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3D MDEFT imaging of the human brain at 4.7 T with reduced sensitivity to radiofrequency inhomogeneity

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Abstract

A modification to the 3D modified driven equilibrium Fourier transform (MDEFT) imaging technique is proposed that reduces its sensitivity to RF inhomogeneity. This is especially important at high field strengths where RF focusing effects exacerbate B_1 inhomogeneity, causing significant signal nonuniformity in the images. The adiabatic inversion pulse used during the preparation period of the MDEFT sequence is replaced by a hard (nonadiabatic) pulse with a nominal flip angle of 130° . The spatial inhomogeneity of the hard pulse preparation compensates for the inhomogeneity of the excitation pulses. Uniform signal intensity is obtained for a wide range of B_1 amplitudes and the high CNR characteristic of MDEFT is retained. The new approach was validated by numerical simulations and successfully applied to human brain imaging at 4.7 T, resulting in highquality T_1 -weighted images of the whole human brain at high field strength with uniform signal intensity and contrast, despite the presence of significant RF inhomogeneity.

Keywords

high field MRI; T_1 -weighted imaging; RF inhomogeneity; human brain imaging; structural brain imaging

The use of high field strength MR systems for imaging the human brain has become increasingly widespread over recent years. High field strength offers increased signal-to-noise ratio (SNR) and greater sensitivity to contrast mechanisms that rely on differences in magnetic susceptibility (e.g., the blood oxygenation level-dependent (BOLD) effect) (1-3). However, there are several factors which make MRI of the human brain more challenging at high field strength. These include (i) inhomogeneity of the RF transmit and receive fields (B_1) caused by field focusing effects (4,5) and (ii) field-dependent alterations of tissue relaxation rates (6). MR pulse sequence development and optimization therefore must be performed in order to achieve optimal image quality at a particular field strength. Despite these potential difficulties, high-resolution functional MRI (7) and T_2 -weighted structural imaging (8,9) have been performed successfully at field strengths of greater than 3 T and demonstrate significant improvements over their low field equivalents.

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For structural imaging of the whole brain, 3D T_1 -weighted rapid gradient echo approaches are generally used. At lower field strength (<3 T), fast low angle shot (FLASH) or magnetization prepared rapid gradient echo methods provide good contrast among gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). However, these methods perform more poorly at higher field strengths due to the longer T_1 values. 3D modified driven equilibrium Fourier transform (3D MDEFT) imaging has been proposed as an alternative technique for achieving good T_1 contrast over the whole brain, initially at 4 T (10) and more recently at 3 and 1.5 T (11). 2D MDEFT has also been used at 8 T for structural T_1 -weighted imaging of a limited number of slices (12). In order to achieve the optimum T_1 contrast, center-out phase encoding is used for the innermost loop of the 3D MDEFT sequence (13). However, this increases the sensitivity of the technique to RF inhomogeneities, which are more prominent at higher field. As a result, tissue signal and contrast will vary considerably over the imaging volume unless additional measures are taken to reduce the B_1 sensitivity of the sequence. Low flip angle adiabatic pulses (e.g., BIR-4 (14)) are impractical as excitation pulses for fast gradient echo sequences at high field strength due to their duration and power requirements, and so alternative B_1 compensation pulses have been proposed. These have spatially varying flip angles in either one (13) or two (15) dimensions, with the shape of the pulse profile designed to counteract the RF inhomogeneity. This technique works well at 2 T where the main source of B_1 variation is the RF coil, which is constant across subjects and can be accurately approximated by a simple function. However, at 4.7 T the dominant source of B_1 inhomogeneity is the RF focusing effect, which depends on factors such as subject positioning relative to the RF coil and subject head size. Therefore, in order to accurately account for this problem using B_1 compensation pulses, it would be necessary to acquire B_1 profiles on a subject-by-subject basis and generate compensation pulses using this information. This would increase the total scan time required, which is undesirable if multiple imaging protocols are required within a single session (e.g., if MDEFT is used as a structural reference scan for a BOLD functional MRI study). Also, multidimensional RF compensation pulses reduce the efficiency of the MDEFT acquisition, because they are inevitably longer than standard nonselective hard pulses and consequently cause an increase in TE and TR. Therefore, a method which automatically corrects for RF inhomogeneities in all directions without prior knowledge of the exact spatial variation of the B_1 field in the head, and without increasing TE and TR, is desirable.

