Bloch Simulation of a Three-point Dixon Experiment Using a Four-dimensional Numerical Phantom

Ryoichi Kose¹, Katsumi Kose¹*, and Yasuhiko Terada²

A 4D numerical phantom, which is defined in the 3D spatial axes and the resonance frequency axis, is indispensable for Bloch simulations of biological tissues with complex distribution of materials. In this study, a 4D numerical phantom was created using MR image datasets of a biological sample containing water and fat, and the Bloch simulations were performed using the 4D numerical phantom. As a result, 3D images of the sample containing water and fat were successfully reproduced, which demonstrated the usefulness of the concept of the 4D numerical phantom.

Keywords: Bloch simulation, Dixon method, three-point Dixon, numerical phantom

Introduction

With the recent dramatic increase in computing power, many studies to reproduce the MR imaging process based on the Bloch equations have been reported.¹⁻⁶ At present, the fundamental developments of computational methods have been almost completed, and their applications to realistic biological systems are underway. Some examples are applications to magnetization transfer phenomena,⁴ flowing systems,⁷ and objects with T₂⁻⁰ distribution and chemical shifts.⁸

We recently published a method to perform Bloch simulations of biological samples with chemical shift and T₂⁻⁰ distributions.⁸ In the proposed method, a 4D numerical phantom, i.e., proton density (PD), T₁ and T₂ in the 4D space with spatial 3D axes, and a resonance frequency axis, was defined for the Bloch simulation. In our previous report, we demonstrated the usefulness of this approach using a simple real phantom consisting of four test tubes filled with doped water, peanut oil, margarine, and fish sausage. The problem with the experimental setup, however, was that each material was homogeneous to each test tube and was spatially separated by the test tubes, and the effectiveness of the proposed method was not fully demonstrated. In this paper, we report a method for creating a 4D numerical phantom for a realistic biological sample, including different materials (water and fat) in the voxels, and evaluate the usefulness of our approach.

Materials and Methods

MRI experiment

A commercially available pork block bacon (size: 38 mm × 48 mm × 80 mm) was used for the MR imaging experiment to create a 4D numerical phantom (Fig. 1a). To prevent the sample from drying, the bacon block was enclosed in a plastic bottle (inner diameter = 48 mm). We used an MRI system with a 1.5 T superconducting magnet (JMTB-1.5/280/SSE; JASTEC, Hyogo, Japan), which has a horizontal room temperature bore (inner diameter = 280 mm), and a digital MRI console (MRTechnology, Ibaraki, Japan). A gradient coil set (inner diameter = 87 mm) designed using the target field method was used. The RF coil was an 8-element birdcage coil (diameter = 64 mm, length = 64 mm), which was used for both transmission and reception.

Pulse sequences were 3D spin echo (SE) sequences with TR/TE = 800 ms/20 ms (proton density-weighted [PDW] sequence), 160 ms/20 ms (T1-weighted [T1W] sequence), and 800 ms/40 ms (T2-weighted [T2W] sequence) (field of view (FOV): 64 mm × 64 mm × 128 mm, image matrix: 128 × 128 × 256, and voxel size: 0.5 mm × 0.5 mm × 0.5 mm). In order to obtain water and fat images using the three-point Dixon method,⁹,¹⁰ the SE refocusing time was shifted by ±2.2 ms from the in-phase time by shifting the timing of the refocusing (180°) RF pulse by ±1.1 ms.

Image processing for the 4D numerical phantom

To separate the water and fat images, the three-point Dixon method¹⁰ was used. To remove phase aliasing caused by a large static field inhomogeneity, the inhomogeneity field was
approximated using a second-order polynomial and the phase shift was corrected by the polynomial.\textsuperscript{10} This operation (virtual shimming) was performed instead of phase unwrapping calculation because 3D phase unwrapping is unstable for noisy image datasets. Residual inhomogeneity of the magnetic field $\Delta B_0$ was calculated from the difference between the phase maps of two out-of-phase images acquired at $\pm 2.2$ ms using the PDW sequences.

