The method for quantitative magnetic resonance imaging of agar phantom with contrast agent

Y Dwihapsari1, E Asdiantoro1 and N Maulidiyah1

1Department of Physics, Institut Teknologi Sepuluh Nopember Surabaya (ITS), Kampus ITS Keputih Sukolilo Surabaya Indonesia 60111

yanuritadh@physics.its.ac.id

Abstract. Magnetic Resonance Imaging (MRI) is one of the reliable instruments in medical physics for diagnostic and treatment monitoring. In MRI scanning, data were acquired using several techniques depending on the parameters being measured. Several quantitative MRI methods were conducted to obtain values of some parameters in MRI, such as spin-spin relaxation time or \( T_2 \). \( T_2 \)-value was generally obtained using spin-echo sequence and the recent development used multiple spin-echo sequence to significantly reduce acquisition time. The quantification of \( T_2 \) is achieved by exponential fitting of echo-time with signal intensity. Although the quantification is quite straightforward, some distortion and errors were found during quantification process due to several factors. In this study \( T_2 \) quantification of agar with various concentrations was conducted and the study was focused on the processing method for \( T_2 \) quantification. The fitting methods based on mono-exponential and bi-exponential models would be applied and the results would be compared to find the best method for quantitative \( T_2 \) MRI of gel phantom. The method would also be applied in agar phantom with addition of CuSO\(_4\) contrast agent to observe the effect of contrast agent on \( T_2 \)-value.

1. Introduction

Magnetic Resonance Imaging (MRI) is one of the reliable instruments in medical physics for diagnostic and treatment monitoring. It is superior to observe the molecular structure and properties of human tissues and metabolites inside human body. Data of images or spectra are generally obtained in MRI scanning by utilizing magnetic properties inside human body and applying a pulse sequence which consists of series of pulses and gradients. In MRI scanning, data were acquired using several techniques depending on the parameters being measured. Several quantitative MRI methods were conducted to obtain values of some parameters in MRI, such as spin-lattice relaxation time (\( T_1 \)) and spin-spin relaxation time (\( T_2 \)).

\( T_2 \)-value was generally obtained using spin-echo sequence by weighting transverse magnetization which causes decay due to spin-spin relaxation and magnetic field inhomogeneity. The recent development used multiple spin-echo sequence to significantly reduce acquisition time. The quantification of \( T_2 \) is achieved by exponential fitting of echo-time (TE) with signal intensity, \( S \), which can be described as mono-exponential model [1, 2]

\[
S(TE) = S_1 \exp \left(-\frac{TE}{T_2}\right)
\]
where $S_1$ is initial magnetization without weighting. In other studies, several models are proposed to describe the relation between TE and signal intensity which give better approximation of $T_2$-value [2]. One of the models is bi-exponential model which can be described as

$$S(TE) = S_1 \exp \left(-\frac{TE}{T_{2,1}}\right) + S_2 \exp \left(-\frac{TE}{T_{2,2}}\right).$$  \hspace{1cm} (2)

Although $T_2$ quantification is quite straightforward, some distortion and errors were found during quantification process due to several factors, such as magnetic field inhomogeneity, refocusing pulses, slice selective gradient and the self-properties of phantom. The accurate $T_2$ quantification is essential in diagnosis of diseases development of phantom and tissue-mimicking materials. One of the issues in $T_2$ quantification is finding the best fitting model which can give $T_2$-value closest to the real value. Several studies have discussed some methods for fitting model [1-3]. The studies were generally conducted in homogeneous phantom using gel or material which best mimics human tissues, such as agarose and agar. The assessment of $T_2$-value in agarose and agar hydrogel had been conducted in several studies and showed reducing $T_2$-value in higher concentration of agar and agarose [4, 5].

In this study $T_2$ quantification of agar with various concentrations was conducted and the study was focused on the processing method for $T_2$ quantification. The fitting method based on mono-exponential and bi-exponential model would be applied and the results would be compared to find the best method for quantitative $T_2$ MRI of gel phantom. In addition, the method would be applied in agar phantom with addition of CuSO$_4$ contrast agent to observe the effect of contrast agent on $T_2$-value.

