T2 Quantification of Agarose with Contrast Agent in Magnetic Resonance Imaging

Y Dwihapsari1*, E Asdiantoro1 and N Maulidiyah1
1Physics Department, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia 60111
yanuritadh@physics.its.ac.id

Abstract. Spin-spin relaxation time or T2 is an important parameter in Magnetic Resonance Imaging (MRI) which provides information on molecular structure inside tissues, properties of human tissues and metabolites inside human body. It also contributes to clinical study by providing more information on pathological properties and delineation between healthy and malignant tissues in brain pathologies and identification of tissue abnormalities. In this study, T2 measurement was performed by acquiring T2 images of agarose hydrogel. T2-weighted imaging sequence was used with variation of agarose concentration, echo-time and repetition time. The signal intensities of samples were acquired and fitted to echo-time to obtain T2-value. In addition, contrast agent of CuSO4 was mixed with agarose solution and the similar T2 measurement was performed with variation concentration of agarose and CuSO4. Although some limitations were found during T2 measurement due to acquisition and instrumental setting, T2 quantification could provide more information about properties inside samples. The quantification could also be used for measurement of the effectiveness of contrast agent for increasing image contrast in MRI scanning.

1. Introduction
The information on spin relaxation rates especially spin-spin relaxation time or T2 in Magnetic Resonance Imaging (MRI) can give additional insight on molecular structure inside tissues and properties of human tissues and metabolites inside human body. It also contributes to clinical study by providing more information on pathological properties and delineation between healthy and malignant tissues in brain pathologies [1, 2] and identification of tissue abnormalities [3, 4].

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 radiofrequency (RF) pulses and gradients. T2-weighted imaging 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 [5].

The spin magnetization, M, which is generated in MRI due to applied magnetic field, B, is described using Bloch equation [6]

\[ \frac{dM}{dt} = \gamma M \times B \]  

(1)
where $\gamma$ is gyromagnetic ratio. In three-dimensional laboratory frame (x-, y- and z-axis), equation (1) can be written in a matrix form as

$$\begin{pmatrix}
\frac{dM_x}{dt} \\
\frac{dM_y}{dt} \\
\frac{dM_z}{dt}
\end{pmatrix} = \gamma \begin{pmatrix}
i & j & k \\
M_x & M_y & M_z \\
B_x & B_y & B_z
\end{pmatrix}. \tag{2}
$$

Spins precess around the static magnetic field in z-direction, $B_z$, has non-zero value and is expressed as $B_0$. The magnetization in z-direction, $M_z$, will stay constant but magnetization in x- and y- (transverse) direction will change from $M_x$ to $M_y$ and so forth. For each component, equation (2) can be written as

$$\frac{dM_x}{dt} = \gamma (M_y B_0 - M_z B_y)$$
$$\frac{dM_y}{dt} = \gamma (M_z B_x - M_x B_0)$$
$$\frac{dM_z}{dt} = 0. \tag{3}
$$

In the presence of additional RF magnetic field, $B_1$, which rotates at frequency of $\omega$, the total magnetic field is given as

$$B = B_1 \cos \omega t \hat{i} - B_1 \sin \omega t \hat{j} + B_0 \hat{k} \tag{4}$$

and by including spin-spin relaxation time, $T_2$, and spin-lattice relaxation, $T_1$, equation (3) is written as

$$\frac{dM_x}{dt} = \gamma (M_y B_0 + M_z B_1 \sin \omega t) - \frac{M_x}{T_2}$$
$$\frac{dM_y}{dt} = \gamma (M_z B_1 \cos \omega t - M_x B_0) - \frac{M_y}{T_2}$$
$$\frac{dM_z}{dt} = -\gamma (M_x B_1 \sin \omega t + M_y B_1 \cos \omega t) - \frac{(M_x - M_0)}{T_1}. \tag{5}
$$

The transformation from laboratory frame to rotating frame will change the representation of magnetization in x-, y- and z-axis, respectively. After generation of RF pulse, the magnetized spin system will return to its equilibrium and the relaxation in transverse and longitudinal direction (equation (5)) in rotating frame becomes

$$\frac{dM_x}{dt} = -\frac{M'_x}{T_2}$$
$$\frac{dM_y}{dt} = -\frac{M'_y}{T_2}$$
$$\frac{dM_z}{dt} = -\frac{(M'_z - M_0)}{T_1}. \tag{6}
$$

where $M'_x$, $M'_y$ and $M'_z$ are magnetization in x-, y- and z-axis, respectively. The solution of equation (6) in x- and y- axis in rotating frame is given by
\[ M_{x'y'}(t) = M_{x'y'}(t = 0+) e^{-\frac{t}{T_2}} \]  

(7)

where \( M_{x'y'}(t = 0+) \) is magnetization in transverse direction immediately after generation of an RF pulse. The quantification of \( T_2 \) therefore can be achieved by varying time \( t \) which gives variation of \( M_{x'y'} \). In the experiment, variation of \( t \) is given by varying echo-time (TE) and magnetization is represented by signal intensity of image produced during experiment. The exponential fitting of echo-time (TE) with signal intensity, \( S \), gives \( T_2 \)-value which can be described as mono-exponential model \[ S(TE) = S_1 \exp \left( -\frac{TE}{T_2} \right) \]  

(8)

where \( S_1 \) is initial signal intensity without TE weighting.

