The Effect of Varying Slice Thickness and Interslice Gap on $T_1$ and $T_2$ Measured with the Multidynamic Multi-echo Sequence

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Purpose: The purpose of our study was to investigate the effect of different slice thicknesses and/or interslice gaps on longitudinal and transverse relaxation times ($T_1$ and $T_2$) measured by a multi-dynamic, multi-echo (MDME) sequence.

Materials and Methods: This retrospective study included nine healthy subjects who underwent MDME sequence (at 3T) with four different combinations of slice thicknesses and/or interslice gaps: slice thickness of 4 mm and interslice gap of 0 mm (TH4/G0), TH4/G1, TH5/G0, and TH5/G1. $T_1$ and $T_2$ were measured in various brain regions by a qualified neuroradiologist with 8 years of clinical experience: the frontal white matter (WM), occipital WM, genu, splenium, frontal cortex, thalamus, putamen, caudate head, and cerebrospinal fluid (CSF). The paired samples $t$-test was used to investigate the effect of different slice thicknesses and interslice gaps (TH4/G0 versus TH4/G1 and TH5/G0 versus TH5/G1). $P < 0.013$ was considered statistically significant.

Results: $T_2$ in all brain regions and $T_1$ in the frontal WM, putamen, and CSF did not significantly change for different slice thicknesses and/or gaps ($P > 0.013$). In addition, $T_1$ in all brain regions of interest did not significantly change between TH4/G0, TH4/G1, TH5/G0 and TH5/G1. However, $T_1$ in some of the brain regions was higher with TH4/G0 than with TH5/G0 (occipital WM, frontal cortex, and caudate head) and with TH4/G1 than with TH5/G1 (occipital WM, genu, splenium and thalamus, all $P < 0.013$).

Conclusion: $T_2$ estimated using the MDME sequence was stable regardless of slice thickness or gap. Although the sequence seems to provide stable relaxation values, identical slice thicknesses need to be used for follow-up to prevent potential $T_1$ changes.

Keywords: interslice gap, multi-dynamic multi-echo sequence, slice thickness, $T_1$-relaxation time, $T_2$-relaxation time

Introduction

A novel quantitative MRI sequence, the 2D fast spin echo (FSE) multi-dynamic multi-echo (MDME) sequence,
application of quantitative MRI. In addition, the resulting absolute quantitative values enable the formation of synthetic images with the intended contrast that is consistent regarding imperfections of the scanner and variations in the pulse sequence.\textsuperscript{3,4} Although the quality of these synthetic images is perceived to be inferior, diagnosis based on synthetic MRI and conventional MRI has shown good agreement.\textsuperscript{5,6} Using the MDME sequence, several previous studies reported promising results for multiple sclerosis, brain metastases, idiopathic normal pressure hydrocephalus, and meningitis.\textsuperscript{7–13}

The current MDME sequence, quantification of relaxation times and proton density by multi-echo acquisition of a saturation recovery using turbo spin-echo readout (QRAPMASTER) is an upgraded version of quantification of relaxation times and proton density by twin-echo saturation-recovery turbo-field echo (QRAPTEST) in which the previous small flip angle excitation pulse was replaced with a 90° pulse and a series of 180° refocusing pulses, which were incorporated to generate a train of spin echoes instead of gradient echoes.\textsuperscript{1,14} The resulting improvements in signal-to-noise ratio (SNR) and the robustness against susceptibility effects are clearly beneficial. However, three different slice-selective radiofrequency (RF) pulses with large flip angles (90°, 120°, and 180°) are indispensably used in the sequence, which may, therefore, be more subject to the imperfection of the RF pulses, particularly at a higher field. Although the MDME sequence allows for simultaneous $B_1$ inhomogeneity correction, residual inhomogeneity may persist at a higher field as previously discussed.\textsuperscript{15} In clinical practice, it is sometimes necessary to modify the slice thickness and gap due to individual differences in brain size and a limited acquisition time. Consequently, the extent of imperfections in RF pulses may also be variable. While previous studies demonstrated the robust performance of the sequence, the majority of studies have been conducted at 1.5T.\textsuperscript{1,2,5,7,16,17} In this report, we investigated the effect of varying the slice thickness and/or interslice gap on the estimated $T_1$ and $T_2$ by the MDME sequence in anticipation of further expanded applications of the sequence in neuroimaging. A set of data acquired from healthy subjects at 3T was retrospectively collected where the potential impact of RF pulse imperfections is expected to be more pronounced.\textsuperscript{18}