In this work, we propose a modification to the 3D MDEFT technique that reduces its sensitivity to RF inhomogeneity while retaining high T_1 contrast in brain tissue. This modification consists of replacing the inversion pulse of the MDEFT preparation period (which is often an adiabatic hyperbolic secant (sech) pulse (16), chosen for its insensitivity to RF inhomogeneity (12)) with a standard nonselective hard pulse with a nominal flip angle of 130° . Although perhaps counterintuitive, the use of a B_1 -sensitive preparation pulse reduces the B_1 sensitivity of the overall sequence, due to the counteracting effects of the preparation pulse and the excitation pulses. In the adiabatic sequence, image nonuniformity occurs as a result of a spatial variation of the excitation flip angle. Regions with higher B_1 have greater signal due to a higher flip angle. However, if the inversion pulse efficiency is also made to vary with B_1 , regions with higher B_1 will be inverted more efficiently, and therefore the amplitude of the longitudinal magnetization at the end of the inversion time delay will be reduced. The two effects of excitation flip angle and inversion efficiency work in opposite directions and will tend to cancel each other out. Therefore, the use of a hard preparation pulse in MDEFT is predicted to reduce image signal nonuniformity. Using this sequence, T_1 -weighted 3D image volumes of the whole human brain have been acquired at 4.7 T with a resolution of $1 \times 1 \times 1 \text{ mm}^3$.

THEORY

The standard 3D MDEFT sequence consists of three main components: (i) a global saturation pulse to null both the longitudinal and the transverse magnetization; (ii) after a recovery time delay (TD), a 180° pulse is applied to invert the longitudinal magnetization; (iii) after an inversion recovery delay (TI), a 3D imaging technique (e.g., spoiled 3D FLASH) is used to acquire image data. The sequence is repeated a number of times in order to build up the whole imaging data matrix, with each repeat acquiring data for different regions of the 3D k space volume. The contrast in an MDEFT image is determined by the state of the longitudinal magnetization at the end of the TI delay, immediately prior to image acquisition. In order to calculate this, we consider the evolution of the tissue magnetization from the time of saturation to the end of the TI delay.

Assuming perfect saturation, the tissue longitudinal magnetization (M_z) following MDEFT preparation is given by

$$M_z(TI) = M_0 (1 - (1 - \cos\phi [1 - \exp(-TD/T_1)] \exp(-TI/T_1))), \quad [1]$$

where M_0 is the value of the longitudinal magnetization at equilibrium, T_1 is the longitudinal relaxation time of the tissue, TD is the time between saturation and inversion pulses, TI is the inversion time, and ϕ is the inversion pulse flip angle. If TD = TI and $\phi = 180^\circ$, Eq. [1] becomes

$$M_z(TI) = M_0 [1 - \exp(-TI/T_1)]^2, \quad [2]$$

which is the standard expression quoted for the signal intensity in an MDEFT image (10,12). However, there is no fundamental reason for TD and TI to have the same value, and it has been shown that an asymmetric MDEFT sequence in which TD < TI provides better GM—WM contrast-to-noise ratio (CNR) at 1.5 and 3 T (11) than the symmetric equivalent. Therefore, for MDEFT parameter optimization at 4.7 T, TD and TI were allowed to have different values.

Numerical simulations were performed to investigate the dependence of the MDEFT signal intensity on RF inhomogeneity and the effect of this on GM/WM SNR and CNR. In order to do this, the following tissue parameters were assumed: $T_1(\text{WM}) = 1.05$ s and $T_1(\text{GM}) = 1.5$ s (based on measurements made in other laboratories at 4 and 4.7 T (6,17)). A parameter optimization scheme described previously was used (11), resulting in sequence timings of TD = 0.25 s and TI = 0.35 s. From Eq. [1], the magnetization excited by the first RF pulse of the imaging sequence is

$$M_{\text{MDEFT}} = M_0 (1 - (1 - \cos\phi [1 - \exp(-TD/T_1)] \exp(-TI/T_1)) \cdot \sin\theta, \quad [3]$$

where θ is the flip angle of the excitation pulse. For these simulations, the contrast in the MDEFT images was assumed to be determined by the values given by Eq. [3], since center-out phase encoding was used for the innermost loop of the imaging sequence (see Methods). The sensitivity of the technique to RF inhomogeneity was assessed by varying θ and examining the effect on M_{MDEFT} . Three variations of the MDEFT sequence were simulated:

- i. MDEFT with an adiabatic hyperbolic secant inversion pulse (which has very good inversion efficiency and is insensitive to RF inhomogeneities), for which ϕ was assumed to have a constant value of 180° .

- ii. MDEFT with a hard inversion pulse, for which ϕ was assumed to vary with θ , with its maximum value (180°) when θ had its nominal value. It was assumed that the flip angles of the excitation and inversion pulses were proportional, so that if the inversion pulse flip angle was 180° when $\theta = 23^\circ$, it would be 90° when $\theta = 11.5^\circ$.
- iii. MDEFT with a reduced flip angle hard pulse preparation, for which the nominal flip angle of the “inversion” pulse was reduced to 130° . This corresponds to the value of the inversion pulse flip angle when θ has its nominal value. As above, the flip angle of this preparation pulse was assumed to vary linearly with θ . Other values of nominal inversion pulse flip angle were also investigated, and 130° was found to result in the greatest degree of insensitivity to B_1 field variations (data not shown).

In all three cases, the initial MDEFT saturation pulse was assumed to completely null all longitudinal magnetization at the beginning of the preparation period. This assumption was justified by the use of adiabatic half passage RF pulses for this purpose.

METHODS

All imaging was performed using a 4.7-T, 90 cm bore diameter magnet (Magnex Scientific Ltd, Oxford, UK) controlled by a console supported by Philips Medical Systems (Eindhoven, Holland) based on a MR5000 design (SMIS Ltd., Guilford, UK). A shielded head gradient coil was used (Magnex Scientific Ltd.), providing gradient fields of up to 36 mT/m with a maximum slew rate of 195 mT/m/ms. Images were acquired using a transmit/receive fourport drive birdcage RF coil with an internal diameter of 28 cm. Six normal healthy volunteers were scanned after informed consent and approval from the University College London Hospital Ethics Committee.

RF pulse calibration was carried out manually on a 5-mm axial slice coincident with the maximum of the B_1 profile in the axial direction using the method of van der Meulen and van Yperen (18). We have previously found that using this method in the human head at 4.7 T, the mean RF flip angle obtained is approximately 15% higher than the desired flip angle (due to the topography of the B_1 maps, with the B_1 maximum being focused in a central spot and regions of lower B_1 forming concentric rings around this spot; for examples of B_1 maps of the human head at 4.7 T, see (19)). Therefore, the value obtained from the calibration was divided by 1.15, and this value was used for the hard RF pulse power. Adiabatic pulse power settings were chosen to ensure that the adiabatic condition was satisfied (16).

3D MDEFT was implemented as described previously (10,11). The image orientation was chosen such that the read gradient was applied along the superior—inferior direction. The image matrix size was 256 (read) $\times$ 224 (PE_{inner}) $\times$ 176 (PE_{outer}). In the read direction, $2 \times$ oversampling was used to avoid signal aliasing from the lower regions of the head/neck (i.e., 512 complex data points were sampled per acquisition). Center-out phase encoding was used in the PE_{inner} loop and the data were acquired in two segments. The first segment covered one half of $k_{PE_{\text{inner}}}$ -space from the center out (112 lines) and the second segment covered the other half of $k_{PE_{\text{inner}}}$ -space from the center out (also 112 lines). Each segment was preceded by its own MDEFT preparation period. This two segment acquisition was repeated 176 times for each step in the PE_{outer} direction. Using a parameter optimization scheme (11) designed to maximize GM/WM/CSF CNR for a given total scan time at 4.7 T (assuming $T_1(\text{GM}) = 1.5$ s, $T_1(\text{WM}) = 1.05$ s, and $T_1(\text{CSF}) = 4.6$ s; spin densities $\rho(\text{GM}) = 0.75$, $\rho(\text{WM}) = 0.65$, and $\rho(\text{CSF}) = 1$ [arbitrary units]; $T_2^* = 25$ ms), the following sequence parameters were chosen: TD = 250 ms; TI = 350 ms; acquisition bandwidth (BW_{acq}) = 50 kHz; nominal excitation flip angle = 23° ; TR = 13.1 ms; TE = 5.2 ms; gradient spoiling in read and PE_{inner} directions and RF spoiling; phase encode gradient rewinding along both PE