Using the magnetic field inhomogeneity $\Delta B_0$, PDW, T1W, and T2W water and fat images with correct sign were separated.\textsuperscript{10} PD, T1, and T2 maps of water and fat were calculated from the parameter-weighted images using the standard SE signal equation. The 4D numerical phantoms were created by mapping the 3D water and fat numerical phantoms along the frequency axis, according to the resonance frequencies and relative spectral intensities reported in the past studies.\textsuperscript{11,12}

**Bloch simulation**
The Bloch simulation of the three-point Dixon experiment was performed using the 4D numerical phantom and a Bloch simulation software package\textsuperscript{5,6} developed by our group. Since the Bloch simulation program was developed for 3D numerical phantoms (PD, T1, and T2 maps) whose coordinate axes were spatial axes (x, y, and z), the MR signal for the 4D numerical phantom was obtained by summing up MR signals simulated for the 3D numerical phantoms with assigned resonance frequencies (= homogeneous offset magnetic fields). The Bloch simulation for the 3D numerical phantom was performed in the uniform offset magnetic field corresponding to the chemical shift.

**Results**
Figure 1b shows 2D cross-sectional images of the bacon block selected from the 3D image datasets acquired with the PDW 3D SE sequences under the in-phase (0 ms) and out-of-phase ($\pm 2.2$ ms) conditions. These images clearly show the water-fat mixed region by the low signal area in the out-of-phase images.

Figure 1c shows the calculation process for the inhomogeneous static magnetic field $\Delta B_0$. At first, the phase shifts of the out-of-phase images caused by the instrumental imperfections were corrected using the phase image of the in-phase images.
image (base phase correction). Next, a large phase shift variation caused by the static magnetic field inhomogeneity was corrected using a quadratic polynomial function that simulated the field inhomogeneity (virtual shimming). This operation corresponds to an ideal second-order shimming of the inhomogeneous static magnetic field. The difference between the phase images acquired at $-2.2$ ms and $+2.2$ ms gave the magnetic field inhomogeneity $\Delta B_0$ that could not be corrected by the virtual shimming. Since the phase difference between water and fat was $\pi$ radian under the out-of-phase condition, the phase difference was corrected by subtracting $\pi$ radian from the phase shift in the fat region, which resulted in the $\Delta B_0$ map. The spot noise observed in the $\Delta B_0$ map was corrected using a median filter and a low pass filter. Using the $\Delta B_0$ map, phase distributions of the real part and imaginary part images were corrected and water and fat images were successfully separated for the central 16 successive axial planes (8 mm thick in total). In the region outside the axial slices, the fitting of the inhomogeneous magnetic field by the quadratic polynomial was not accurate, and it was impossible to eliminate the phase aliasing.

Figure 2a shows the central cross-sections of the separated PDW, T1W, and T2W images of water and fat. Figure 2b shows the PD, T1, and T2 parameter maps of water and fat calculated from the parameter-weighted images shown in Fig. 2a using the standard SE signal equation. Since the $\Delta B_0$ map could be calculated for 16 successive axial planes, parameter maps were obtained for the 3D rectangular region (128 $\times$ 128 $\times$ 16 voxels), including the central axial plane of the sample.

Figure 3 shows the schematic view of the 4D numerical phantom created from the 3D parameter maps of water and fat. The 4D phantom consists of the 3D water phantom located at 0 Hz and the 3D fat phantom located at 43, −119, −152, −166, −194, −213, and −238 Hz resonance frequency because the fat spectrum can be approximated by seven major resonance lines. The relaxation times of the fat protons are different for individual resonance lines, but for simplicity, they were assumed to be identical for all resonance lines. Typical T1 and T2 values of the numerical phantom were 940 and 29.5 ms for the water, and 272 and 34.5 ms for the fat, respectively, as determined by the peaks in the histograms of the T1 and T2 maps shown in Fig. 2b.

