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Four-angle method for practical ultra-high-resolution magnetic resonance mapping of brain longitudinal relaxation time and apparent proton density

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Abstract

Changes in longitudinal relaxation time (T_1) and proton density (PD) are sensitive indicators of microstructural alterations associated with various central nervous system diseases as well as brain maturation and aging. In this work, we introduce a new approach for rapid and accurate high-resolution (HR) or ultra HR (UHR) mapping of T_1 and apparent PD (APD) of the brain with correction of radiofrequency field, B_1 , inhomogeneities. The four-angle method (FAM) uses four spoiled-gradient recalled-echo (SPGR) images acquired at different flip angles (FA) and short repetition times (TRs). The first two SPGR images are acquired at low-spatial resolution and used to accurately map the active B_1^+ field with the recently introduced steady-state double angle method (SS-DAM). The estimated B_1^+ map is used in conjunction with the two other SPGR images, acquired at HR or UHR, to map T_1 and APD. The method is evaluated with numerical, phantom, and *in-vivo* imaging measurements. Furthermore, we investigated imaging acceleration methods to further shorten the acquisition time. Our results indicate that FAM provides an accurate method for simultaneous HR or UHR mapping of T_1 and APD in human brain in clinical high-field MRI. Derived parameter maps without B_1^+ correction suffer from large inaccuracies, but that this issue is well-corrected through use of the SS-DAM. Furthermore, the use of the SPGR imaging, with short TR and phased-array coil acquisition permits substantial imaging acceleration and enables robust HR or UHR T_1 and APD mapping in a clinically acceptable time frame with whole brain coverage obtained in less than 2 min or 5 min. The method exhibits high reproducibility and benefits from the use of the conventional SPGR sequence, available in all

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability Statement

The datasets generated for this study are available on request to the corresponding author.

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preclinical and clinical MRI machines, and very simple modelling addressing a critical outstanding issue in neuroimaging.

Keywords

Relaxation time mapping; Proton density mapping; Spoiled-gradient recalled-echo sequence; Ultra-high-resolution imaging; Quantitative MRI

Introduction

Magnetic resonance (MR) longitudinal relaxation times and proton density (PD) depend on the concentration of macromolecules such as proteins, phospholipids, and fats, as well as water content and mobility. Thus, changes in longitudinal relaxation time (T_1) and PD can be sensitive indicators of microstructural alterations associated with myelin degradation, axonal loss, inflammation, edema, or matrix destruction in the central nervous system [1–3]. Indeed, quantitative T_1 and PD values obtained through magnetic resonance imaging (MRI) represent potential biomarkers for multiple sclerosis [3–8], Parkinson's disease [9–11], mild cognitive impairment [12, 13], Alzheimer's disease [12–15], schizophrenia [16, 17], epilepsy [18], as well as for aging and developmental plasticity [1, 19–22].

A myriad of MRI approaches have been developed to measure T_1 or PD [23, 24]. The most popular methods are those that collect a series of inversion recovery-prepared images, such as the Look-Locker technique or its variants [25–29], or a series of spoiled gradient recalled echo (SPGR) images acquired at several flip angles (FAs) or repetition times (TRs) [30–36]. However, these methods, while rapid and accurate, require specialized MRI sequences or complex modeling, and are highly sensitive to inhomogeneities in the radiofrequency (RF) transmit field, B_1^+ [30, 31, 35, 37, 38]; this requires additional measures for calibration which greatly extend the acquisition time while adding further complexity to the overall process. Therefore, these methods have not been well-integrated into clinical use, resulting in an ongoing need for a practical, accurate, and fast T_1 and PD mapping methods.