Materials and Methods

Study population

Our institutional review board approved the study protocol, and informed consent was waived. Ten healthy subjects underwent brain MRI scans with the MDME sequence for health check-ups in October 2015. Data from one subject were excluded due to motion artifacts. Finally, nine subjects (all men; mean age of 24 years; age range of 23–27 years) were included in this study. No abnormal radiologic signs were revealed in the brain MRI scans.

MR examination

All subjects underwent MR examination using a 3T clinical scanner (Discovery MR750w; GE Medical Systems, WI, USA) with a 32-channel head coil. Axial images were acquired using the 2D MDME sequence 1) (flip angles = 120° [saturation], 90° [excitation], and 180° [refocusing]). All subjects were scanned using four combinations of different slice thicknesses (TH:mm) and interslice gaps (G:mm): TH4/G0, TH4/G1, TH5/G0, and TH5/G1. The in-plane resolution was maintained at 0.75 × 0.75 mm². The scan was set to cover the same range of the brain by adjusting the number of slices. Consequently, TRs were automatically adjusted accordingly. The detailed sequence parameters are shown in Table 1.

Data post-processing

Least squares fitting was performed on the signal intensity ($S$) of each pixel of the images per section to calculate $T_1$ by assuming a single exponential decay according to the following Eq. (1):

\[
sS = A \cdot PD \cdot \exp \left( -\frac{TE}{T_z} \right) \cdot \frac{1 - [1 - \cos(B, \theta) \cdot \exp \left( -\frac{TI}{T_1} \right) - \cos(B, \theta) \cdot \exp \left( -\frac{TR}{T_1} \right)]}{1 - \cos(B, \alpha) \cdot \cos(B, \theta) \exp \left( -\frac{TR}{T_1} \right)}
\]

where $A$ is the overall intensity scaling factor considering the coil sensitivity, RF chain amplification and voxel volume; $\alpha$ is the applied excitation flip angle; and $\theta$ is the saturation pulse flip angle. $T_2$ was also calculated by least squares fitting. Quantitative MRI maps of $T_1$ and $T_2$ were generated using vendor-provided software (SyMRI 7.2; Synthetic MR, Linköping, Sweden).

Image analysis

To accurately and consistently place ROIs in the intended brain regions across the $T_1$ and $T_2$ maps obtained from different slice thicknesses and/or gaps, first, all quantitative maps were downloaded as Digital Imaging and COmmunications in Medicine (DICOM) files after data post-processing using the SyMRI software. Second, a folder of all quantitative maps for each subject was loaded into a DICOM viewer (RadiAnt DICOM Viewer, version 3.4.2; Meixant, Poznan, Poland). The number of slices was 38 for TH4/G0, 30 for TH4/G1 and TH5/G0, and 26 for TH5/G1 to encompass the entire brain. Finally, ROIs were placed in a total of nine brain regions by a qualified neuroradiologist with 8 years of clinical experience: the frontal white matter (WM), occipital...
Table 1: Multi-dynamic, Multi-echo sequence parameters

|                  | TH4/G0 | TH4/G1 | TH5/G0 | TH5/G1 |
|------------------|--------|--------|--------|--------|
| TR (ms)          | 6073   | 4510   | 4553   | 4000   |
| TE (ms)          | 21.4/85.8 | 21.6/85.8 | 21.6/86.6 | 21.6/86.6 |
| Number of sections | 38     | 30     | 30     | 26     |
| Scan time        | 7 min 42 s | 5 min 43 s | 5 min 46 s | 5 min 04 s |
| TI (ms)          | Automatically calculated 4 different TI |
| FOV (mm²)        | 240 × 192 |
| Scan matrix      | 320 × 256 |
| Asset factor     | 2 |
| Echo-train length | 12   |
| Bandwidth (kHz)  | 22.73  |
| NEX              | 1 |

G, interslice gaps (mm); NEX, the number of excitations; TI, inversion delay; TH, slice thicknesses (mm).

