of the sample (SAR), and also off-resonance effects due to the broad resonance peaks caused by the significant tissue magnetic susceptibility effects observed at higher magnetic fields.

Moore et al. (14) extended the composite pulse principle to include slice selection using field gradients and investigated the use of repetitive trains of pulses of five and eight composite RF pulses to achieve signal excitations of low angles up to 90° . Such RF pulses showed some intolerance to B_1 amplitude at a field strength of 7T in MRI of the human head, which is a primary focus of our current work.

This study aims to improve radiofrequency (RF) excitation homogeneity at high magnetic fields using novel radio frequency (RF) pulse shapes (both 90° and 180° excitations and their use together in a practical spin echo sequence). In this case, the methodology is based on a series of sinc-shaped RF pulses with associated gradient pulse waveforms. Our overall hypothesis was that efficient combinations of traditional RF and gradient waveforms with specific phase offsets would produce more uniform excitation and spin-refocusing throughout the human brain over a wide range of B_1 amplitudes. This in turn would produce improved MRI signal intensity and homogeneity in multi-slice spin-echo imaging of the human brain at ultra-high fields (e.g. 7T). The methodology has recently been patented by Ordidge (15) with the significance that it has the potential to improve image quality and signal strength for high magnetic field MRI scanners at 7T and above.

In MRI, the image is usually reconstructed with a “magnitude” Fourier transformation and the requirement for phase coherence from signal across the whole field of view of the sample is no longer a requirement. Even when phase is important, the phase difference between two co-located pixels in two images (with and without contrast e.g. such as flow encoding) is often the measurement of

significance. Therefore, the inherent phase distribution of the image is not usually of importance, marking a significant difference with MRS, and this principle is exploited in this paper. Either 90° and 180° RF excitation pulses can be used in isolation, and we seek to demonstrate principles on which these pulses can be designed, optimized and used for improvements in head MRI to confirm the practicality of the approach with available hardware at 7T.

With regard to spatially localized MRS (16), including MR Spectroscopic Imaging (MRSI) (17), the phase distribution across the entire sample becomes substantially less important because the important factor is the phase distribution across the localized sample volume, which is usually insignificant. Therefore, newly optimized simpler composite RF pulses can be used to mitigate the effects of RF non-uniformity in most MRI and MRS applications, and this is especially useful in ultra-high (7T) MRI where the effects are much greater.

New variations of composite RF and gradient waveforms have been developed that are designed to be tolerant of RF non-uniformity, show some tolerance to off-resonance signal effects (due to their brevity), and require low or only modest increases in sample heating (SAR, depending on the sequence and settings). The SAR increase approximately doubles comparing 7T and 4T field strengths (18) and, therefore, can be a particular problem at field strengths of 7T and above. We have named these new composite waveforms: composite Serial Transmit Excitation Pulses (STEP) because of the serial nature of combining traditional RF and gradient waveforms. To address the above aims, we present in this paper a theoretical framework, simulation results, and experimental results using this methodology in multi-slice spin-echo imaging of the human brain at 7T.

THEORY

90° Excitation RF Pulse

The use of a composite RF excitation pulse (90° pulse) consisting of two elements in a defined amplitude ratio of 0.5 to 1 (named $\overline{0.5} - 1$: where the bar indicates a phase shift e.g. $\overline{0.5}$ represents a

45° RF pulse with a phase shift of $\pm 90^\circ$) is an example of a pulse that enables effective correction of non-uniform RF excitation over a range of B_1 amplitudes. Such a pulse is shown in Figure 1(A) comprising two block pulses. This RF pulse excites the nuclear magnetization into the transverse plane for a range of macroscopic B_1 field strengths that might be encountered in the human head at 7 Tesla.

Figure 1(B) shows the trajectory and final magnetization position for a non-slice selective 45°-90° excitation (rectangular RF pulses) in the $\overline{0.5} - 1$ composite STEP pulse. Rotation around a B_1 field in the x-axis, is followed by rotation around a B_1 field in the y-axis to cause the final position of magnetization to be in the x-y plane with an attendant B_1 -dependent phase shift relative to both axes.

The effects of RF pulses and gradients were simulated using a purpose-written Matlab program (version R2013b) that used rotation matrices to simulate solutions of the Bloch equations (written in-house) to determine the final effect on a uniform sample and the effect of a range of B_1 amplitudes ($B_1 = 1$ for a 90° sinc excitation). The result for a 90° excitation $\overline{0.5} - 1$ STEP RF pulse is shown in Figure 1(C) where the net magnetization in the transverse plane (M_{xy}) is plotted for increasing B_1 amplitude in the horizontal axis (arbitrary units) after application of a $\overline{0.5} - 1$ STEP pulse (dashed line) and a sinc pulse. (solid line). The simulation was initiated with all magnetization along the +z axis. Three maxima, labeled (1), (2) and (3) for the $\overline{0.5} - 1$ STEP RF pulse show maximal transverse magnetization (M_{xy}) for pulse rotations of 45°-90°, 90°-180° and 135°-270° respectively (all in the ratio 0.5:1) with a minimal reduction in M_{xy} between these rotation conditions. All three of the labelled excitations result in the final magnetization vector being excited exactly by 90° into the transverse (x-y plane) albeit with different final phases in the transverse plane of approximately -45°, 0° and +45°. Relative to a single sinc RF pulse (solid line), the total range of B_1 fields providing a tolerable excitation is corrected by up to three-fold (dependent on choice of acceptable minimum required M_{xy} excitation). At excitation angles between the three conditions mentioned above, the correction is not exact, but there is a distinct improvement on the results from a single RF pulse.

180° Refocusing RF Pulse

A $1 - \bar{1} - 1$ 180° composite STEP pulse is hypothesized to have a superior refocusing performance ability vs. B_1 amplitude since it can be formed by the combination of two 90° excitation composite STEP pulses (the standard STEP pulse and a time reversed STEP pulse;) . Namely:

$$(1 - \bar{0.5}) + (\bar{0.5} - 1) \cong (1 - \bar{1} - 1) \text{Equation (1)}$$

This combination helps to reduce the overall 180° RF pulse to three components rather than four. For rectangular RF pulses, the nominal excitation angles with increasingly high B_1 amplitudes would be 90°-90°-90° ($B_1 = 1.0$); 180°-180°-180° (twice B_1 amplitude), and 270°-270°-270° (thrice B_1 amplitude) all of which cause signal refocusing, giving a modified response versus B_1 field akin to the $\bar{0.5} - 1$ STEP pulse shown in Figure 1(C).

To address the fact that the areas of very low signal intensity in head images correspond to tissue volumes that experience low B_1 fields, it is beneficial to produce RF pulses that give maximum signal from these tissue areas for both the excitation and refocusing RF pulses.

90° – 180°- Spin Echo Sequence

The net signal from a spin-echo signal has been shown to vary according to the function:

$$S = S_0 * \sin(\alpha) * [\sin(\beta/2)]^2 \quad \text{Equation (2)}$$

where α is the excitation angle of the first RF pulse in the spin-echo sequence (nominally 90°) and β is the excitation angle of the refocusing RF pulse in the sequence (nominally 180°) (19).

Therefore, a combination of the two STEP pulses above ($\bar{0.5} - 1$ excitation and $1 - \bar{1} - 1$ 180° refocusing pulses) would be predicted to improve the performance of signal from the slice selective spin-echo imaging sequence on the human head at 7T.

These RF pulses and combinations were modified to produce slice selective RF excitation and were investigated by simulation. Their performance was compared in MR images of the human head to investigate whether improved spin-echo type imaging can be performed, e.g. for Diffusion-Weighted

Imaging (DWI) (20) and T₂-weighted MRI, both of which can be susceptible to B₁-related inhomogeneity but are important applications of MRI at high magnetic fields.

METHODS

Simulations

Whilst rectangular RF pulses may be useful for localized spectroscopy and 3D MRI (e.g. in combination with MRSI), generally MRI sequences should be slice-selective. In the **0.5 – 1** composite STEP excitation pulse, each of the two RF elements may be made slice-selective using standard sin(x)/x (sinc x) RF pulse shapes in combination with slice selective and refocusing gradients. With uni-polar selection gradients applied during the pulses, negative re-focusing gradient are needed both between the two RF pulse elements (a full single lobe (gradient x time) area) and half this area after the second element. For a bi-polar gradient waveform, as shown in Figure 2, only an additional final re-focusing gradient of approximately half the single lobe (gradient x time) area is required which provides a significant saving in time. Inspection of the pulse/gradient timing diagram illustrates that the second positive gradient provides refocusing of signal from the first RF pulse sub-component and simultaneously enables slice selection for the second RF sub-component pulse. Signals excited by both RF sub-components are fully rephased by the end of the pulse.