Figure 4a shows the central cross-sectional images of the block bacon acquired using the PDW 3D SE sequence (TR/TE = 800 ms/20 ms) under the in-phase and out-of-phase conditions. Figure 4b shows the PDW SE images simulated using the 4D numerical phantom shown in Fig. 3. The calculation time for one 4D image (number of voxels: 128 $\times$ 128 $\times$ 16 [x, y, and z directions], number of subvoxels: 1 $\times$ 1 $\times$ 4 [x, y, and z directions], and number of spectra: 8) was about 190 s using a GPU (GeForce RTX 2080 Ti; NVIDIA, Santa Clara, CA, USA). The number of subvoxels in the readout direction (z direction) was set to 4 in order to accurately simulate the real condition of the MR data acquisition. The simulated images were reconstructed after summing up the eight sets of MR signals calculated for the water and fat phantoms.

Figure 4c shows the difference between the images obtained from the experiment and the simulation. The
difference between the images was calculated after equating the sum of the absolute values of each image. The ratio of the sum for the absolute values of the difference images to the sum of the absolute values of the original images was 18.4%, 12.8%, and 18.3% for the out-of-phase (–2.2 ms), in-phase (0 ms), and out-of-phase (+2.2 ms) images, respectively.

Discussion

**Difference between images acquired with experiment and simulation**

As shown in Fig. 4, there were 10% to 20% differences between the images acquired with the experiment and the simulation. There are many possible causes for the errors, but most of them were produced in the creating process of the numerical phantoms. This is because the Bloch simulation program can reproduce images with high accuracy (error within 1%) if appropriate numbers of sub-voxels are defined.\[5\] Below, we consider the errors in the numerical phantom creation process.

To separate water and fat images using the Dixon method, the phase image is required. However, when water and fat are contained in a voxel, the sum of the nuclear magnetization of water and fat in a voxel can be close to zero in the out-of-phase images.\[13\]–\[15\] In such a case, there will be a large error in the phase calculation due to the background noise. This leads to a large error in the calculation of the separated water and fat images. To overcome this problem, the three images should be measured at three unequally spaced time points, instead of at three equally spaced time points used in this study.

Errors also occur when calculating parameter maps from the parameter-weighted (PDW, T1W, and T2W) water and fat images. This is because TR/TE used in the 3D SE sequences (800 ms/20 ms, 160 ms/20 ms, and 800 ms/40 ms) were not optimal for measuring T1 and T2 of the water and fat in the bacon block. The relaxation times of the resonance lines of subcutaneous fat measured at 7T11 are reported to be 320 to 1080 ms for T1 and 30 to 67 ms for T2. For the 4D numerical phantom, T1 and T2 for fat were set to 272 ms and 34.5 ms, respectively, for all resonance lines. Therefore, T1 and T2 might be underestimated, although frequency (magnetic field) dependence of T1 and T2 of fat is not available. To overcome this problem, it is desirable to use more efficient...
pulse sequences such as 3D multiple SE sequences for creating the numerical phantom.

**Number of spectral lines used for the fat spectrum**
The nuclear magnetic resonance (NMR) spectrum of fat protons consists of many resonance lines. In this study, we assumed that fat consists of a single resonance line for the analysis of the experimental data acquired by the three-point Dixon method, and the fat consists of seven resonance lines for the Bloch simulation. We used the single-line approximation for the analysis of the experimental images because the number of the images was insufficient for the multiple line fitting. However, because the number of resonance lines is not limited for the creation of the 4D numerical phantom, we used seven resonance lines for the Bloch simulation. Of course, in order to represent the fat spectrum with many spectral lines more precisely, the relaxation time of each line should be determined using other experimental data. Therefore, the 4D numerical phantom can be used for the Bloch simulation of advanced pulse sequences such as IDEAL (iterative decomposition of water and fat with echo asymmetry and least-squares estimation)\textsuperscript{16} and other multiple echo pulse sequences.

**Effects of $B_0$ and $B_1$ inhomogeneities on the Bloch simulation**
Although the effects of $B_0$ and $B_1$ inhomogeneities were not introduced in the Bloch simulation performed in this study,
these effects appeared in the images obtained by the Bloch simulation. For example, the effect of the $B_1$ inhomogeneity caused by the 8-element birdcage coil is shown in the dark areas at the four corners and the bright areas at the top and bottom in both the experimental and simulated images shown in Fig. 4. As for the $B_0$ inhomogeneity, the signal readout direction is perpendicular to the axial plane, which has the effect of deforming the image perpendicular to the plane shown in Fig. 4. Because the numerical phantoms were created using the experimental images, the effects of $B_0$ and $B_1$ were already introduced into the numerical phantom.