Fig. 1: Representative T₁ and T₂ maps from a subject and the location of the ROI for the frontal white matter (WM). (A and F) coronal and sagittal T₁ maps (generated from the axial T₁ maps by the RadiAnt DICOM Viewer; Meixant, Poznan, Poland). (B–E) magnified axial T₁ maps (B and G) slice thickness of 4 mm and interslice gap of 0 mm (TH4/G0), (C and H) TH4/G1, (D and I) TH5/G0, and (E and J) TH5/G1. The ROI was carefully drawn to avoid the partial volume effect on the axial T₁ map with TH4/G0 (B) and copied and pasted on the rest of the T₁ (C–E) and T₂ (G–J) maps. These pasted ROIs were further adjusted if necessary. The mean T₁ and T₂ values in the frontal WM were not significantly different for the four slice groups with different thicknesses and gaps.

WM, genu, splenium, frontal cortex, thalamus, putamen, head of the caudate nucleus, and cerebral spinal fluid (CSF). All quantitative maps were adjusted to show the same slice and magnified focusing on the same brain region to minimize the partial volume effect. An ROI was drawn on each of the most representative regions in the T₁ maps with TH4/G0 and copied and pasted onto the remaining quantitative maps for each subject (Figs. 1 and 2). The positions of the pasted ROIs were examined, and, if necessary, carefully adjusted. A mean pixel value was obtained for each ROI. As a result, four T₁ and four T₂ values were simultaneously obtained for each of the nine brain regions.

Statistical analysis
Continuous data were expressed as mean ± standard deviation (SD). The Kolmogorov–Smirnov test was applied to the quantitative values for normality (P < 0.05 indicates a non-normal distribution). If data distributions were normal (P-value > 0.05), the paired samples t-test was used to investigate the effect of different slice thicknesses (TH4/G0 versus TH5/G0 and TH4/G1 versus TH5/G1) and interslice gaps (TH4/G0 versus TH4/G1 and TH5/G0 versus TH5/G1). If the data distributions were non-normally distributed (P-value ≤ 0.05), the Wilcoxon signed rank test (paired) was used. The significance level for paired samples t-test or Wilcoxon signed rank test.
Slice Thickness and Gap on MDME Sequence

was adjusted to \( P < 0.013 \) for the Bonferroni correction. Statistical analyses were performed using commercially available software (IBM SPSS Statistics, version 20 [IBM Corporation, Armonk, NY, USA]).

**Results**

Figures 1 and 2 show representative \( T_1 \) and \( T_2 \) maps of the brain from a subject. The high SNR and contrast in the quantitative maps are clearly shown for all combinations of slice thicknesses and interslice gaps. Representative locations of the ROIs are also shown for the frontal WM (Fig. 1) and frontal cortex (Fig. 2), which are the largest (~122 pixels) and the smallest (~6 pixels) in ROI size, respectively. The potential effect of the partial volume is clearly negligible.

Table 2 summarizes the \( T_1 \) and \( T_2 \) values for the nine regions of the brain for the four slice groups. Data distributions of all brain regions except the CSF were normal (\( P_s > 0.05 \), Kolmogorov–Smirnov test). The \( P \)-values calculated from the paired samples \( t \)-tests or the Wilcoxon signed rank test between the slice groups are summarized in Table 3.

For all brain regions, \( T_2 \) did not differ between any of the slice groups (\( P_s > 0.013 \)). For all brain regions, \( T_1 \) did not differ significantly between TH5/G0 and TH5/G1 and between TH4/G0 and TH4/G1 (\( P_s > 0.013 \)), despite the large difference in TR for the latter. However, the use of different slice thicknesses influenced the \( T_1 \) values for various brain regions.