Again, the effects of RF pulses, this time with gradients, were simulated using a purpose-written Matlab program (version R2013b) that used rotation matrices to simulate solutions of the Bloch equations (written in-house) to determine the final effect on a one-dimensional uniform sample and the effect of a range of B₁ amplitudes and gradient waveforms.

For slice selective refocusing 180°, the refocusing capability of the simulated pulses was measured using the equation $|M_x^{100} + M_y^{010}|$ according to the methodology of Moore et al., where a value of zero indicates perfect refocusing (14). In order to measure the absolute signal that can be refocused, the phase of the initial **1 – 1 – 1** STEP pulses was adjusted for each B₁ value to provide a final M_{xy} to +M_y

rotation whose integral value provides the integral signal refocused across the selected slice (the integrated anti-symmetric M_x magnetization is zero). To remove the possibility of any gradient-echo signal contributions, signal-crushing gradients were added in the simulation.

Experimental Details

For comparison of techniques, a spin-echo sequence was used because this requires both a good RF excitation pulse followed by an effective refocusing RF pulse. Equation (2) demonstrates that if either RF pulse causes a non-optimal excitation angle, then the signal will be degraded, and particularly severely in the case of the refocusing RF pulse. Images were produced on a whole-body 7T research scanner (Siemens Healthcare, Erlangen, Germany) fitted with a NOVA RF head coil. All human imaging was performed on volunteers under approval from the University of Melbourne Human Ethics Committee.

Sinc RF pulses were used as the basic RF pulse shapes since they can be implemented, and their effect easily compared, on all scanners and the RF settings can be used as a useful comparative benchmark. The technology can be used with any desired RF pulse shape.

The NOVA head coil used has a birdcage transmit coil outer coil (circularly polarized) with a 32-channel receive-only inner coil. The total RF power available was 8 kW (single channel). Image reconstruction was performed using standard Siemens parallel-receive methodology.

Following simulations, complete waveforms were generated and exported as text files for incorporation into a Siemens® IDEA VB17A sequence program. The sequence was cloned from a multi-slice gradient-echo sequence with the excitation pulse replaced by an externally specified RF and gradient waveform file. In this way, all combinations of excitation and refocusing using the STEP and traditional sinc RF waveforms could be compared using the exact same image acquisition parameters.

Since our aim was to produce useable sequences for a Siemens 7T MRI scanner with a maximum RF power of 8kW, experimental implementation started with determining the minimum possible inter-

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pulse delay based on gradient rise times and RF pulse duration. Such an optimization must be based on reasonable experimental values: we used a basic sinc shaped RF sub-component pulse (central lobe only) of 660 μ s duration to provide a selected slice-thickness of 2.8mm with a frequency bandwidth of 3kHz. For the 45 $^{\circ}$ excitation in the STEP sequence, we used a shorter $\overline{0.5}$ pulse of 330 μ s pulse duration. The gradient slew rate was 200 T/m/s with a maximum gradient value of 70 mT/m. A rise time of 300 μ s was used for the $\overline{0.5} - 1$ STEP pulse to accommodate the larger gradient required by $\overline{0.5}$ RF pulse, and a 80 μ s rise-time was used for the $1 - \overline{1} - 1$ (where the gradient was half that for 1 pulse used in the 90 $^{\circ}$ pulse, and the range of slice selection gradients in the complete STEP sequence therefore varied by a factor of four). Hence, the over-all selected slice profile has been improved by making the width of the selective 180 $^{\circ}$ slice larger, in this case by a factor of two. The RF and gradient pulse timing diagram is shown in Figure 2(B) compared with the single-lobe spin-echo sequence of Figure 2(A). This also emphasizes the differences in RF amplitudes of the pulses in the two sequences.

Other MRI techniques and imaging parameters were:

B_1 -maps: Images were generated using the standard Siemens B_1 -mapping method using a fitted result from two images obtained with α - and 2α - excitation-angle gradient echo images.

B_0 -maps: Images were generated using the standard Siemens B_0 -mapping using a fitted result from two images obtained with different gradient echo times.

Human Brain Imaging: The parameters used for spin-echo brain imaging were: TE = 42ms, TR = 5 seconds, slice thickness = 2.8 mm, STEP sub-component single-lobe sinc pulses of 660 μ s duration, inter-pulse interval in $\overline{0.5} - 1$ pulse = 600 μ s, inter-pulse interval in the $1 - \overline{1} - 1$ pulse = 160 μ s ; the multi-slice sequence consisted of 11 slices, image matrix size = 128x128, FOV = 25 cm, bandwidth per image point = 500 Hz, total scan time = 640 seconds. The TR of 5 seconds eliminates the majority of T_1 -weighting of the brain tissue signals (1.2% error for grey matter and 7.6% error for white matter based on published T_1 values measured at 7T (22)).

RF Calibration: Maximum RF voltage was determined to be approximately 450V for the sinc spin-echo sequence and the RF voltage used for the STEP sequence was chosen accordingly (using the results of simulations) and found to be 400V for the average head (see Results for selection criteria).

RESULTS

Simulations

For the first simulations of single STEP pulses using shaped RF waveforms, a 5-lobe sinc pulse was used both for a standard RF waveform and as an RF pulse as a sub-component of the STEP pulse. Figure 3 shows the simulated responses for excitation RF pulses, for a uniform sample along the selection axis, with signal intensity integrated across the spatial selected slice profile plotted on the vertical axis versus B_1 amplitude (normalized to 1.0 for a 90° sinc pulse) along the horizontal axis. To obtain the net signal from the slice, the magnitude of the M_{xy} magnetization was integrated across the nominal slice width of the simulation with the net signal accounting for the refocus-able signal obtained under standard refocusing conditions after a magnitude Fourier Transform, e.g.:

$$\text{Total signal from selected slice} = [(\int_{-\Delta Z/2}^{\Delta Z/2} M_x dz)^2 + (\int_{-\Delta Z/2}^{\Delta Z/2} M_y dz)^2]^{0.5} \quad \text{Equation (3)}$$

where ΔZ = slice thickness.

Figure 3(A) shows slice selective 90° pulse performance (normalized to $B_1 = 1.0$ for a 90° sinc pulse (red line), $\overline{0.5} - 1$ pulse (blue line), $1 - \overline{0.5}$ pulse (time-reversed, yellow line), $\overline{1} - 1$ pulse (grey line), and optimized $\overline{0.5} - 1$ pulse (green line).

Figure 3(A) shows the greater tolerance of STEP RF pulses to B_1 non-uniformity through the appearance of a broader signal response than the sinc pulse (e.g. blue line c.f. red line). The yellow line shows the performance of $1 - \overline{0.5}$ STEP pulse which is again superior to the sinc pulse but not as good as for the $\overline{0.5} - 1$ STEP pulse. The simulated response of the time reversed $1 - \overline{0.5}$ selective 90° RF

pulse is also shown because, according to Equation (1), it forms a useful sub-component of the refocusing 180° RF pulse.

The attributes of using a **0.5:1** combination of RF amplitudes is demonstrated by inspection of the result for a $\bar{1} - 1$ STEP pulse (grey line), which is similar to the sinc in performance. However, the $\bar{1} - 1$ STEP pulse may be useful with very low B_1 fields because the signal response is broader at these low B_1 values: the maximum signal occurs at approximately 75% of the amplitude for the sinc RF pulse (i.e. a significantly lower B_1 amplitude). The maximum signal amplitude achieved from the slice for the $\bar{1} - 1$ STEP pulse is almost identical to the sinc RF pulse.

Finally, the green line plot in Figure 3(A) shows significant further improvement of the $\overline{0.5} - 1$ STEP pulse optimized by adjustment of gradient amplitudes (reduced slice selection for the $\overline{0.5}$ pulse of 80% gradient magnitude with an additional positive gradient of 11% between the two pulse sub-components for correct refocusing of the signal from the first pulse sub-component). A notable improvement in pulse performance is achievable with minimal slice profile broadening (see typical selective pulse spatial profiles: Figure 4).