Since the effects of $B_0$ and $B_1$ on MR images vary greatly depending on the signal readout direction, pixel bandwidth, RF pulse, RF coil, etc., the numerical phantoms created by the present method should be carefully used for the Bloch simulations using other pulse sequences. Therefore, it is desirable to use pulse sequences less affected by the inhomogeneity of $B_0$ and $B_1$, such as 3D SE sequences with a homogeneous volume coil and a large pixel bandwidth, to create the numerical phantoms using the method proposed in this study.

Conclusion

A 4D numerical phantom for the Bloch simulation was created using 3D MR images of a bacon block acquired with the 3D SE sequences designed for a three-point Dixon experiment. The 4D numerical phantom was used for the Bloch simulation of the pulse sequences of the three-point Dixon experiment, which were used for the creation of the numerical phantom. The images obtained by the Bloch simulation well reproduced the images acquired with the experiment. Although further research is needed for clinical application, we thus concluded that the 4D numerical phantom is useful for the Bloch simulation of biological systems consisting of water and fat, such as muscle, liver, and breast, if their numerical phantoms could be created using the method developed in this study.

Conflicts of Interest

Ryoichi Kose and Katsumi Kose are directors of MRIsimulations Inc. Yasuhiko Terada has no conflict of interest on this topic.

References

1. Benoit-Cattin H, Collewet G, Belaroussi B, et al. The SIMRI project: a versatile and interactive MRI simulator. J Magn Reson 2005; 173:97–115.
2. Stöcker T, Vahedipour K, Pflugfelder D, et al. High-performance computing MRI simulations. Magn Reson Med 2010; 64:186–193.
3. Xanthis CG, Venetis IE, Chalkias AV, et al. MRISIMUL: a GPU-based parallel approach to MRI simulations. IEEE Trans Med Imaging 2014; 33:607–617.
4. Liu F, Velikina JV, Block WF, et al. Fast realistic MRI simulations based on generalized multi-pool exchange tissue model. IEEE Trans Med Imaging 2017; 36:527–537.
5. Kose R, Kose K. BlochSolver: a GPU-optimized fast 3D MRI simulator for experimentally compatible pulse sequences. J Magn Reson 2017; 281:51–65.
6. Kose R, Setoi A, Kose K. A fast GPU-optimized 3D MRI simulator for arbitrary k-space sampling. Magn Reson Med Sci 2019; 18:208–218.
7. Fortin A, Salmon S, Baruthio J, et al. Flow MRI simulation in complex 3D geometries: application to the cerebral venous network. Magn Reson Med Sci 2018; 80:1655–1665.
8. Kose R, Kose K, Terada Y, et al. Development of a method for the Bloch image simulation of biological tissues. Magn Reson Imaging 2020; 74:250–257.
9. Dixon WT. Simple proton spectroscopic imaging. Radiology 1984; 153:189–194.
10. Glover GH, Schneider E. Three-point Dixon technique for true water/fat decomposition with $B_0$ inhomogeneity correction. Magn Reson Med 1991; 18:371–383.
11. Ren J, Dimitrov I, Sherry AD, et al. Composition of adipose tissue and marrow fat in humans by $^1$H NMR at 7 Tesla. J Lipid Res 2008; 49:2055–2062.
12. Zhong X, Nickel MD, Kannengiesser SA, et al. Liver fat quantification using a multi-step adaptive fitting approach with multi-echo GRE imaging. Magn Reson Med 2014; 72:1353–1365.
13. Wen Z, Reeder SB, Pineda AR, et al. Cramér-Rao bounds for three-point decomposition of water and fat. Magn Reson Med 2005; 54:625–635.
14. Pineda AR, Reeder SB, Wen Z, et al. Iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL): application with fast spin-echo imaging. Magn Reson Med 2005; 54:636–644.