**Table 2** \( T_1 \) and \( T_2 \) for the four combinations of slice thicknesses and interslice gaps

| ROI size (mm²) | \( T_1 \) relaxation time (ms) | \( T_2 \) relaxation time (ms) |
|----------------|-------------------------------|-------------------------------|
|                | TH4/G0 | TH4/G1 | TH5/G0 | TH5/G1 | TH4/G0 | TH4/G1 | TH5/G0 | TH5/G1 |
| Frontal WM     | 68.6 ± 32.5 | 734 ± 33 | 722 ± 20 | 700 ± 33 | 690 ± 23 | 68 ± 5 | 67 ± 4 | 67 ± 5 | 66 ± 4 |
| Occipital WM   | 19.9 ± 6.3 | 725 ± 32 | 721 ± 31 | 686 ± 27 | 687 ± 29 | 75 ± 5 | 75 ± 2 | 75 ± 2 | 75 ± 4 |
| Genu           | 25.0 ± 10.5 | 641 ± 43 | 640 ± 41 | 609 ± 29 | 608 ± 44 | 62 ± 2 | 61 ± 3 | 61 ± 2 | 60 ± 2 |
| Splenium       | 31.6 ± 5.6 | 717 ± 42 | 705 ± 19 | 681 ± 34 | 656 ± 34 | 70 ± 3 | 69 ± 2 | 69 ± 3 | 68 ± 2 |
| Frontal cortex | 3.4 ± 2.4 | 1206 ± 108 | 1254 ± 158 | 1135 ± 99 | 1138 ± 97 | 82 ± 5 | 81 ± 5 | 82 ± 6 | 79 ± 5 |
| Thalamus       | 64.3 ± 10.9 | 913 ± 33 | 897 ± 32 | 872 ± 39 | 870 ± 38 | 66 ± 3 | 66 ± 3 | 66 ± 3 | 66 ± 2 |
| Putamen        | 38.3 ± 11.9 | 1142 ± 53 | 1119 ± 49 | 1097 ± 43 | 1094 ± 58 | 65 ± 2 | 65 ± 2 | 65 ± 2 | 64 ± 3 |
| Head of caudate nucleus | 18.5 ± 5.5 | 1153 ± 64 | 1142 ± 71 | 1101 ± 57 | 1097 ± 46 | 70 ± 2 | 69 ± 2 | 70 ± 2 | 69 ± 2 |
| CSF            | 26.1 ± 14.3 | 4088 ± 158 | 4154 ± 43 | 4152 ± 38 | 4141 ± 18 | 1359 ± 401 | 1024 ± 392 | 1125 ± 483 | 914 ± 336 |

Data are means ± standard deviation. CSF, cerebrospinal fluid; G, interslice gaps (mm); TH, slice thicknesses (mm); WM, white matter.
Table 3 Results of the paired samples t-tests

|                  | TH4/G0 versus TH4/G1 | TH5/G0 versus TH5/G1 | TH4/G0 versus TH5/G0 | TH4/G1 versus TH5/G1 |
|------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Frontal WM       | 0.370                 | 0.366                 | 0.043                 | 0.026                 |
| Occipital WM     | 0.609                 | 0.794                 | 0.003<sup>a</sup>     | 0.002<sup>a</sup>     |
| Genu             | 0.905                 | 0.984                 | 0.044                 | 0.009<sup>a</sup>     |
| Splenium         | 0.527                 | 0.028                 | 0.055                 | 0.004<sup>a</sup>     |
| Frontal cortex   | 0.136                 | 0.912                 | 0.006<sup>a</sup>     | 0.021                 |
| Thalamus         | 0.268                 | 0.807                 | 0.015                 | 0.004<sup>a</sup>     |
| Putamen          | 0.238                 | 0.868                 | 0.033                 | 0.247                 |
| Head of caudate nucleus | 0.562             | 0.809                 | 0.007<sup>a</sup>     | 0.076                 |
| CSF              | 0.373                 | 0.859                 | 0.373                 | 1.000                 |

<sup>a</sup>Adjusted P < 0.013 values were considered statistically significant. The P values were calculated from the paired samples t-tests (all brain regions except the cerebral spinal fluid [CSF]) or the Wilcoxon signed rank test (CSF). G, interslice gaps (mm); TH, slice thicknesses (mm); WM, white matter.