Figure 3(B) show slice selective 180° refocusing pulse performance versus B_1 amplitude, measured by simulating actual slice refocused signal magnitude for the sinc (red line) and the $1 - \bar{1} - 1$ pulse (blue line). The signal accounts for the refocus-able signal obtained under standard refocusing conditions using a modified Equation 3 with substantial simulated gradient crushing of signal before and after the 180° pulse, and taking account of the inherent phase shift of the $1 - \bar{1} - 1$ 180° STEP pulse (see Methods section). Please note the B_1 amplitude scaling factor of 2 when comparing the two pulses (i.e. 2 for the sinc pulse c.f. 1 for the $1 - \bar{1} - 1$ pulse). The refocusing capability for each pulse (14) is shown as corresponding dashed lines (see Methods: value integrated across the slice profile). Also shown (in diagrams (i), (ii), (iii) and (iv)), are the spatial performance of the refocusing capability for each pulse at the B_1 positions depicted on the vertical lines for each pulse. The $1 - \bar{1} - 1$ 180° STEP

pulse response demonstrates a superior refocusing slice profile that integrates to a larger net signal from the slice across a wide range of B_1 amplitudes.

The difference between the plot in Figure 1(C) (for rectangular pulses) and those in Figure 3(A) reflect the degradation in selected slice profile shape away from nominally rectangular shape, as the RF amplitude is increased (see Figure 4).

To address the possibility of a change of slice thickness caused by the application of the $\overline{0.5} - 1$ STEP excitation pulse, a simulation is shown in the Appendix: Figure A1, where the spatial slice selection profile for this pulse (upper two plots for excited M_x and M_y magnetization) is shown compared to those for a sinc RF excitation pulse (lower plots). The slice selection gradient in the simulation has been chosen to obtain the same slice thickness as in later brain imaging (2.8mm).

Two other features are immediately evident. Firstly, the $\overline{0.5} - 1$ STEP (90° excitation) generates a larger net signal from the slice for most B_1 values (Figure 3A), presumably as a consequence of having a “sharper” slice profile with better-defined slice edges. This should be of no surprise since B_1 tolerance also applies to sharpening of the selected slice profiles where B_1 is necessarily reduced on the selected slice edges, therefore sharpening of the slice profile also results in increased signal from within the selected slice. Secondly, the tolerance of the a $\overline{0.5} - 1$ STEP RF pulse is much better in net slice-signal magnitude at larger B_1 fields, although because of poorer slice-shape definition, intolerance to B_1 is less than the theoretical ideal of a factor of 3 (i.e. approximately a factor of approx. 2). Also, the maximum signal for the a $\overline{0.5} - 1$ RF pulse occurs at a slightly higher B_1 field compared to the sinc pulse.

The $1 - \overline{1} - 1$ 180° STEP pulse clearly shows superior refocusing ability vs. B_1 amplitude (Figure 3(B)), as was hypothesized because it is the combination of two good 90° STEP pulses: namely, the $(1 - \overline{0.5})$ and $(\overline{0.5} - 1)$ pulses (Equation 1).

The $\frac{1}{2} - \frac{1}{2} 180^\circ$ STEP pulse also only requires 50% of the maximum RF amplitude of the sinc pulse because, at the minimum level of operation, only a 90° rotation is required rather than an 180° rotation. Therefore, in the simulation, the axes of the two pulses in Figure 3(B) has been adjusted to give a fair comparison between the pulses (with a nominal 90° sinc shaped excitation normalized to $B_1 = 1.0$).

Optimization of Spin-Echo STEP Sequence

The above simulations showed the potential benefits of the STEP approach for single pulses. However, in addition, the composite RF pulse STEP spin-echo sequences suffer from two main disadvantages, both of which are related to off-resonance effects:

- (i) The time delay between pulse sub-components allows time for significant off-resonance signal evolution which disrupts the pulse performance; notably by altering the phase for off-resonance signal so that later RF pulse sub-components do not have the desired effect.
- (ii) The bi-polar slice selection gradients employed in both 90° and 180° STEP pulses cause non-overlap of the spatially selected slices in positive and negative gradients.

The solution to (i) is simply to minimize the time duration between RF pulse sub-components by minimizing RF sub-component pulse durations and using the highest gradient slew rate available in the MRI scanner. This inter-pulse time delay may also be reduced in the $\frac{1}{2} - \frac{1}{2}$ excitation pulse by making the first pulse sub-component half the duration but applied at the same RF amplitude as the next $\frac{1}{2}$ RF pulse sub-component with gradient alteration to maintain the same slice thickness.

The solution to (ii) is to alter the slice thickness selected to achieve maximum overlap of the slices selected by the negative and positive gradients. This is achieved by reducing the gradients for the 180° refocusing RF pulse, typically by a factor of up to 50-60% when the inter-slice separation is at least twice the desired slice thickness. For multi-slice imaging, the SAR limit usually means that contiguous

slice imaging is not possible anyway for complete brain coverage. In addition, a moderate reduction of the gradient applied for the $\overline{0.5}$ excitation by 33% does not significantly affect the spatial slice profile. The simulation of slice behavior for the complete spin echo sequence was performed by including both STEP pulses with crushing gradients before and after the selective 180° RF pulse, although these could only be applied in the slice direction for this one spatial-dimension simulation. All RF pulses were simulated as single lobe sinc pulses and as pulse sub-components for STEP pulses. Accuracy of the spin-echo simulations was improved (by a few %) by setting the z-magnetization to zero before the 180° RF pulse to remove the possibility of gradient echo contamination in the spin-echo signal. The spatial slice profiles are shown for the complete sequence in Figure 4, for a range of B_1 amplitudes (B_1 values shown on left of each plot; 1.0 being ideal for the 90° pulse of a 90° - 180° - echo sequence). Spatial slice profiles from the simulation are shown in arbitrary spatial units (see Experimental Details above for the actual gradient magnitudes and timing used in the 7T MRI scanner) and simulations were performed in the absence of relaxation terms. The integrated refocused slice signal (in arbitrary units) is shown to the right of each plot and shows that the net signal from the slice is preserved by at least 56% over a B_1 range that varies by a factor of three.

The simulated integrated slice signal behavior for the complete spin-echo STEP sequence is shown in Figure 5(A) (dashed line) and compared to the equivalent sinc spin-echo sequence (solid line). The $(\overline{0.5} - 1) - (1 - \overline{1} - 1)$ STEP sequence was applied at half the maximum B_1 amplitude of the sinc sequence. The same STEP sequence was also simulated with a maximum RF voltage of 0.9 times that used in the sinc sequence (dotted line; see Experimental details for choice of this factor) which substantially recovers signal that would have been lost at low B_1 amplitudes. This is demonstrated by the horizontal line that is tangential to the maximum of the sinc performance profile. At this tangential point, the performance of the STEP sequence matches that of the sinc sequence and the same image signal will be obtained from each sequence (which occurs at the center of the human brain), but at all lower B_1 values the STEP sequence will provide superior results. The line drawn at $B_1 = 0.5$ shows an

approximate 330% increase in STEP slice signal compared to a sinc sequence and this is confirmed by later experimental results from the human head. Therefore, a notable improvement in pulse performance is achievable with minimal slice profile broadening (see pulse profiles of Figure 4).

In order to evaluate the complete sequence for off-resonance effects (both of the above effects), a frequency offset was added to the complete sequence and the effect on the integrated slice signal was plotted versus frequency offset, as shown in Figure 5(B). Two sequences were simulated: sequence STEP-A with a 90° phase shift of alternate STEP RF sub-components, and sequence STEP-B with a 270° (-90°) phase shift. Again, the sequence was simulated for the exact RF amplitudes and timing as described in the Experimental section so that the effect of off-resonance frequencies were accurately reflected in the data. The bandwidth of the RF pulses used experimentally was 3 kHz. Firstly, the off-resonance curves have a central half-height width of approximately 480 Hz (the bandwidth of off-resonance tolerance). Secondly, sequence STEP-B shows a frequency response shifted by up to approximately 100 Hz (that is dependent on exact experimental timing) and can be used to experimental advantage. The curves also show further maxima (although reduced) at ± 750 Hz. This occurs where the slices defined in positive and negative gradients begin to be shifted significantly outside the main selected slice overlap region into areas that contain “fresh” magnetization that only see a part of each of the STEP pulses.