In this study, we propose a new approach to simultaneously map T_1 and apparent PD (APD) at high-resolution (HR) or ultra HR (UHR) in the clinical high-field setting. This four-angle method (FAM) also uses a series of conventional SPGR images acquired with different FAs and short TRs, and so may be implemented with all preclinical and clinical MRI systems. We use a total of four such images for efficiency, while maintaining accuracy. Briefly, two low-resolution images are used to map, voxel-wise, the B_1^+ field using the recently introduced steady-state double angle method (SS-DAM) [39]. This known B_1^+ map is then used in conjunction with two additional HR or UHR images to map T_1 and APD through a nonlinear least-squares fit of the magnitude of the SPGR signal to an appropriate model. Our extensive analyses with numerical simulations, phantom experiments, and in-vivo data further demonstrate the great potential of the FAM to provide accurate, reproducible, and accelerated HR or UHR T_1 and APD maps with correction of B_1^+ inhomogeneity. Furthermore, our results show that FAM is consistent with modern imaging acceleration techniques, addressing a critical outstanding issue in neuroimaging of practical, accurate, reproducible, and rapid whole-brain coverage parameter mapping.

Material and Methods

Four-angle method (FAM)

Assuming a longitudinal steady-state has been reached, the magnitude of the SPGR signal is conventionally given by the Ernst equation through

$$S_{\text{SPGR}}(\zeta\theta, \text{TR}) = |\text{APD}\sin(\zeta\theta)(1 - \exp(-\text{TR}/T_1))/(1 - \exp(-\text{TR}/T_1)\cos(\zeta\theta))| \quad [1]$$

where the dimensionless quantity ζ denotes the local, voxel-wise, B_1^+ scaling factor, APD is the apparent proton density representing the signal amplitude and is proportional to the true PD, reception field amplitude B_1^- , and machine factors, θ is the nominal excitation FA, TR is the repetition time, and T_1 is the longitudinal relaxation time.

FAM uses four SPGR images acquired with short TRs at different FAs to estimate ζ , APD, and T_1 . First, two SPGR images are used to estimate ζ voxel-by-voxel using the recently introduced steady-state double angle method (SS-DAM) [39], which is based on the signal intensity ratio of two SPGR images acquired with different FAs, but with very short TR. It exploits the linearity of the SPGR signal as a function of FA around $\theta = 180^\circ$ [40, 41]. In this linear regime, the intensity ratio, Q , of two SPGR images acquired with different FAs (e.g. θ values of 120° and 240°) is independent of T_1 and depends only on ζ . To calculate ζ voxel-wise, Q is computed for a large range of ζ , assuming a reasonable but arbitrary value of T_1 (e.g. $T_1 = 2000$ ms) to create a look-up table of Q vs. ζ . Experimental values of Q are determined from the acquired SPGR images, and ζ is then estimated in each voxel using a linear interpolation based on the pre-defined look-up table. As the ζ field varies smoothly over the imaged volume [33, 38–44], only modest spatial resolution imaging is required. Second, these values of ζ , obtained with the SS-DAM, are used in conjunction with the two remaining SPGR images, acquired with at HR or UHR, to map the T_1 and APD based on the Ernst equation defined above [30, 31]. Of note, as a pre-processing step, all acquired images must be reconstructed to the same spatial resolution to ensure accuracy of the voxel-wise ζ correction. All analyses were performed with MATLAB (MathWorks, Natick, MA, USA).

Simulation analysis

Numerical simulations were conducted to assess the performance of the FAM for T_1 and APD mapping. Noise-free SPGR brain T_1 -weighted images were generated, using the Ernst equation above, at four FA/TR combinations of $120^\circ/35$ ms, $240^\circ/35$ ms, $4^\circ/6$ ms, and $16^\circ/6$ ms, using predefined T_1 , PD, and ζ maps. The input T_1 map was generated from synthetic structural images obtained from BrainWeb database [45] with values of 800 ms, 1500 ms, and 4000 ms assigned respectively to white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF). Similarly, the input APD map was generated with values of 75, 90, and 100 for WM, GM, and CSF respectively. The input ζ map was generated assuming a Gaussian distribution defined over the spatial extent of the image with values between 0.65, at the edges, and 1.4, in the center, corresponding to a large ζ variation.