2. Materials and Methods

Data acquisition was performed using 1.5 T MRI scanner (Signa, General Electric, US) with head coil. Phantom was constructed from agar gel by mixing distilled water and agar powder purchased from local market with various concentrations of 2.5, 5, and 7.5 w/v%. In addition to pure agar hydrogel, CuSO$_4$ was added as a contrast agent by mixing CuSO$_4$ with concentration of 50% and 75% to agar solution. In total, 9 phantoms were formed and placed inside plastic tube before being scanned. Samples and their conditions are given in Table 1.

| Sample | Agar Concentration (w/v%) | CuSO$_4$ Concentration (v/v%) |
|--------|---------------------------|-----------------------------|
| 1      | 2.5                       | 0                           |
| 2      | 5                         | 0                           |
| 3      | 7.5                       | 0                           |
| 4      | 2.5                       | 50                          |
| 5      | 5                         | 50                          |
| 6      | 7.5                       | 50                          |
| 7      | 2.5                       | 75                          |
| 8      | 5                         | 75                          |
| 9      | 7.5                       | 75                          |
All phantoms were divided into 9 slices with slice thickness of 5 mm and images were acquired using multiple spin-echo sequence by varying echo-time (TE) from 20 to 200 ms. In this experiment, several parameters were used as follows: field-of view (FOV) = 100 mm × 100 mm, matrix size = 256 × 256, repetition time (TR) = 1000 – 2000 ms, echo-time (TE) = 10 – 200 ms, and slice thickness = 5 mm. To ensure repeatability of this experiment, the experiments were conducted three times with variation of repetition time (TR) of 1000, 1500 and 2000 ms.

Images were processed using a program in Matlab (Mathworks, US) to obtain signal intensity mapping. The signal intensities were used to obtain $T_2$-value by fitting TE with signal intensity using mono-exponential and bi-exponential models. The fitting of TE vs signal intensity using mono-exponential model was conducted according to Eq. 1 and bi-exponential model according to Eq. 2 using Levenberg-Marquardt non-linear least square algorithm [6]. The fitting was conducted without offset in the first attempt and with offset in the second attempt.

3. Results and Discussion

Images from acquisition with TR of 1500 ms in a slice was shown in Fig. 1 and showed different signal intensity across various TE. The graph of TE vs signal intensity from a 5% phantom in a slice was shown in Fig. 2. The mono-exponential fitting between those parameters was based on Eq. 1. The first attempt did not count the offset and the fitting was merely based on the original value from data and resulted in incorrect $T_2$-value compared to established $T_2$-value from other studies [4, 5].

![Figure 1. Images from acquisition with TR of 1500 ms in a slice](image)

The second attempt used offset and considered the different offset for each phantom. The best offset value was automatically chosen which represented the closest $T_2$-value. The offset was considered as baseline especially in case of $T_2$ decay was not converged towards zero. The mono-exponential fitting to obtain $T_2$-value using offset and without offset was shown in Fig. 3. The fitting without offset showed that the fitting did not represent all data points and caused misreading in $T_2$-value.
Figure 2. The graph of signal intensity vs TE from agar and agar + CuSO$_4$ 50% (☐ = agar 2.5%, ○ = agar 5%, Δ = agar 7.5%, + = agar 2.5% + CuSO$_4$ 50%, - = agar 5% + CuSO$_4$ 50%, x = agar 7.5% + CuSO$_4$ 50%)

The different offset value in mono-exponential fitting was contributed from the imperfect magnetization which might arose due to magnetic field inhomogeneity and distorted slice selection gradient. It is especially true when multiple spin echo sequence is used where distortions due to gradient and refocusing pulses are higher. A study by Milford et al. also shows the importance of offset value which depends on magnetic field homogeneity, refocusing pulses, and noise from the system [3].

Figure 3. The fitting of TE and signal intensity to obtain $T_2$-value using mono-exponential model (- - -) without offset and (⋯) with offset
The fitting using bi-exponential model was conducted based on Eq. 2. The similar steps were applied to bi-exponential fitting, the offset was not used at the first attempt and used in the second attempt in bi-exponential model. The fitting using bi-exponential model without and with offset was shown in Fig. 4. The result also showed that the fitting was not converged to zero without offset. Although bi-exponential without offset showed better fitting compared to mono-exponential model, $T_2$-values obtained from this model were not in a good agreement to values established by other comparable studies. The bi-exponential fitting with offset resulted in two $T_2$-values where one $T_2$ was very small and negligible and another $T_2$ was comparable to $T_2$ from mono-exponential model.