By simulation of the individual 90° and 180° STEP pulse components (Figure 3), the combination of the two STEP pulses above ($0.5 - 1$ excitation and $1 - 1 - 1$ 180° refocusing pulses) would be predicted to improve the signal from the slice in a spin-echo by a net factor of approximately 35% (in the absence of B_1 non-uniformity), consisting of signal improvements of 9% and 28% from the selective 90° and 180° STEP pulses respectively compared with the sinc pulses. The actual simulated improvement when both pulses are simulated together in a spin-echo sequence (with B_1 normalized to 1.0 for the sinc pulse) is approximately 36%, despite a complex interaction of different slice shapes

and phases. This also indicates that further improvements could be attainable by optimizing the pulse combinations rather than each pulse in isolation.

MR Brain Imaging Results

Figure 6 shows a comparison between STEP (image 6(A)) and standard single sinc-pulse (image 6(B)) spin-echo axial images of an upper section through the human brain (one subject from $n=6$). The single sinc sequence was performed with a maximum RF voltage of approx. 450V; the hardware maximum being 500V. The STEP pulse sequence was performed with a maximum RF voltage of 400V (see horizontal line of Figure 5(A); this voltage means that the image signal matches that of the sinc sequence when $B_1 = 1.0$ and exceeds the sinc-generated signal for all lower B_1 fields). The images were from an 11 slice multi-slice procedure which was performed comfortably within the SAR limit for the average head for both sequences. The sagittal and axial B_1 maps of the same image section are shown in Figures 6(C) and 6(D) (units are approximate angular frequency in Hz for a block RF pulse). Although these B_1 maps show a factor of almost three in variation on a sagittal map through the middle of the brain; the non-uniformity can reach a slightly greater reduction factor in the off-axis temporal regions.

Application of the 400V RF amplitude for the STEP sequence provides an increase of approximately 1.8 in B_1 -amplitude (transmit field) in all areas of the brain (as calculated by the lower amplitude required by the refocusing STEP pulse (a factor of 2) multiplied by the factor of increased voltage relative to the standard STEP sequence (0.9). Preservation of the tissue signal associated with the STEP pulses, enables images with greater signal to be obtained from a larger volume of the brain than available using standard sinc pulses. Figure 6(A) also shows the improvement in Signal to Noise Ratio (SNR) in a defined brain volume of STEP vs. sinc results (circular volumes: mean 828 vs. 357; images 6(A) compared to 6(B)). Noise was measured in a diagonally offset region of the image of equivalent

volume outside the brain. The axial B_1 map of this upper section of the brain (Figure 6(D)) shows considerable B_1 non-uniformity, and improvement in grey/white matter T_2 contrast becomes more apparent off center (compared to sagittal mid-center) in the images.

Figure 7 is from a lower brain axial section and contains the B_0 anomaly in the sinus brain region (as seen by hyper-intensity in the B_0 map (following shimming) of the volume in Figure 7(B) approximately delineated by an ellipse). In this region, the average localized frequency shift was +582 Hz compared to the main brain volume (0 Hz) and the lower brain (several hundred negative Hz). The upper left image (Figure 7(A) acquired with sinc pulses) can be compared with images obtained from sequences STEP-A and STEP-B [Figure 7(C) and 7(D)], where a clear (but not perfect) improvement is seen in the image with sequence STEP-B for the problematic region [depicted in Figure 7(C)].

Figure 8 shows the full 22 sections obtained in a single procedure from a single sinc sequence figure 8(A) vs. the STEP-A pulse sequences figure 8(B). Due to SAR limits, the images were obtained in two segments of 11 slices, but these could have otherwise been obtained with a single sequence with a TR = 10 seconds (with the same SAR). The residual signal intensity variation of the center of the images compared to the edges is caused by the spatial characteristics of signal reception from the 32-channel head coil. Figure 8(C) shows a color map of the SNR improvement in all 22 slices, demonstrating that there is a substantial improvement of SNR, even in axial slices of the brain for which B_0 and B_1 adjustments are commonly optimized in 7T scans. The percentage increase in SNR rises toward the edges of the images and is 350% or more (as predicted by the simulation results of Figure 4). The improvement in the center of the images, where the sinc RF pulses produce good spin-echo signal due to better spin flip values, is much lower or even zero in some limited locations as indicated by the horizontal line in the simulation of Figure 4(A). The very low B_1 field in the left and right medial regions of the brain (Figure 8) cause image degradation in image intensity and contrast of a magnitude that cannot be entirely corrected by the STEP sequence in all of the brain axial sections.

Figure 9 shows a comparison between a Siemens single slice FSE image (Figure 9(A)) and the equivalent axial section obtained using the above STEP sequence and parameters (Figure 9(B)). The image produced by this Siemens sequence is commonly referred to as T_2 -weighted image. However, in this sequence the signal drop-out is minimized by using the gradient echo magnetization from the refocusing pulse. This “extra” signal is T_2^* -weighted in areas of signal drop-out in the pure spin-echo image. The darkening in the frontal regions of both images is a result of the previously described off-resonance slice position effect. In the Siemens image, the use of different gradient magnitudes in the slice selective excitation and refocusing pulses causes misalignment of the slices due to different off-resonance spatial shifts. In Figure 9(A), the selected slice is also spatially offset in the off-resonance areas, whereas for the STEP sequence the selected slice is from the overlap between spatially shifted images selected in positive and negative gradients, and therefore, is centered about the desired brain region.

In lower brain sections, the overall SNR is decreased (even in the STEP images), presumably due to combined drop-off the response of both transmitter and receiver coils. However, the STEP improvement is still maintained as a large percentage improvement.

The effectiveness of the STEP pulses at recovering signal can be improved by applying an RF voltage of up to 500V so as to provide maximum signal recovery in the outer regions of the image. However, degradation of the central brain volumes can then be observed due to the inability of the STEP pulses to correct for large B_1 amplitudes present in these inner volumes.

DISCUSSION

The STEP pulses show clear improvements for high-field imaging in terms of SNR (see Figure 8). The alternative solutions are often complicated, time consuming and expensive but may have other benefits.

STEP pulses are easily implemented and offer the possibility of reduced SAR (90%) if the STEP sequence is used at half the maximum RF amplitude of the equivalent sinc sequence. However, in this application the RF voltage was increased to give an SAR increase of 284% (i.e. a factor of approx. 0.9 in max. STEP RF voltage c.f. maximum RF voltage for sinc pulses). It is difficult to see how the volumes of brain tissue experiencing low B_1 can otherwise be effectively imaged using this approach.

The simulations also confirm that increasing the RF voltage improves the outer brain regions but at the expense of poorer SNR and theoretical contrast from the very center of the brain, where the B_1 -field is the strongest and the STEP pulses start to partially lose their ability to correct the B_1 -field.

Alternative strategies involving multiple rapid whole sequences are being investigated where the best advantages of both high and lower voltage sequences can be combined in rapid succession. An alternative is to extend the duration of the RF pulses to give larger spin excitation angles in the areas of lower B_1 field, but this must be combined with the above strategy to preserve image quality in central brain regions. The disadvantage of extending RF pulse durations is the associated increase in sensitivity to B_0 resonance offset effects.

The inter-spacing of the $\mathbf{1} - \bar{\mathbf{1}} - \mathbf{1}$ 180° refocusing pulses sub-component pulses of $660 \mu\text{s}$ means that the pulses can cope with B_0 field offsets in a range that approximates to 480 Hz; a variation typically seen for most of the human head at 7T. However, more coverage can be obtained by setting up the standard STEP-A sequence with a +240Hz offset or using the STEP-B sequence. Alteration of the sequences between STEP-A and STEP-B shifts this range by +100Hz so that, using STEP-B the B_0 abnormality at the base of the brain around the frontal region can be imaged with more acceptable image distortion and image quality.

The results demonstrate that, for complete coverage of the human head using a spin-echo sequence, the optimal approach involves changing the multi-slice sequence “on the fly” together with the associated imaging parameters, as the multi-slice sequence passes through the parts of the brain affected by the

“B₀ field bubble” (for a axial multi-slice imaging set). Significant re-programming is needed to bring these changes into reality.