The study of contrast agent for enhancement of resolution and contrast in diagnostic MRI had been developed since 1980s using ferric chloride for gastrointestinal tract [9]. Since then, the development of contrast agent has been one of the main topics in MRI study. The contrast agent decreases water signal intensity and shortens spin-spin relaxation time (\( T_2 \)) by creating local magnetic field gradients dephase transverse magnetization effectively and cause spins to relax back to equilibrium faster.

In this study, \( T_2 \) images of phantom from agarose hydrogel were assessed using \( T_2 \)-weighted imaging sequence with variation of agarose concentration and repetition time (TR). The images were acquired within 30 minutes for all samples and processed to obtain \( T_2 \)-value. In addition, contrast agent of CuSO4 was mixed with agarose solution and the similar \( T_2 \) measurement was performed with variation concentration of agarose and CuSO4. The results over variation of agarose and CuSO4 concentration were analysed and the effect of CuSO4 on \( T_2 \)-values was examined.

2. Materials and Methods

The images were obtained using MRI 1.5 Tesla (General Electric, US) with birdcage coil. The samples consisted of pure agarose solution and the mixture of agarose solution and CuSO4 contrast agent. The variation of agarose concentration is 2.5, 5, and 7.5 w/v% respectively and the variation of CuSO4 concentration is 0%, 50% and 75% respectively. Agarose samples were obtained from agarose solution mixed with distilled water which was poured into nine different tubes and positioned accordingly to obtain MRI images. \( T_2 \)-weighted imaging (T2WI) with multiple spin-echo sequence was used to obtain images with parameters of matrix size = 256 × 256 and field-of-view (FOV) = 40 mm × 40 mm. Scanning was performed in one slice which was positioned in the middle of the tube with slice thickness of 5 mm. The whole scanning was conducted with repetition time (TR) of 1000 ms, 1500 ms, and 2000 ms respectively. The echo-time (TE) ranged between 20 and 200 ms were used to obtain \( T_2 \) images. Images were then processed to obtain signal intensities by randomly selecting 5 regions of interest (ROI) of round shape with approximate diameter of 21 mm² using a free image processing software, ImageJ (NIH, US). \( T_2 \)-values were acquired by plotting signal intensities exponentially against echo-time (TE). \( T_2 \)-values of various agarose concentrations were analyzed and the effect of CuSO4 on \( T_2 \)-values was examined.

3. Results and Discussion

The signal intensities of agarose hydrogel in 5 ROIs in all samples at TR = 2000 ms and TE = 50 ms as well as their mean and standard deviation were shown in table 1. Signal intensity was varied across ROIs and the variation was found bigger in the samples with the highest concentration of contrast agent. The variation of signal intensity appeared due to magnetic field inhomogeneity and electronic noise from the instrument. The lowest mean signal intensity was found in the samples of agarose 2.5%. The addition of contrast agent caused shortening effect and resulted in a further reduction of signal intensity. The
reduction was found in all agarose concentrations and showed that contrast agent could be used to increase image contrast in MRI scanning.

Table 1. Image intensity (mean and standard deviation, SD) from 5 ROIs selected randomly from all samples. Intensity was obtained at TR = 1500 ms and TE = 50 ms

| Sample | Concentration (Agarose, CuSO₄) | Intensity | Mean | SD |
|--------|--------------------------------|-----------|------|----|
| 1      | (2.5%, 0%)                      | 164.31    | 161.73 | 160.81 | 154.58 | 158.77 | 160.04 | 3.64 |
| 2      | (5%, 0%)                        | 229.08    | 230.46 | 212.96 | 202.77 | 215.81 | 218.22 | 11.62 |
| 3      | (7.5%, 0%)                      | 258.81    | 259.35 | 248.62 | 209.00 | 226.50 | 240.45 | 22.05 |
| 4      | (2.5%, 50%)                     | 88.39     | 92.50  | 85.08  | 90.92  | 91.58  | 89.69  | 3.00 |
| 5      | (5%, 50%)                       | 179.96    | 211.46 | 192.89 | 185.96 | 214.42 | 196.94 | 15.34 |
| 6      | (7.5%, 50%)                     | 185.42    | 228.73 | 204.85 | 174.42 | 237.12 | 206.11 | 26.96 |
| 7      | (2.5%, 75%)                     | 86.42     | 78.54  | 84.62  | 107.23 | 93.77  | 90.12  | 11.00 |
| 8      | (5%, 75%)                       | 181.39    | 206.96 | 179.69 | 172.23 | 188.04 | 185.66 | 13.17 |
| 9      | (7.5%, 75%)                     | 177.81    | 211.15 | 173.42 | 168.92 | 183.35 | 181.93 | 16.77 |