The two low-resolution SPGR images generated with voxel size of 2 mm x 2 mm x 2mm and FA/TR of $120^\circ/35$ ms and $240^\circ/35$ ms were used to estimate ζ voxel-by-voxel using the SS-DAM. This ζ map was then up-sampled to voxel size of 1 mm x 1 mm x 1 mm using

linear interpolation and used in conjunction with the high-resolution SPGR images generated with voxel size of 1 mm x 1 mm x 1 mm, FA/TR of 4°/6 ms and 16°/6 ms to simultaneously estimate, voxel-by-voxel, T_1 and APD. Results were derived from the noiseless SPGR images, and from SPGR images generated with SNR values of 25 and 200 corresponding to high- and low-resolution clinical imaging conditions. Noisy images were created by adding zero-mean Gaussian noise, of standard deviation (SD) σ , with the SNR defined as the signal of WM at FA of 4° divided by σ . For each estimated parameter (*i.e.* T_1 , PD, or ζ), relative difference maps, RDM, were calculated voxel-by-voxel according to $RDM(\%) = 100 \times |P_{est} - P_{ref}|/P_{ref}$, where P_{est} and P_{ref} are the estimated and reference parameters, respectively. The mean and SD of the RD values were also calculated over parenchymal voxels.

Phantom analysis

We evaluated the performance of FAM on a large phantom (9 cm diameter $\times$ 22 cm high) consisting of a bottle of water doped with copper sulfate. Four 3D SPGR images were acquired with FA/TR/TE combinations of 120°/35 ms/5.1 ms, 240°/35 ms/5.1 ms, 4°/7.5 ms/3.5 ms, and 16°/7.5 ms/3.5 ms; these are the minimum TE values achievable. All images were obtained with SENSE factor of 2 applied in the left/right direction, field-of-view (FoV) of 190 mm x 150 mm x 140 mm, and acquisition voxel size of 2 mm $\times$ 2 mm $\times$ 2 mm for the pair of SPGR images obtained with FAs of 120° and 240°, and of 1 mm $\times$ 1 mm $\times$ 1 mm for the pair of SPGR images obtained with FAs of 4° and 16°. All images were reconstructed to 1 mm $\times$ 1 mm $\times$ 1 mm. The total acquisition time was ~5 min. To analyze the effect of ζ on T_1 and PD determination, all derived T_1 and APD maps were obtained with and without ζ correction. For these measurements, RDM, defined by $RDM(\%) = 100 \times |P_{corr} - P_{uncorr}|/P_{corr}$, where P_{corr} and P_{uncorr} are the corrected and uncorrected parameter maps, respectively, were also computed. The mean and SD of the RD values calculated over all phantom regions were also displayed. All experiments were performed on a 3T whole body Philips MRI system (Achieva, Best, The Netherlands) using the internal quadrature body coil for transmission and an eight-channel phased-array head coil for reception.

In-vivo analysis

To evaluate FAM in-vivo, four 3D SPGR images were acquired from the brains of four healthy participants (3 males of ages 23, 38, and 53, and 1 female of age 41). Images were acquired with FA/TR/TE combinations of 120°/35 ms/4.7 ms, 240°/35 ms/4.7 ms, 4°/6.5 ms/3 ms, and 16°/6.5 ms/3 ms; these are the minimum TE values achievable. All images were obtained with SENSE factor of 2 applied in the left/right direction, and FoV of 200 mm x 200 mm x 180 mm. The SPGR images obtained at FAs of 120° and 240° were acquired with voxel size of 3.1 mm x 3.1 mm x 5 mm, while the SPGR images obtained at FAs of 4° and 16° were acquired with voxel size of 1.2 mm x 1.2 mm x 1.2 mm and reconstructed to 1 mm x 1 mm x 1 mm using zero-filling in k -space. The total acquisition time was ~4 min. Frequency-encoding was applied along the head/foot direction to avoid aliasing from the shoulders and upper body regions. To analyze the effect of ζ on T_1 and APD determination, all derived T_1 and PD maps were obtained with and without ζ correction. Corresponding RDM defined by $RDM(\%) = 100 \times |P_{corr} - P_{uncorr}|/P_{corr}$, where P_{corr} and P_{uncorr} are the corrected and uncorrected parameter maps, respectively, were also calculated. Mean and SD