The slice thickness used for this study is relatively large (2.8mm) as a consequence of using short RF pulses in order to minimize the inter-sub-pulse time interval. Reduction of the slice thickness can be achieved by replacing only one of the RF pulses in the full STEP sequence with a longer pulse with a larger number of sinc zero-crossings in the RF time shape. The optimum location of this pulse within the 5 pulse sub-component STEP sequence is yet to be determined, and as shown, all RF pulses do not have to select the same slice thickness. An alternative is to saturate the slice edge regions with pre-pulses to narrow the slice widths, bearing in mind that the slice-to-inter-slice space ratio of multi-slice sequences is larger at high fields due to SAR limitations on the number of slices. A suitable RF pulse that is relatively independent of RF amplitude and yet uses low RF power is the tailored noise pulse, which could be applied in a band-pass design allowing saturation of signal immediately outside the desired selected slice thickness (22). It is also beneficial, as with many multi-slice sequences, to increase the effective slice width of the refocusing RF pulse to achieve better spatially defined slice shapes and increased SNR.

Finally, to avoid the interaction of T₁-effects with T₂-contrast effects, a TR of 5 seconds was employed so that reasonably complete relaxation occurs following each slice excitation. Otherwise, steady-state M_z magnetization effects may be caused by off-resonance and B₁ non-uniformity effects on the selected slice during this complicated sequence. A solution is to apply a selective post-saturation RF pulse immediately after the STEP sequence, so that all magnetization returns to the longitudinal axis from a value of zero. A suitable RF pulse that is essentially independent of applied B₁ value could again be the selective noise RF pulse (22), which could be applied as a complete slice thickness saturation pulse with a relatively low RF amplitude. This would allow shorter TR values to be used, with a concomitant reduction in total scan time but maintain predictable relaxation performance.

The composite STEP sequence potentially allows improvement of spin-echo imaging e.g. Diffusion-Weighted Imaging (DWI) (20) and T₂-weighted MRI; both of which can be substantially improved by correction of B₁-related inhomogeneity and are important applications of MRI at high magnetic fields. Furthermore, the distribution of phase angles of the measured magnetization as measured by the STEP sequence can also be used to directly report on the RF field non-uniformity if a phase image is used and interpreted. A method of B₁ mapping using similar composite RF pulses has also been published by Morrel which uses the phase of the resulting excitation to encode the flip-angle (23).

CONCLUSIONS

The potential benefits of STEP MRI pulse sequences are that they may make high field MRI, and potentially MR spectroscopy (MRS), shorter (the lack of pre-scans makes the studies shorter and increases the signal strength), potentially cheaper (when no extra hardware such as parallel RF transmission channels are required), and safer (if lower SAR can be achieved using 90° rather than 180° RF pulses, and when patient movement between the pre-scan and the main scan causes potential changes to SAR conditions in imaging using parallel RF transmission).

The slice selective composite STEP pulses presented here differ in several aspects from other composite RF pulses. The 90_x-180_φ excitation pulse proposed by Levitt (13) where φ is ideally 135° and the train of pulses proposed by Moore et. al (14) do not show comparable characteristics of slice selection and spin-echo imaging performance respectively, thereby limiting their applicability.

For composite pulses to achieve any degree of correction for B₁ non-uniformity, the total spin excitation angles of the pulses must exceed the desired spin rotation, i.e. 90° and 180° for a spin echo sequence. The results presented in this study show that STEP pulses are capable of increasing the SNR and homogeneity of spin-echo images across the human brain and particularly in the temporal and cerebella areas.

However, it is also clear that such an approach could yield valuable improvements that will be of benefit to ultra-high field MRI and MRS particularly for diffusion, spin-echo fMRI, and PRESS sequences that all require a spin-echo. In addition, because of improved definition of slice profiles, STEP pulses may also improve lower field scanners by providing more SNR and/or lower SAR. All of this can be achieved without additional hardware.

In addition, this sequence can be easily combined with other approaches (e.g. parallel imaging, B_1 shimming etc.) in order to mitigate the B_0 and B_1 effects of ultra-high field MRI and contribute to the development of a greater range of MR pulse sequences for 7T.

APPENDIX A

To address the possibility of a change of slice thickness caused by the application of the $\overline{0.5} - 1$ STEP excitation pulse, a simulation is shown in Figure A1 where the spatial slice selection profile for this pulse (upper two plots for excited M_x and M_y magnetization) is shown compared to those for a sinc RF excitation pulse (lower plot). The vertical lines show the FWHM (Full Width Half Maximum) for the selected slices with minimal differences between the two pulses. When comparing the simulated slice integrals, it should be noted that the STEP composite pulses were constructed with the same sinc pulse shapes. Therefore, the effective time bandwidth product remained the same. When the sequences were transferred to the MRI scanner, the desired slice thickness and positions could be set by the console software. As seen in Figure A1, there is no significant increase in slice thickness, but the gradient in the simulation has been chosen to obtain the same slice thickness as in brain imaging (2.8mm).

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FIGURE CAPTIONS

Figure 1(A) shows the $\overline{0.5} - 1$ STEP RF pulse amplitude vs. time. Figure 1(B) shows the effect of the RF pulse on macroscopic magnetization (black line: trajectory; grey arrow: final magnetization position). Figure 1(C) shows simulated M_{xy} (transverse) magnetization (percentage) following a $\overline{0.5} - 1$ STEP RF pulse (solid line) and Sinc excitation pulse (dashed line) vs. B_1 amplitude (1.0 = 100% signal). The three maxima for the $\overline{0.5} - 1$ pulse correspond to conditions of $45^\circ - 90^\circ$, $90^\circ - 180^\circ$ and $135^\circ - 270^\circ$ spin rotations.

Figure 2. Shows a comparison of the spin-echo pulse and gradient sequence timing diagrams for: figure 2(A) the single sinc sequence and figure 2(B) the $(\overline{0.5} - 1) - (1 - \overline{1} - 1)$ STEP sequence (bi-polar gradients).

Figure 3(A) shows slice selective 90° pulse performance (normalized to $B_1 = 1.0$ for a 90° sinc pulse (red line), $\overline{0.5} - 1$ (blue line), $1 - \overline{0.5}$ (yellow line), $\overline{1} - 1$ (grey line), and optimized $\overline{0.5} - 1$ (green line) pulses. Figure 3(B) shows slice selective 180° refocusing pulse performance versus B_1 amplitude, measured by simulating actual slice refocused signal magnitude for the sinc (red line) and the $1 - \overline{1} - 1$ pulse (blue line). Please note the B_1 amplitude scaling factor of 2 when comparing the two pulses. The refocusing capability for each pulse (integrated across the selected slice) is shown as corresponding dashed lines. Also shown (in diagrams (i), (ii), (iii) and (iv)), are the spatial performance of the refocusing capability for each pulse at the positions depicted on the vertical lines for each pulse.

Figure 4. Shows simulated spatial slice profiles for the complete STEP $(\overline{0.5} - 1) - (1 - \overline{1} - 1)$ spin-echo sequence for a range of B_1 amplitudes (values shown on left of each plot; 1.0 being ideal for a 90° - 180° - echo sequence). The Integrated Refocused Slice Signal (in arbitrary units) is shown to the right of each plot.

Figure 5(A): Shows simulated slice integral signal performance for the STEP and sinc sequences. The $(\overline{0.5} - 1) - (1 - \overline{1} - 1)$ STEP sequence was applied at half the maximum B_1 amplitude (dashed line) and also at a value of 0.9 compared to the sinc (dotted line). Figure 5(B) shows the off-resonance effects on the STEP sequence plotted versus frequency offset for sequences STEP-A and STEP-B.

Figure 6. Axial images for the same mid-brain slice acquired obtained during multi-slice sequences. Figure 6(A) shows the image for a single sinc. Figure 6(B) shows the image for a $(\overline{0.5} - 1) - (1 - \overline{1} - 1)$ STEP sequence. Figure 6(C) shows a sagittal B_1 -map depicting the average relative B_1 values in selected brain regions. Figure 6(D) shows an axial B_1 -map of the slice selected in Figures 6(A) and 6(B). A comparison of SNR from comparable image volumes shows a large improvement of SNR off-center of the image axes.

Figure 7 shows axial sections from a brain slice above the eye-level showing the problem of B_0 non-uniformity (see B_0 map of Figure 7(B) with a mean +582 Hz resonance shift in the depicted brain area). Figure 7(A) was obtained using the single sinc sequence, Figure 7(C) used STEP-A and Figure 7(D) shows the improvement in the section obtained with sequence STEP-B.