directions; FOV = $256 \times 176 \times 224 \text{ mm}^3$ to give $1 \times 1 \times 1 \text{ mm}^3$ spatial resolution. The total scan time was 12 min 8 s. In order to minimize the echo time, an asymmetric echo acquisition was used in the read direction so that the peak signal occurred at point 192 rather than point 256 (the center of the 512 point acquisition). For the MDEFT saturation pulse, two successive adiabatic half passage sech pulses were used. For the MDEFT inversion, three types of pulse were used: (i) adiabatic sech pulse ($\mu = 5$, $\beta = 1250 \text{ s}^{-1} \cdot \text{BW} = 1989 \text{ Hz}$); (ii) hard nominal 180° pulse (duration $680 \mu\text{s} \cdot \text{BW} = 1471 \text{ Hz}$); and (iii) hard nominal 130° pulse (same duration as 180° pulse). Standard hard pulses were used for RF excitation in the imaging section of the sequence. Images were generated using a 3D-FT with a Hanning filter applied to the first and last 12.5% of the data in all three dimensions. No other image processing or intensity correction schemes were used to enable straightforward comparison of images and assessment of signal intensity variation.

In order to assess the practical utility of the three MDEFT sequences, the image data sets were partitioned into WM, GM, and CSF maps using a segmentation algorithm based on a modified “mixture model” cluster analysis method (20). Following segmentation, an assessment of “image uniformity” was performed. In order to achieve this, it was necessary to remove the contrast due to tissue type (GM, WM, and CSF). Using the WM and GM maps created from the hard 130° MDEFT images, voxels with a probability greater than 0.8 of being either WM or GM were identified. The corresponding voxels were selected from each of the three original data sets to generate images containing signal from GM and WM only. The image intensity of the voxels that were identified as being GM were multiplied by a factor greater than 1 to remove differences in pixel intensity due to tissue type (the value of this factor was based on the average ratio of SI for GM and WM over the whole brain). The images were smoothed by convolution with a boxcar kernel of 8-mm width. To remove the confounding effect of zero intensity pixels, which occur at tissue boundaries in the combined GM/WM images (where partial volume effects cause the probabilities of GM/WM to be less than 0.8), the smoothed images were normalized using a mask created from the combined GM/WM images and convolved with the same smoothing kernel. The resulting image uniformity maps have an intensity that directly reflects the degree of SI nonuniformity present in the image data.

RESULTS

Figure 1 shows the results of the simulation studies. The horizontal axes of the graphs in Fig. 1 correspond to the amplitude of the B_1 field and are represented in terms of the flip angle of the RF excitation pulse, which is proportional to B_1 . In the case of the sech inversion pulse (Fig. 1a), only the flip angle of the excitation pulse varies with RF power, because the inversion pulse is insensitive to variations in B_1 . Consequently, there is a strong dependence of signal intensity (SI) on B_1 field amplitude. If a nominal 180° hard pulse is used for inversion, the actual inversion efficiency varies with B_1 . In Fig. 1b, the nominal flip angle of the excitation pulse is 23° and the nominal flip angle of the inversion pulse is 180° . Variations in B_1 cause the excitation pulse flip angle to be higher or lower than 23° and the inversion pulse flip angle to be correspondingly higher or lower than 180° . However, it is important to note that in both cases the inversion efficiency decreases. This results in the behavior shown in Fig. 1b. When B_1 is less than or equal to its nominal value, the SI in WM and GM is relatively uniform, leading to a nearconstant WM—GM signal difference. This is because the loss of signal due to a lower flip angle is compensated for by the reduction in inversion efficiency. However, as the B_1 field amplitude increases to higher than its nominal value, the SI begins to increase rapidly for both WM and GM. This is because the high flip angle and reduced inversion efficiency both cause an increase in the amount of excited magnetization. This will cause regions in the center of the brain, where the B_1 field has its maximum value due to field focusing effects (21), to have high SI. The problem of SI