RD values calculated over all brain regions were also displayed after manual segmentation performed to eliminate non-parenchymal regions. Moreover, to further reduce the acquisition time of the FAM, we investigated two different imaging acceleration methods. The first method consisted of using a SENSE factor of 2 in both left/right and anterior/posterior directions, leading to a total acquisition time of ~2.1 min. The second method consisted of combining the first method and half-scan acquisition, leading to a total acquisition time of ~1.3 min. All other parameters were identical to those described previously. Mean RD values in T_1 and APD were also calculated over large parenchymal regions for both accelerated and unaccelerated maps. Images were acquired from the brains of the three male subjects.

To evaluate the robustness of FAM to noise, T_1 and APD maps were also obtained using FAM from very high-resolution 3D SPGR images acquired at FAs of 4° and 16° from the brain of the 38-year-old participant, with voxel size 0.7 mm x 0.7 mm x 0.7 mm. We designate these as ultra-HR (UHR), since they are of substantially greater resolution than conventional clinical images. The images were acquired with TR = 10.2 ms and TE = 4.8 ms, and reconstructed to 0.35 mm x 0.35 mm x 0.35 mm using zero-filling in k -space. All other parameters were identical to those described previously. The total acquisition time was ~13 min. Here as well, the SPGR images were obtained with the acceleration methods described above using a SENSE factor of 2 in both left/right and anterior/posterior directions, leading to a total acquisition time of ~7 min, and in combination with half-scan acquisition, leading to a total acquisition time of ~5 min.

Further, the reproducibility of FAM for HR or UHR mapping of APD and T_1 was assessed by acquiring four independent 3D HR and UHR datasets from the brain of the female subject. For both levels of resolution, all corresponding datasets were linearly registered to the first dataset, using the FSL tool FLAIR [59], in order to correct for any motion that may have occurred between the scans. The calculated matrix of transformation was then applied to the corresponding APD and T_1 -derived parameter maps. Finally, for each derived parameter, the voxel-wise coefficient of variation (CoV) map was calculated over the four datasets and presented along with the four APD and T_1 maps for three different representative slices.

Finally, for all subjects, the mean and SD of T_1 and APD values were calculated in several brain regions. For that, the HR SPGR image of each subject was registered using nonlinear registration to the MNI standard space image using the FSL software tools FLIRT and FNIRT [59]. The derived transformation matrix was then applied to the T_1 and APD maps for that corresponding subject. Twelve regions of interest (ROIs) were defined encompassing WM and deep GM regions of the brain. Eight WM ROIs were derived from the MNI structural atlas [59], corresponding to frontal lobes, parietal lobe, occipital lobe, temporal lobe, cerebellum, splenium of corpus callosum, body of corpus callosum, and internal capsule, while the four deep GM regions, corresponding to insula, caudate, putamen, and thalamus, were derived from the Johns Hopkins University (JHU) ICM-DTI-81 atlas [59].

The nature of the experimental procedures was fully explained to all subjects, from whom written informed consent was obtained prior to participation. The MRI protocol was

approved by the MedStar Research Institute and the National Institutes of Health Intramural Ethics committees, and all examinations were performed in compliance with the standards established by the National Institutes of Health Institutional Review Board. All experiments were performed on a 3T whole body Philips MRI system (Achieva, Best, The Netherlands) using the internal quadrature body coil for transmission and an eight-channel phased-array head coil for reception.