Figure 8. Axial sections from a 22 multi-slice procedure obtained in a single procedure using: figure 8(A); sinc pulses; and figure 8(B); STEP-A sequence. Figure 8(C) shows a color map of the

percentage SNR improvement in all 22 slices, demonstrating a substantial improvement of SNR value; calculated as the difference of the signal in each image pixel for (STEP-sinc)/sinc amplitudes.

Figure 9 shows a comparison between a Siemens single slice FSE image. Figure 9(A) was obtained with the same gradients and parameters as the equivalent axial section obtained using the described STEP-A sequence as shown in Figure 9(B).

CAPTION for APPENDIX

Figure A1. The spatial slice selection profile for the $\overline{0.5} - 1$ STEP excitation pulse (upper two plots for excited M_x and M_y magnetization) is shown compared to those for a sinc RF excitation pulse (lower plot). The vertical lines show the Full Width Half Maximum (FWHM) for the selected slices and for a slice thickness of 2.8mm.

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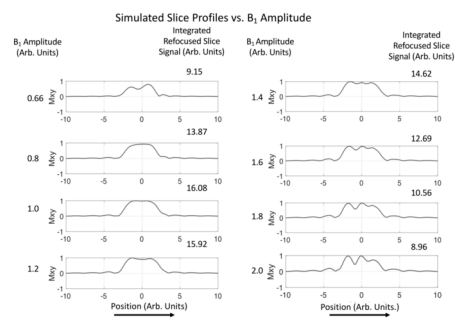
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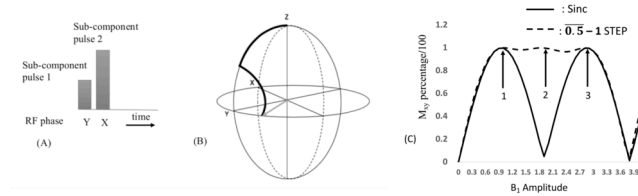
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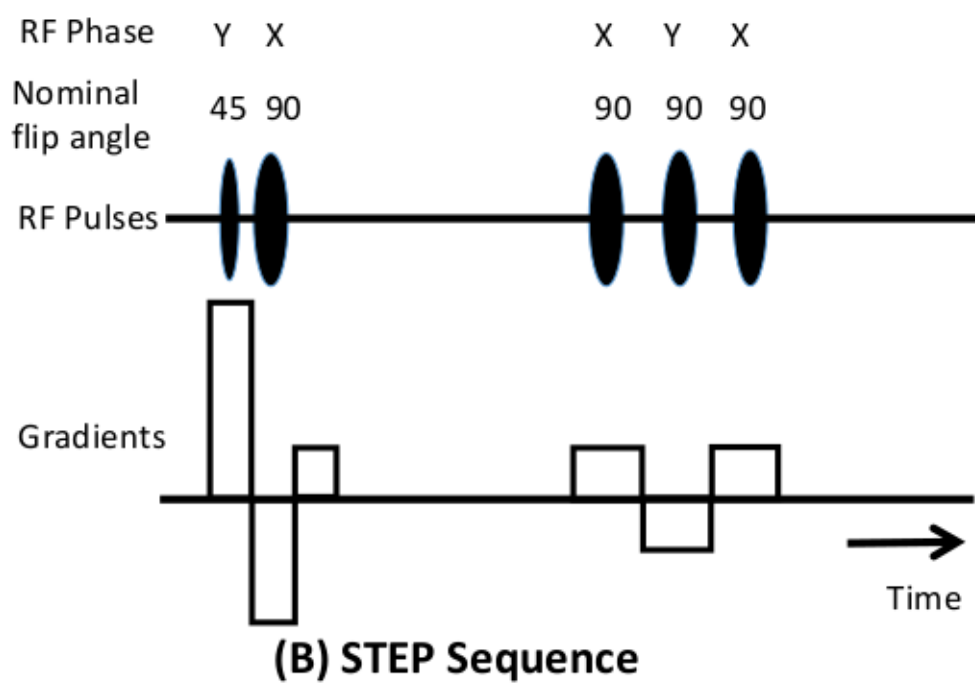
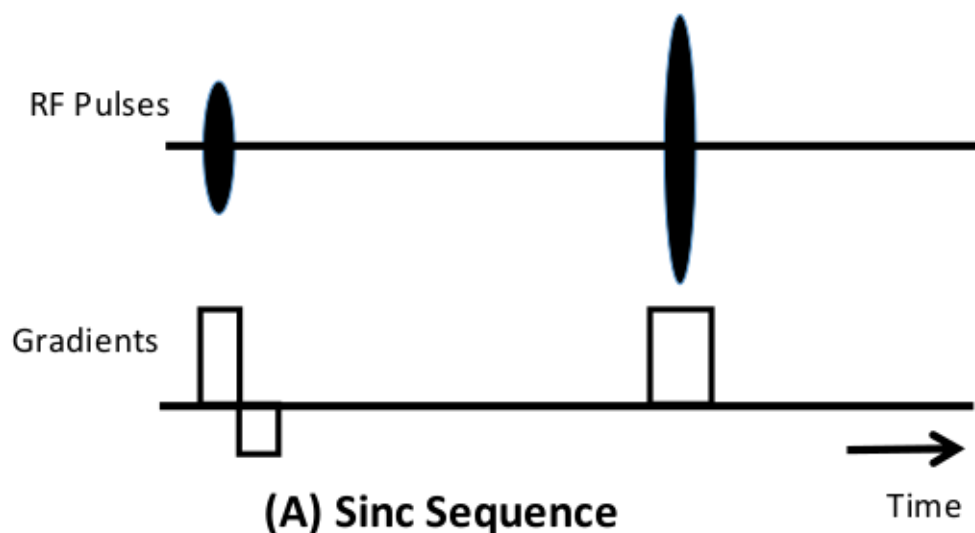
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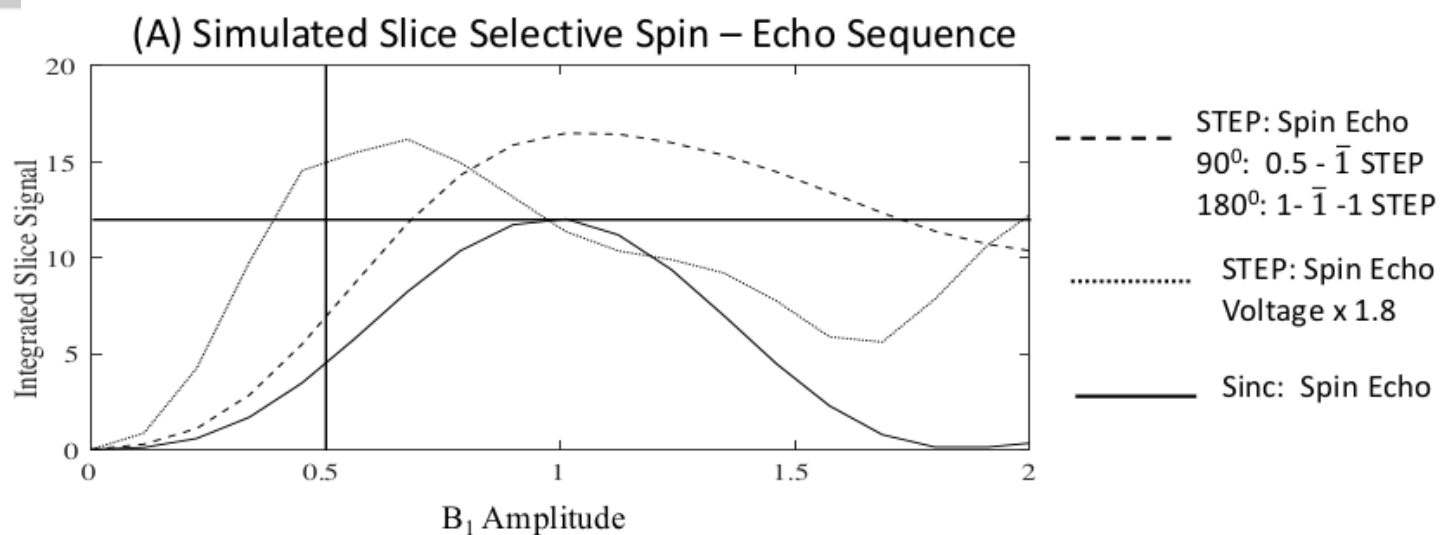
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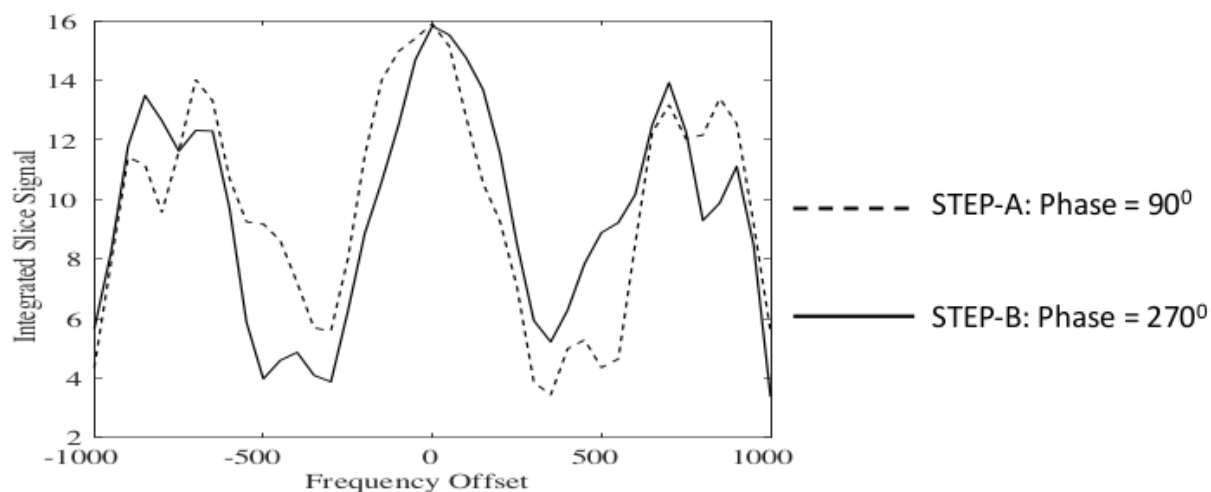
NBM_4445_24092020Fig1.tiff