increase at high B_1 can be eliminated by reducing the nominal flip angle of the inversion pulse from 180 to 130°, as shown in Fig. 1c. In this case, the increase of flip angle with B_1 continues to be opposed by an increase in inversion efficiency, even at levels higher than the nominal values. Therefore, the SI of WM and GM is reasonably constant over the wide range of B_1 values represented in Fig. 1 and, importantly, there is no overlap in the range of SI covered by each of the tissue types, i.e., the minimum of the WMSI curve is greater than the maximum of the GM SI curve. A relatively constant CNR is achieved, as indicated by the flatness of the WM—GM difference curve shown in Fig. 1c.

Figure 2 summarizes the predicted range of WM and GM signal intensities resulting from a range of B_1 fields that correspond to flip angles from 13 to 34° for the three sequences (as in Fig. 1). This figure contains the same information as presented in Fig. 1, but makes it easier to appreciate two crucial points about the MDEFT sequence with the 130° hard pulse: first, the much reduced extent of the variation of signal intensity for both WM and GM, and second, the lack of overlap between the WM and GM ranges. Also, it is important to note that the difference between the mean WM signal and the mean GM signal (shown by the horizontal bars in the graph in Fig. 2) for the hard 130° MDEFT sequence is similar to that of the two other sequences (0.020, 0.022, and 0.022 in the units of Fig. 2 for the sech, hard 180°, and hard 130° sequences, respectively). This means that, on average, there is no loss of WM—GM CNR when using the hard 130° preparation pulse. All these factors should combine to help to facilitate automatic tissue-based image segmentation.

Examples of human brain images acquired at 4.7 T using the three variants of the 3D MDEFT sequence are shown in Fig. 3. Note that no image processing or intensity correction schemes have been applied in the generation of these images. Several of the predictions made by the simulations are apparent in these images. First, the B_1 -dependent signal dropout in the standard MDEFT sequence is visible in the outermost areas of the brain, particularly in the inferior regions of the cerebellum and the superior region of the cerebrum (Fig. 3a). This corresponds to the predictions from Fig. 1a: the SI increases with B_1 , i.e., from peripheral to central brain areas, leading to low SI at the edges. By using a hard 180° inversion pulse (Fig. 3b), the SI in these regions of dropout increases, but a SI “hotspot” appears in the region of highest B_1 at the center of the brain. This corresponds to the predictions from Fig. 1b: SI is constant when B_1 is low (i.e., no considerable losses in peripheral areas), but there is a strong increase in SI when B_1 is high, leading to the intensity hotspot in the center of the brain. This actually worsens the overall SI uniformity compared to the MDEFT sequence with the adiabatic inversion. Signal uniformity is considerably improved by using a hard 130° inversion pulse, as predicted in Fig. 1c and shown in Fig. 3c. The result is high-quality T_1 -weighted images with uniform intensity and good contrast among WM, GM, and CSF.

Figure 4 shows the image uniformity maps for three MDEFT sequences, with a structural image of the same transverse slice for anatomic reference. It is clear that SI uniformity of the images acquired using the 130° hard pulse MDEFT sequence (Fig. 4d) is superior to that of the other sequences. Profiles along a line through the image uniformity maps illustrate the difference in the flatness of the maps. Analysis of a 6-cm transverse midbrain slab showed that the SD of the image uniformity map was 23.0, 34.8%, and 13.8% for the sech, hard 180°, and hard 130° sequences, respectively. Also, it is interesting to note that the mean value of the hard 130° MDEFT uniformity map is higher than that of the other two sequences (as predicted in Fig. 1), resulting in overall higher image SNR.