The T<sub>1</sub> values of the occipital WM, frontal cortex and head of caudate nucleus were significantly higher with TH4/G0 than with TH5/G0 (P = 0.003 for the occipital WM, P = 0.006 for the frontal cortex and P = 0.007 for the head of caudate nucleus). In addition, the T<sub>1</sub> values of the occipital WM, genu, splenium, and thalamus were found to be higher with TH4/G1 than with TH5/G1 (P = 0.002 for the occipital WM, P = 0.009 for the genu, P = 0.004 for the splenium and P = 0.004 for the thalamus). Box-and-whisker representations in Fig. 3 illustrated the T<sub>1</sub> and T<sub>2</sub> values in the frontal WM and occipital WM with different slice thicknesses and/or interslice gaps.

Discussion

The MDME sequence enabled simultaneous acquisition of the tissue relaxation parameters T<sub>1</sub> and T<sub>2</sub>, whereas most
of the past quantitative MRI methods allowed only one parameter per scan. One advantage of this method is that the quantitative MRI results are in absolute values for tissue properties, which are independent of scanners or variations in the pulse sequence.

The MDME sequence used in our study employs three different RF pulses for saturation, excitation, and refocusing with relatively large flip angles of 120°, 90° and 180°, respectively. In a prior article, Warnnjes et al. thoroughly investigated the impact of the resulting imperfections of the pulse profiles on the estimation of $T_1$, $T_2$, and PD with different uses of an agarose phantom and simulations at 1.5T. The fitting algorithms for quantification were also modified accordingly by fine-tuning the intensity of the echoes for the $T_2$ correction and the relationship between the effective flip angles of the saturation and excitation pulses for PD estimation. The promising applicability of the sequence in neuroimaging has been previously reported. However, to our knowledge, the majority of previous studies investigated the robustness of the sequence at 1.5T. Given that the potential impact of the imperfection of RF pulses on quantitative MRI can be more pronounced at a higher field, we investigated the effect of differences in slice thickness (4 versus 5 mm) and interslice gap (with and without a 1-mm gap) at 3T. For further expansion of the clinical application of the MDME sequence, the effect of such fundamental sequence variations, such as the slice thickness and interslice gap, needs to be investigated at a higher field. This was the motivation for our study. A previous study reported comparable performances for sequences at 1.5 and 3T; however, these were performed only qualitatively based on the quality of synthesized images (or semi-quantitatively based on 5-level image quality scores) not quantitatively in terms of the actually measured $T_1$ and $T_2$ values. To exclude the partial volume effect in our analysis, all ROIs were carefully selected.

Our $T_1$ and $T_2$ results at 3T are comparable with previous findings ($T_1$ of gray matter [GM]: 1200–1820 ms, $T_2$ of WM: 650–847 ms, $T_2$ of GM: 71–99 ms and $T_2$ of WM: 56–69 ms). In response to the presence/absence of interslice gaps, we did not find significant difference in $T_1$ and $T_2$ values for all brain regions. Therefore, although further investigation is required with a larger number of subjects, the effect of cross-talk may not result in substantial quantitative errors in the $T_1$ and $T_2$ estimation for slice thicknesses of less than 5 mm. Our results support the advantage of the linear slice order employed by the MDME sequence instead of the standard interleaved slice order. Our comparison of the $T_1$ and $T_2$ values for TH4/G0 and TH4/G1 also demonstrates that the influence of the large difference in TR is minimal.