NBM_4445_24092020Fig2.tiff

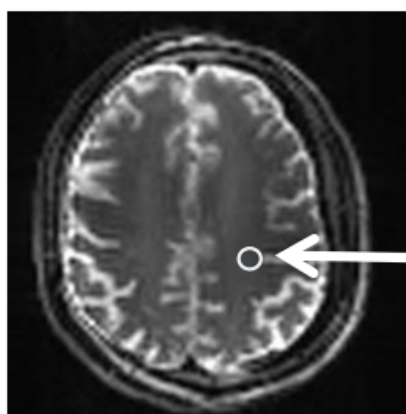


(B) Simulated Effect of Off-Resonance on STEP Spin – Echo Sequence



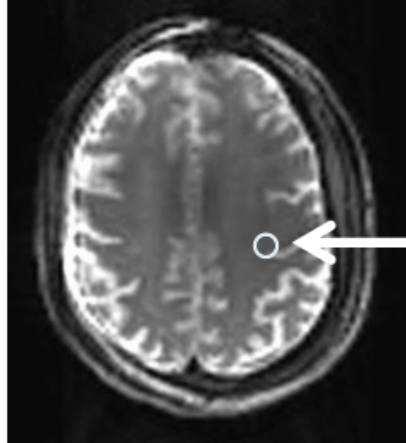
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(A) Axial spin-echo Sinc pulses