Results

Figure 1a shows simulation results for estimated T_I and APD maps obtained using the FAM from SPGR T_I -weighted images generated at three different SNR values of infinity (*i.e.* noiseless case), 200, and 25, encompassing ideal and clinical SNR conditions. Results are displayed with and without ζ correction. Visual inspection shows that, for all SNRs, ζ -corrected T_I and PD maps were similar to the reference maps. This is further supported by the quantitative analysis showing negligible RD values. We note that the higher RD seen in CSF regions at low SNR (*i.e.* SNR = 25) is due to the very low signal intensities in the T_I -weighted images in those regions due to the long T_I of CSF. As expected, small ζ variations lead to very large errors in derived T_I and APD maps; this further supports the necessity to correct for ζ effects in the estimation of T_I and APD. We note that the B_I^+ mapping method described here has previously been validated [39], with the current extension being incorporation of the SPGR data to also perform HR or UHR APD and T_I mapping. Finally, the zoomed ζ images (Fig. 1b) as indicated by the very negligible influence of tissue in derived ζ values; this further highlights the accuracy of the SS-DAM.

Figure 2 shows examples of derived T_I and APD maps obtained from the phantom imaging data using FAM. As expected, the ζ map exhibits a smooth decrease in ζ as a function of distance from the center of the phantom, in accordance with previous observations [39–41]. More importantly, derived T_I and APD maps with ζ correction exhibit homogeneity across the phantom, reflecting the homogeneity of the phantom itself. In contrast, the T_I and APD maps derived without ζ correction exhibit strong heterogeneity that follows the pattern of ζ variation. Finally, RDM and mean and SD RD values calculated between corrected and uncorrected T_I and APD maps showed large differences, especially in regions where $\zeta \neq 1$. Again, these results demonstrate the importance of ζ mapping for accurate determination of T_I and APD and the great potential of the FAM.

Figure 3a shows examples of T_I and APD maps derived using FAM from the in-vivo HR imaging data from the brain of three participants. The maps are shown with and without ζ correction. Here again, as expected, the ζ maps exhibit a smooth decrease in ζ as a function of distance from the center of the brain. More importantly, derived T_I and APD maps with ζ correction exhibit a high degree of homogeneity across the brain in contrast to those derived without ζ correction, which exhibit substantial heterogeneity; this is also readily seen in the RDM, showing large differences in regions where ζ deviates substantially from 1. Finally, in agreement with the numerical simulations results, the zoomed ζ images (Fig. 3b) show a negligible tissue influence in derived ζ maps highlighting the high degree of accuracy of the SS-DAM.

Figure 4 shows examples of T_1 and APD maps derived using the FAM from HR SPGR images acquired with two different imaging acceleration methods from the brain of the three participants. Visual inspection shows that the T_1 and APD maps are very similar to the reference T_1 and APD maps derived without acceleration. Mean RD values between accelerated and unaccelerated maps for T_1 and APD, calculated over large parenchymal regions, were ~7% and ~3% for SENSE acceleration, and ~9% and ~4% for SENSE and half-scan acceleration. In addition to noise, we note that an important factor influencing these differences is motion artifacts resulting from the lengthy acquisition time required to acquire all scans for the comparison study. This lengthy acquisition time would not be required for simple implementation of FAM. Greater RD values are also seen from CSF regions, which show relatively high sensitivity to noise as described above (Fig. 1). Combining SENSE acceleration and half-scan imaging permits whole brain T_1 and APD mapping in less than 2 min using the FAM.

Figure 5 shows examples of T_1 and APD maps derived using the FAM from HR or UHR SPGR images. The UHR images were acquired with a voxel size of 0.7 mm x 0.7 mm x 0.7 mm, corresponding to a voxel volume of 0.34 mm³ which is ~5 times smaller than the voxel volume of the HR images. Visual inspection shows that HR and UHR derived parameter maps were very similar in all brain regions. In addition, derived T_1 and APD maps from UHR SPGR images acquired with the two imaging acceleration methods described above were virtually identical to the reference T_1 and APD maps derived from imaging data acquired without acceleration (Fig. 6).