DISCUSSION

3D MDEFT is an efficient method for providing structural T_1 -weighted images of the human brain at high field strength. In this paper, a modification to the standard MDEFT approach is proposed, in which the adiabatic inversion preparation pulse is replaced by a hard pulse with a nominal flip angle of 130° . This modification, which is straightforward to implement and requires no extra pulse calibration, is designed to reduce the sensitivity of 3D MDEFT to RF inhomogeneity. It has been shown that using the standard MDEFT sequence at 4.7 T, the inherent B_1 inhomogeneity caused by RF focusing effects is sufficiently large to cause significant nonuniformities in signal intensity across the brain. Using the modified approach, these signal intensity variations are substantially reduced and high-quality T_1 -weighted images with uniform intensity and good contrast between different tissue types are obtained.

Another common method that is used to reduce the appearance of image nonuniformities is intensity correction during image postprocessing. Although this can result in images with apparently uniform intensity, it is important to note that if images are corrected in this way, differences in tissue contrast due to flip angle/ B_1 inhomogeneity will still occur across the image. By addressing the issue of B_1 inhomogeneity at the pulse sequence stage, the method proposed here achieves both uniform contrast and SI across the imaging volume. Residual variation in SI that remains due to the receive profile of the RF coil can be corrected for using image postprocessing. The proposed method is equally valid if different coils are used for transmission and reception, e.g., if a birdcage transmit coil is used with an array coil receiver. In this case, image postprocessing is a standard part of the image reconstruction, which takes account of the large differences in the spatial sensitivities of the array coil elements. Finally, while the effectiveness of the new method has been shown here for neuroimaging at 4.7 T, the principle is also applicable at any field strength where T_1 -weighted imaging using magnetization preparation suffers from problems caused by RF focusing and B_1 inhomogeneity (e.g., 3 T).

In summary, a modification of the 3D MDEFT technique has been described that reduces the variation in image signal intensity caused by inhomogeneities in the RF field and allows the acquisition of high-quality whole-brain T_1 -weighted images with good GM—WM CNR at 4.7 T.

ERRATA

Erratum to: Thomas DL et al. 3D MDEFT imaging of the human brain at 4.7 T with reduced sensitivity to radiofrequency inhomogeneity. *Magn Reson Med* 2005;53:1452-1458.

In our article by Thomas DL et al. 3D MDEFT imaging of the human brain at 4.7 T with reduced sensitivity to radiofrequency inhomogeneity, *Magn Reson Med* 2005;53:1452-1458, a typographical error resulted a loss of brackets in Eqs. 1 and 3. The correct equations appear below:

$$M_z(TI) = M_0 (1 - (1 - \cos\phi [1 - \exp(-TD/T_1)]) \exp(-TI/T_1)), \quad [1]$$

$$M_{\text{MDEFT}} = M_0 (1 - (1 - \cos\phi [1 - \exp(-TD/T_1)]) \exp(-TI/T_1)) \cdot \sin\theta, \quad [3]$$

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FIG. 1.

Variation of MDEFT signal intensity with B_1 field using (a) a sech inversion pulse, (b) a hard 180° inversion pulse, and (c) a hard 130° inversion pulse. Values shown are for white matter (WM, $\blacklozenge$) gray matter (GM, $\circ$), and the difference (WM—GM,*). The horizontal dashed lines in (b) and (c) represent the lowest and highest values of the WM—GM difference in (a). Signal intensity is plotted against the actual excitation pulse flip angle, with the nominal value being 23° for all three sequences (indicated by the vertical dotted line)

FIG. 2.

Range of signal intensity (SI) variation for B_1 fields corresponding to the range of flip angles $13\text{-}34^\circ$ for the three variants of the MDEFT sequence. The symbols represent the extremes of the SI ranges and the horizontal lines represent the mean SI value. Use of a hard 130° preparation pulse greatly reduces the range of SI for both white and gray matter while maintaining good contrast.

FIG. 3.

Selection of sagittal images from a 3D MDEFT data set acquired using (a) sech inversion, (b) hard 180° , and (c) hard 130° preparation pulses. Use of the 130° preparation pulse eliminates the signal dropout seen at the edge of the brain with the sech preparation and the SI hotspot in the center of the brain seen with the hard 180° preparation.

FIG. 4. (a) Anatomic reference image and “image uniformity” maps of the (b) sech inversion, (c) hard 180°, and (d) hard 130° MDEFT sequences. Also shown in (b—d) are profiles taken from the horizontal line through the “uniformity” map at the position indicated (dashed line).