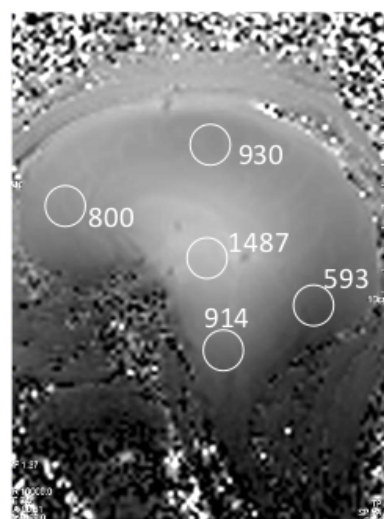
SNR = 357

(B) Axial STEP-A pulses

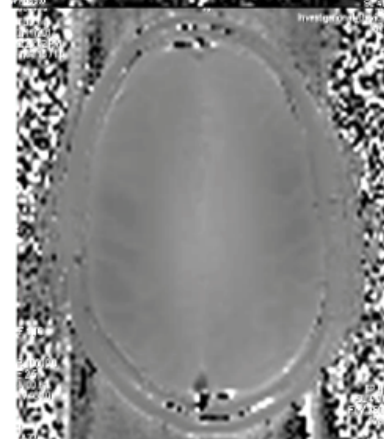


SNR = 828

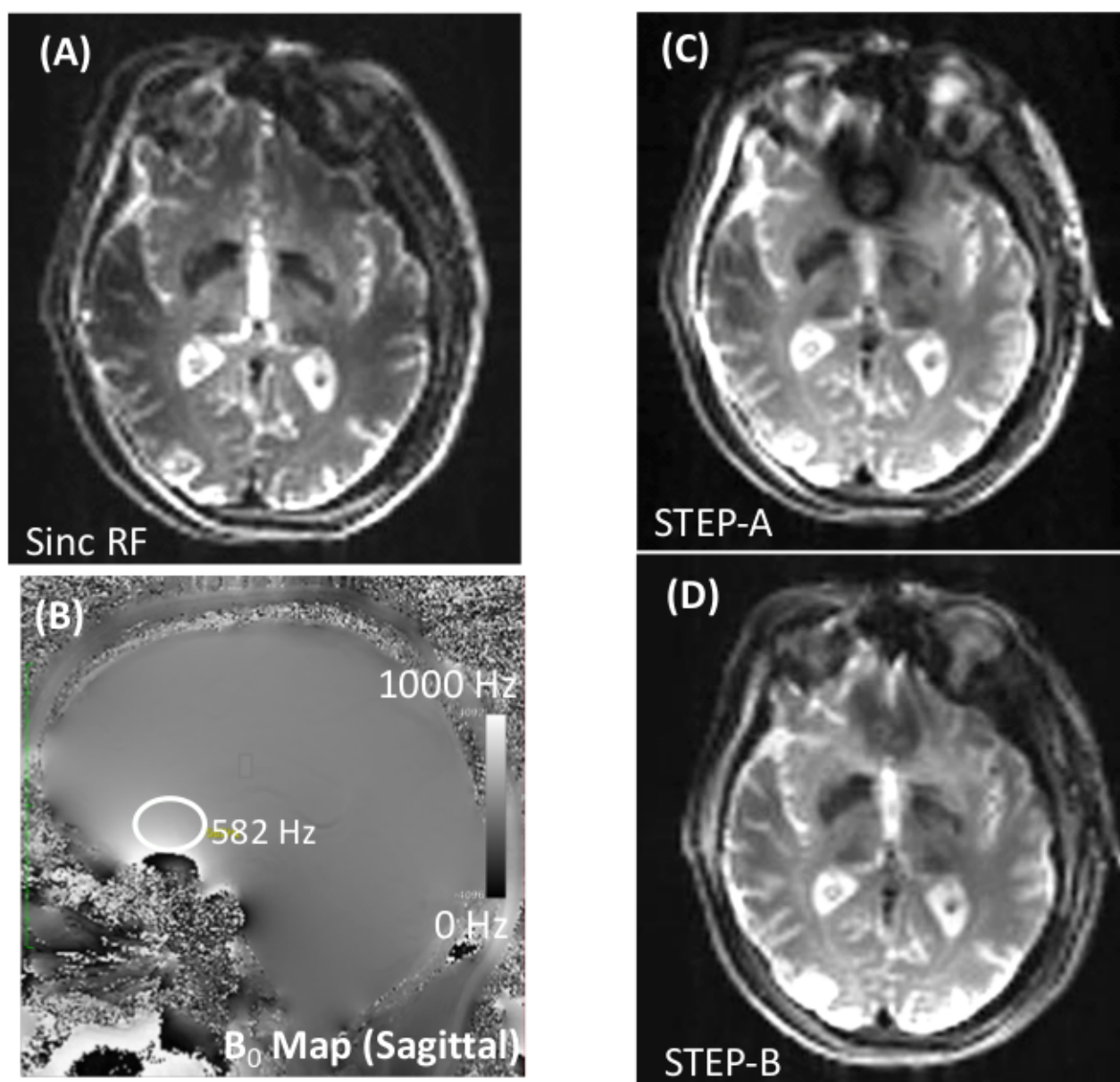
(C) Sagittal B₁ Map



(D) Axial B₁ Map

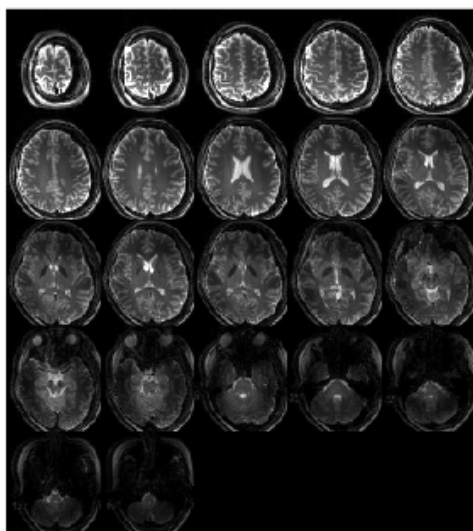


NBM_4445_24092020Fig6.tiff

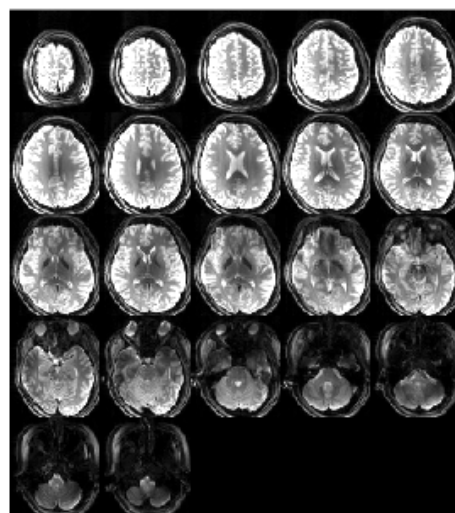


NBM_4445_24092020Fig7.tiff

(A) Axial Head Images:
Sinc RF Pulses



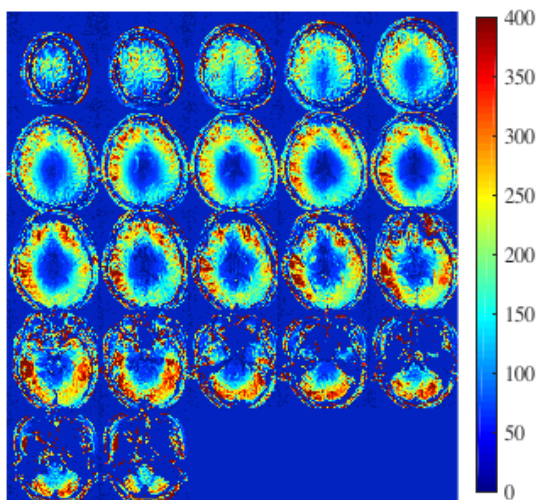
(B) Head Images:
STEP-A
RF Pulses



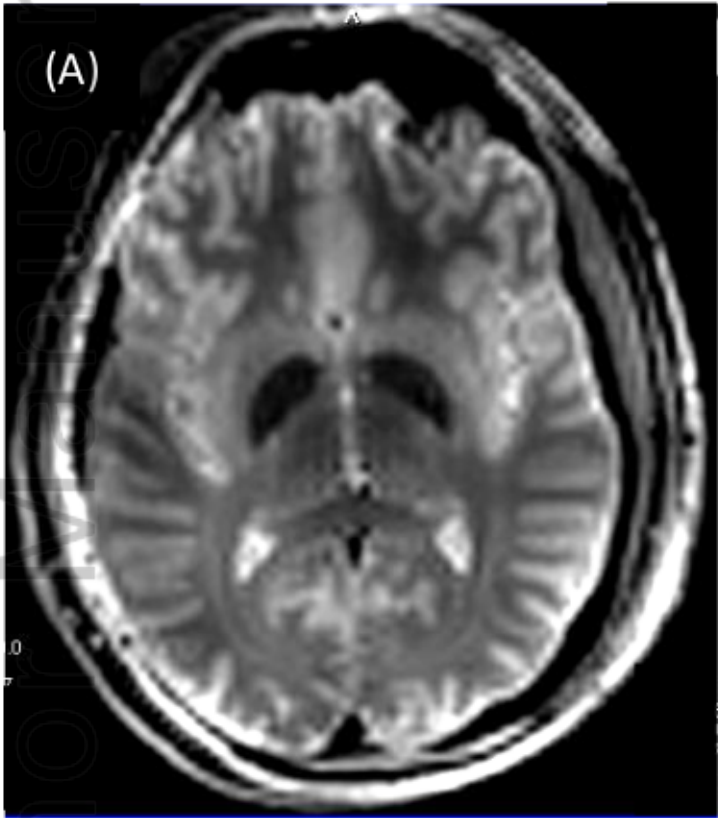
100%

0

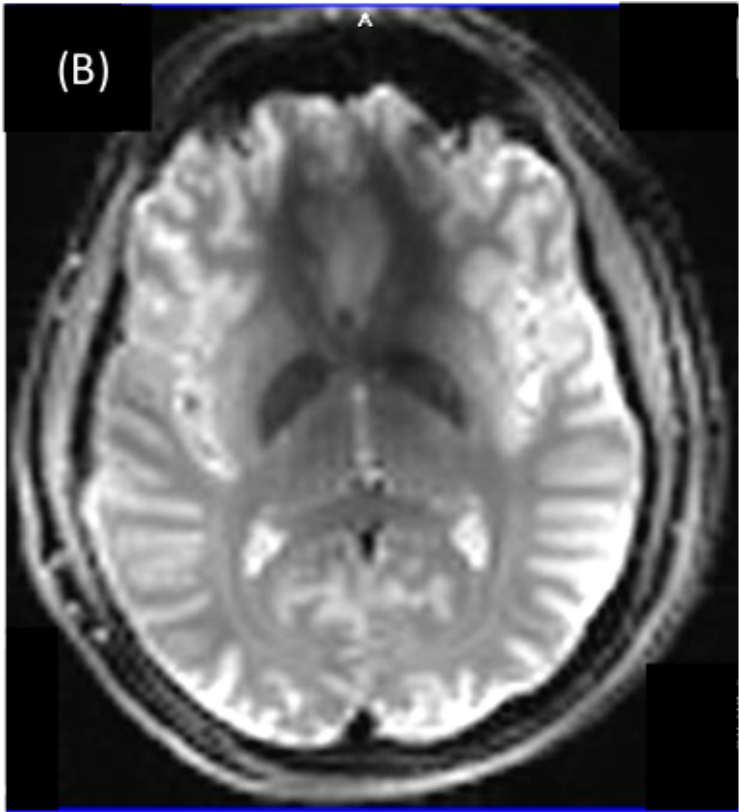
(C) Difference Images:
[(STEP-A) – Sinc] intensity
(shown as percentage of
Sinc RF intensity)



NBM_4445_24092020Fig8.tiff

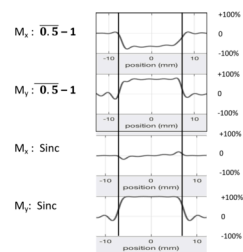


Siemens FSE: Single Echo

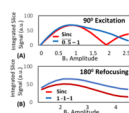


STEP-A Sequence

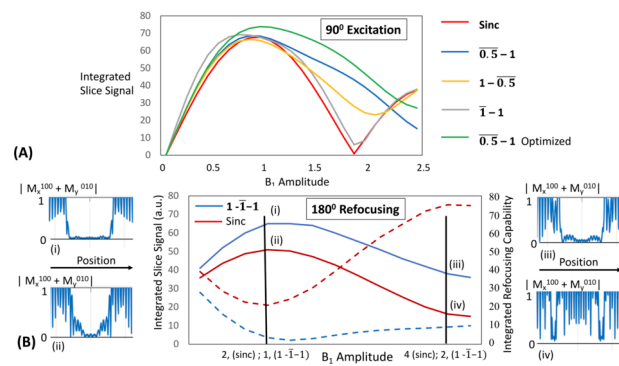
NBM_4445_24092020Fig9.tiff



NBM_4445_24092020Sinc_12.tiff



NBM_4445_26102020Fig3(2).tiff



NBM_4445_26102020Fig3.tiff