![Figure 4. The fitting of TE and signal intensity to obtain $T_2$-value using bi-exponential model (---) without offset and (•••) with offset](image)

The example of $T_2$-value from mono-exponential and bi-exponential fitting using offset and without offset was shown in Table 2. The result of mono-exponential fitting is in a good agreement with results from previous studies which found reducing $T_2$ as concentration of agar was added. The same behavior was also found in agar phantom with CuSO$_4$ contrast agent. The higher agar concentration reduced $T_2$-value of phantom with contrast agent. The addition of contrast agent in the same agar concentration reduced $T_2$-value even further although there was a limitation on the concentration of contrast agent could be added to get lower $T_2$-value.

The fitting using mono-exponential and bi-exponential models were also valid for phantom with contrast agent. $T_2$-value from mono-exponential model using offset was comparable to values from other studies. The offset was needed to correct for magnetic field inhomogeneity and distorted slice selection gradient during experiment. The two $T_2$-values from bi-exponential fitting, either using offset or without offset, showed that one $T_2$ was insignificant and another value was comparable to $T_2$-value from mono-exponential model. In our experiment, mono-exponential model with offset was a good model to fit data for $T_2$ quantification and the results from this model were in line with results from other studies [4, 5].
Table 2. Example of T2-value from mono-exponential and bi-exponential fitting using offset and without offset

| Sample | S1  | T2,1 | S2  | T2,2 | Offset |
|--------|-----|------|-----|------|--------|
| Mono-exponential model with offset |      |      |     |      |        |
| 1      | 562.6  | 30.85 | 102.3 |
| 2      | 621.7  | 29.14 | 79.32 |
| 3      | 669.5  | 28.84 | 65.62 |
| 4      | 938.5  | 25.06 | 110.1 |
| 5      | 860.8  | 24.76 | 94.62 |
| 6      | 904.5  | 22.44 | 74.06 |
| Mono-exponential model without offset |      |      |     |      |        |
| 1      | 501.2  | 75.39 | 0   |
| 2      | 547.1  | 57.58 | 0   |
| 3      | 595.5  | 49.47 | 0   |
| 4      | 769.2  | 52.98 | 0   |
| 5      | 702.5  | 51.03 | 0   |
| 6      | 725.8  | 41.29 | 0   |
| Bi-exponential model with offset |      |      |     |      |        |
| 1      | 562.6  | 30.85 | 0.226 | 0.385 | 102.3 |
| 2      | 621.7  | 29.14 | 0.539 | 0.698 | 79.32 |
| 3      | 669.5  | 28.84 | 0.628 | 0.292 | 65.63 |
| 4      | 938.5  | 25.06 | 0.983 | 0.730 | 110.1 |
| 5      | 860.8  | 24.76 | 0.561 | 0.882 | 94.61 |
| 6      | 904.5  | 22.44 | 0.198 | 0.489 | 74.03 |
| Bi-exponential model without offset |      |      |     |      |        |
| 1      | 501.2  | 75.39 | 0.162 | 0.794 | 0     |
| 2      | 547.1  | 57.58 | 0.286 | 0.757 | 0     |
| 3      | 595.5  | 49.47 | 0.841 | 0.254 | 0     |
| 4      | 769.2  | 52.98 | 0.602 | 0.263 | 0     |
| 5      | 702.5  | 51.03 | 0.076 | 0.054 | 0     |
| 6      | 725.7  | 41.30 | 0.350 | 0.197 | 0     |

4. Conclusion
The correct fitting method is important for T2 quantification. In our experiment, mono-exponential fitting with offset is the best model for fitting TE vs signal intensity and gives T2-values which are comparable to T2 from other studies.

5. References
[1] Clark PR and St Pierre TG 2000 Mag. Res. Imaging 18 431
[2] Carneiro AAO, Vilela GR, de Araujo DB, Baffa O 2006 Braz. J. Phys. 36 9-15
[3] Milford D, Rosbach N, Bendszus M, Heiland S 2015 PLoS One 10 e0145255
[4] Mitchell MD, Kundel HL, Axel L, Joseph PM 1986 Magn. Reson. Imaging 4 263-266
[5] Dwihapsari Y, Maulidiyah N, Darminto 2018 IOP Conf. Series: Mat. Sci. Eng. 395 012025
[6] Whittall KP and Mackay AL 1989 J. Magn. Res. 84 134-152

Acknowledgments
Authors wishing to acknowledge Kemenristekdikti and ITS for support of Research Grant.