Figure 7 shows examples of HR or UHR APD and T_1 maps from the brain of one participant derived using FAM. Results from four HR or UHR datasets acquired in immediate succession with the same experimental parameters are shown. Visual inspection of these APD and T_1 maps shows that the details of the voxel-by-voxel variation is consistent between the four datasets, indicating a high degree of reproducibility, especially in the white and gray matter regions. This reproducibility is quantified in the CoV maps. For the HR datasets, the mean CoV values calculated over large parenchymal regions of the brain were ~1% and ~4% for APD and T_1 , respectively, while for the UHR, the CoV values were ~3% and ~7%; this higher variation is expected as the UHR derived parameters are more sensitive to noise as compared to HR. Furthermore, we note a large variation in APD and T_1 values in the CSF regions; this is consistent with our simulation results and is the consequence of the experimental protocol being optimized for brain parenchyma rather than CSF. We note that some of the variation between scans may be attributed to interscan motion not entirely compensated for by the registration procedure described above.

Finally, the variation in T_1 and APD values across the four volunteers (Figure 8) agrees strongly with prior literature reports [1–14, 30–31, 50–51], indicating the sensitivity of the FAM to intersubject variations in T_1 and APD. Further, as expected, T_1 and APD values derived with or without ζ correction are different, especially in brain regions where ζ deviates significantly from 1.

Discussion

The FAM provides a rapid and robust approach for simultaneous mapping of T_1 and APD with B_1^+ correction. FAM is based on the use of four magnitude SPGR images measured with different excitation FAs, very short TRs, and simple modeling. Our results indicate the utility of exploiting the relatively large spatial scale of B_1^+ variability through combining low-resolution acquisitions appropriate for this scale, with high-resolution acquisitions appropriate for the desired HR or UHR APD and T_1 maps. Less favorable alternatives include the use of uniformly low-resolution images for constructing these maps, resulting in low-resolution parameter maps, or using uniformly high-resolution images, which is considerably slower. Thus, the method introduced in this paper has significant practical advantages over existing mapping methods.

The robustness of the FAM to noise was demonstrated with numerical, phantom, and *in-vivo* analyses, suggesting its utility in conjunction with imaging acceleration methods. We therefore demonstrated that FAM, with half-scan and SENSE reconstruction [46–48], permits whole brain HR or UHR T_1 and APD mapping in less than 2 min or 5 min (Figs. 4–6). Aside from its accuracy and precision, advantages of the FAM include rapid data acquisition, high reproducibility (Fig. 8), simple modeling, use of a conventional MRI sequence, *i.e.* SPGR, available on all preclinical and clinical MRI machines, and rapid processing time. All of this suggests the possibility of integrating the FAM into clinical investigations enabling much more accurate and clinically feasible imaging of a wide variety of CNS disorders, including demyelination and stroke. FAM applies equally well to other tissues and organs where B_1^+ inhomogeneity is a particular problem.

As expected, UHR, as compared to HR, mapping allows for greater depiction of detail in T_1 and APD maps (Figs. 5–7). Furthermore, UHR imaging results in a substantial reduction of the partial volume effects seen in several brain regions, especially at the interfaces between gray and white matter and between gray matter and CSF (Figs. 5–6). However, UHR imaging comes at the expense of increased acquisition time and decreased SNR. Nonetheless, our results showed that UHR whole brain T_1 and APD mapping could be obtained in less than 5 min. The possibility of UHR mapping within a clinically feasible time frame may be of substantial benefit in clinical studies requiring resolution of small brain structures or detection of small brain lesions [49–53].

While our results showed, overall, parameter values consistent with previous studies that used SPGR with variable FAs, derived values were different from those obtained using the inversion recovery or Look-Locker sequences [1–14, 30–31, 50–51] (Fig. 8). This is expected since any APD or T_1 mapping method would require B_1^+ correction and an exact correspondence of APD or T_1 values obtained using different “gold standard” sequences, including inversion recovery or Look-Locker, is not to be expected, since each of these sequences incorporates confounding effects to different degrees and represents an imperfect model (60–62). Finally, we note that with this small number of subjects, no statistical conclusions can be drawn regarding age or sex differences. The goal of these analyses is to indicate the reproducibility and utility of the FAM analysis of brain in human subjects, and to establish consistency with previous findings.