By increasing the slice thickness from TH4/G0 to TH5/G0, significantly different $T_1$ values were obtained in the occipital WM, frontal cortex, and head of caudate nucleus. Given that the ROI sizes of these brain regions are the three smallest, the different SNRs of the images for the two slice groups could be responsible for the different $T_1$ values. Upon the negligible effects of partial volume and cross-talk, these spatially dependent changes in $T_1$ in response to the increased slice thickness might also be due to spatially dependent residual inhomogeneity of $B_0$ at 3T as previously discussed. By increasing the slice thickness from TH4/G1 to TH5/G1 in the presence of interslice gaps, significantly different $T_1$ values were obtained in the occipital WM, genu, splenium, and thalamus. These brain regions do not coincide with those for TH4/ G0 versus TH5/G0, and they include those with a relatively large ROI size, such as the thalamus. These spatially dependent changes in $T_1$ might also be due to spatially dependent residual $B_0$ inhomogeneity. Given the proximity of these brain regions to the ventricle, flow artifacts may also be responsible for the different $T_1$ values. While the brain coverages are all identical for the four different slice groups, the coverages of the individual slices are all different for the different slice groups due to different slice thicknesses and the presence/absence of interslice gaps. Therefore, $T_1$ changes in response to the increased slice thickness with and without interslice gaps can occur in different brain regions due to the presence of factors that render the performance of the sequence spatially dependent, such as residual $B_0$ inhomogeneity and flow artifacts.

In our study, although the $T_1$ values for several brain regions were measured differently in response to increased slice thicknesses, the $T_1$ values were robust regardless of the slice thickness or presence of interslice gaps. Thus, our study corroborates the advantage of the MDME sequence, which is that there is no propagation of errors between $T_1$ and $T_2$, even if the quantification is simultaneously performed. Several previous studies reported $T_2$ values for various brain pathologies, such as multiple sclerosis, stroke, epilepsy, Parkinson’s disease, and in a developing preterm brain. In terms of the clinical follow-up, the robust performance of the MDME sequence for $T_2$ estimation in our study is quite promising. Finally, the substantially large $T_1$ and $T_2$ values of the CSF did not differ between any of the slice groups. Therefore, our results demonstrate the excellent dynamic range of the sequence using the current setting.

There are several limitations of our study. First, as was noted in the “Methods” section, we covered the same range of the brain for the subjects by adjusting the number of slices. In the current version of the sequence, TR is automatically adjusted according to the number of slices for minimum scan time. As a result, different TRs were used for all four groups. However, the shortest TR used for the TH5/G1 slice group is already as long as 4000 ms at 3T. Therefore, potential quantitative errors resulting from the different TRs can be negligible in most brain tissues. Further shortening of the TR due to a fewer number of slices would increase the weight of the short relaxation components of the total $T_1$ relaxation behavior, and hence, the effective mono-exponential approximation would be somewhat shorter. However, changes in the number of slices and TR result in only minor changes in the echo times of the...
acquisition (Table 1) and have a negligible influence on the $T_2$ estimation. Second, because our study was a retrospective study, the number of subjects was limited. This may also explain that the previously reported extent of the cross-talk effect of the sequence\(^1\) was not observed in our study. Third, we did not compare our results with thinner slices, which might be useful for various CNS diseases. Although a scan with a 3-mm slice thickness was tested in a preliminary study, it was not included in this study due to the poor SNR of the images. Finally, a separate $B_1$ mapping using a gold standard method would have clarified the extent of the potential residual $B_1$ inhomogeneity in $T_1$ estimation, which may not completely be excluded in our study at 3T as discussed above and previously.\(^15\) Nonetheless, the simultaneous $B_1$ inhomogeneity correction provided by the MDME sequence is clearly beneficial and of great importance in quantitative MRI.

**Conclusion**

In conclusion, while the slightly variable $T_1$ values obtained using the MDME sequence for the different slice thicknesses require further investigation with a larger sample size, the robust performance of the sequence for $T_1$ estimation at 3T supports the expanded applicability of the sequence in neuroimaging.

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**Conflicts of Interest**

None. Technical support was provided by a GE Healthcare employee (Moonjung Hwang) regarding the sequence modifications and implementation with our MRI. Authors not associated with GE Healthcare maintained full control of the data at all times.

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