For simplicity, the T_I and APD maps were derived from SPGR images obtained with FAs of 4° and 16° . The use of these specific FA values was motivated by previous studies of T_I and APD determination [30–31, 33, 63]. However, the choice of the FAs is crucial to improve accuracy and precision of T_I and APD determination, and must be optimized in regard to the characteristics of the tissue or pathophysiology under investigation. Cramer-Rao lower bound or Monte Carlo simulations have been shown to be effective tools for such analysis, and are extensively used for experimental design [30–31, 33, 63–65].

Further, it is important to note that Eq. 1 used in our work is valid only in the case of homogenous excitation within the imaged volume, e.g. for 3D imaging. Indeed, Bouhrara and Bonny have shown that the use of selective pulses for slice selection in 2D imaging biases B_I^+ determination, emphasizing the importance of considering the slice profile distortions over off-resonance frequencies in the calculation of B_I^+ [66]. While a similar approach could be adopted for accurate determination of T_I and APD when selective pulses are used, a thorough analysis is still needed to investigate the influence of transverse coherence from outside the bandwidth of the selective pulse [66].

Our analysis of APD mapping does not account for the spatial variation of receiver coil sensitivity, B_I^- . Separating PD from coil sensitivity is an ill-posed problem [54]. Nevertheless, FAM may readily be applied in conjunction with several PD-estimation techniques [54]. While the need for B_I^+ is necessary as shown by our results, B_I^- variations could be neglected in the case of weak variation in reception. Further, we assumed perfect spoiling of the transverse magnetization prior to each RF pulse in the SPGR sequence. However, it has been shown that there may be a degree of preservation of transverse coherence in fast RF spoiled sequences with concomitant deviation of the signal behavior from the idealized model. While imperfect spoiling has negligible effect on the accuracy of B_I^+ mapping using the SS-DAM [39], it may influence the accuracy of T_I determination [55–57]. Improved accuracy may be obtainable through incrementation of the excitation RF phase pulse [58]. In our work, we used the default setting of the SPGR sequence which incorporate gradient spoiling combined with RF spoiling.

Conclusion

The FAM presented here permits fast, accurate, and practical simultaneous mapping of the active B_I field, T_I and APD within a clinically acceptable acquisition time. High-resolution whole brain coverage can be achieved in less than 2 min.

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Figure 1a.

Simulation results. Reference ζ , T_1 , and APD maps, and estimated ζ , T_1 , and APD maps using FAM from SPGR T_1 -weighted brain images generated at three different SNRs of infinity (i.e. noiseless case), 25, and 200. T_1 and APD results are shown with (corrected) and without (uncorrected) ζ correction. For each SNR and parameter, corresponding relative difference maps (RDM) and mean and standard deviation RD values, calculated over brain voxels, are displayed. We note that the ζ maps were derived from low-resolution SPGR images generated with a voxel size of 2 mm x 2 mm x 2 mm. The ζ maps were then up-

sampled using linear interpolation to a voxel size of 1 mm x 1 mm x 1 mm and used in conjunction with the high-resolution SPGR images generated with a voxel size of 1 mm x 1 mm x 1 mm to derive corresponding T_1 and APD maps.

Figure 1b.

Zoom on the ζ maps shown in Fig. 1a. The ζ maps are shown with a restricted color scale as compared to the ζ maps shown in Fig. 1a. The maps do not exhibit rapid ζ variations, especially in the edges of tissue boundaries; this indicates that the influence of tissue in derived ζ is very negligible. These results further highlight the accuracy of the SS-DAM.

Figure 2.

Phantom results. Estimated ζ , T_1 , and APD maps using FAM from SPGR T_1 -weighted phantom images. T_1 and APD maps derived from SPGR images with (corrected) or without (uncorrected) ζ correction, where APD is presented in arbitrary units (a.u.), are shown. For each parameter, relative difference maps (RDM), calculated between corrected and uncorrected maps, and corresponding mean and standard deviation RD values are displayed. We note that the ζ maps were derived from the low-resolution SPGR images acquired with a voxel size of 2 mm x 2 mm x 2 mm. The ζ maps were then up-sampled using linear interpolation to a voxel size of 1 mm x 1 mm x 1 mm and used in conjunction with the high-resolution SPGR images acquired with a voxel size of 1 mm x 1 mm x 1 mm to derive corresponding T_1 and APD maps.

Figure 3a. In-vivo results. Estimated ζ , T_1 , and APD maps using FAM from high-resolution SPGR images obtained from the brain of three participants. For each participant, results are shown for two sagittal slices with (corrected) and without (uncorrected) ζ correction. For each parameter, a relative difference map (RDM) calculated between corrected and uncorrected maps, and corresponding mean and standard deviation RD values are displayed. We note that for each participant, the ζ map was derived from the low-resolution SPGR images acquired with a voxel size of 3.1 mm x 3.1 mm x 5 mm. The ζ maps were then up-sampled using linear interpolation to a voxel size of 1 mm x 1 mm x 1 mm and used in conjunction with the high-resolution SPGR images acquired with a voxel size of 1.2 mm x 1.2 mm x 1.2 mm and reconstructed to a voxel size of 1 mm x 1 mm x 1 mm to derive corresponding T_1 and APD maps. 0.343

Figure 3b.

Zoom on the ζ maps shown in Fig. 3a. The ζ maps are shown with a restricted color scale as compared to the ζ maps shown in Fig. 3a. The maps do not exhibit rapid ζ variations, especially in the edges of tissue boundaries; this indicates that tissue influence in derived ζ is negligible. These results further highlight the accuracy of the SS-DAM.

Figure 4.

In-vivo results. Estimated T_1 and APD maps using FAM from high-resolution SPGR images acquired with two different imaging acceleration methods from the brains of the three participants. For each method, results are shown for two representative sagittal slices. We note that for each participant, the ζ map was derived from the low-resolution SPGR images acquired with voxel size of 3.1 mm x 3.1 mm x 5 mm. The ζ maps were then up-sampled using linear interpolation to a voxel size of 0.35 mm x 0.35 mm x 0.35 mm and used in conjunction with the high-resolution SPGR images acquired with a voxel size of 0.7 mm x 0.7 mm x 0.7 mm and reconstructed to a voxel size of 0.35 mm x 0.35 mm x 0.35 mm to derive corresponding T_1 and APD maps.

Figure 5.

In-vivo results. Estimated T_1 and APD maps obtained using FAM from SPGR images acquired at high-resolution (HR) or ultra-high-resolution (UHR) from the brain of one participant. For each method, results are shown for four representative sagittal slices.

Figure 6.

In-vivo results. Estimated T_1 and APD maps using FAM from ultra-high-resolution SPGR images acquired with two different acceleration methods from the brain of one participant. For each method, results are shown for four representative sagittal slices.

Figure 7a.

In-vivo results. Estimated T_1 and APD maps obtained using FAM from SPGR images acquired at high-resolution (HR) from the brain of one participant. T_1 and APD maps were derived from four HR datasets acquired in immediate succession and with the same experimental parameters. Coefficient of variation (CoV) maps calculated over all datasets are also displayed. Results are shown for three representative axial slices.

Figure 7b.

In-vivo results. Estimated T_1 and APD maps obtained using FAM from SPGR images acquired at ultra-high-resolution (UHR) from the brain of one participant. T_1 and APD maps were derived from four UHR datasets acquired in immediate succession and with the same experimental parameters. Coefficient of variation (CoV) maps calculated over all datasets are also displayed. Results are shown for three representative axial slices.

Figure 8.

Mean and standard deviation T_1 and APD values calculated in different brain regions from derived HR maps of the four imaged subjects. Results are shown with and without ζ correction.