The signal intensity decreases as TE increases because of T₂ decay, magnetic field inhomogeneities, magnetic susceptibility variation and chemical shift of the samples. The effect of magnetic field inhomogeneity was even higher in longer TE although long TE was found advantageous for image acquisition in T2WI sequence [10]. The decreasing signal intensity along with increasing TE was plotted to obtain T₂-values and described in figure 1, the example was given at TR = 2000 ms. The signal intensity was perfectly fit to TE and indicated the suitable fitting model for our experiment (equation (8)).

![Figure 1. Fitting of echo-time (TE) vs intensity to obtain T₂-values at TR = 1500 ms](image-url)
The decay of exponential fitting was slower in lower concentration agarose compared to higher concentration agarose and resulted in higher $T_2$-value. The result was in line with the result published from other studies of higher $T_2$-value from lower concentration agarose [11, 12]. $T_2$-value was determined by chemical properties of samples, particularly by interaction between water structure with polar sites of samples. The lower agarose concentration had more water content and therefore higher interaction with polar sites of samples. The imperfect $T_2$ measurement was shown in exponential fitting and caused by several factors, such as pulse sequence selection and instrumental setting. Several methods to minimize the imperfection had been proposed including modification of pulse sequence, selection of RF pulses and use of additional gradients [13, 14].

The contrast agent was proven to manipulate spin relaxation and caused the spin relaxation to be faster. The contrast agent caused faster decay in exponential fitting as shown in figure 1. The decay of agarose with addition of 75% CuSO$_4$ was faster compared to decay of agarose without contrast agent in figure 1. The faster decay was consistent in all agarose concentrations. The other studies also reported decreasing $T_2$ relaxation time with increasing concentration of contrast agent [11, 15]. $T_2$-values for all samples with TR = 1500 ms, 2000 ms and 2500 ms, respectively were given in table 2. Although $T_2$-value changed with different TR, the variation of TR showed the same trend on $T_2$-values where higher agarose concentration resulted in lower $T_2$. The longer TR had insignificant effect in agarose with high concentration of contrast agent as shown in table 2. Agarose without contrast agent was highly affected by longer TR and increasing concentration of contrast agent would reduce the effect of longer TR. The result of $T_2$ in table 2 could provide more information on the effect of contrast agent to increase image contrast compared to the assessment of signal intensity in table 1 which highly depended on magnetic field homogeneity.

The longer TR which caused longer acquisition time could be compensated by applying short TR and adjusting number of averages. Therefore, finding the best optimal TR for image acquisition was essential for obtaining the best image with high resolution and SNR within the minimum acquisition time. Although some limitations were found during $T_2$ measurement due to acquisition and instrumental setting, $T_2$ quantification could provide more information about properties such as water content inside samples. The quantification could also be used for measurement of the effectiveness of contrast agent for increasing image contrast in MRI scanning.

4. Conclusion
The higher agarose concentration resulted in lower $T_2$. The contrast agent reduced $T_2$ further to some degrees and the effect was higher in lower agarose concentration. The attempt to find the best optimal TR for image acquisition was essential for obtaining the best image with high resolution and SNR within the minimum acquisition time. Although some limitations were found during $T_2$ measurement due to

| Sample | Concentration (Agarose, CuSO$_4$) | $T_2$ (ms) TR 1000 ms | $T_2$ (ms) TR 1500 ms | $T_2$ (ms) TR 2000 ms |
|--------|----------------------------------|-----------------------|-----------------------|-----------------------|
| 1      | (2.5%, 0%)                       | 64.43 ± 14.58         | 70.33 ± 15.51         | 99.91 ± 10.37         |
| 2      | (5%, 0%)                         | 52.90 ± 9.82          | 57.59 ± 10.77         | 78.81 ± 7.41          |
| 3      | (7.5%, 0%)                       | 47.64 ± 8.33          | 49.47 ± 8.61          | 72.81 ± 8.31          |
| 4      | (2.5%, 50%)                      | 46.05 ± 9.65          | 52.99 ± 10.85         | 62.19 ± 10.43         |
| 5      | (5%, 50%)                        | 43.97 ± 9.20          | 51.03 ± 10.52         | 60.33 ± 10.01         |
| 6      | (7.5%, 50%)                      | 36.04 ± 7.47          | 41.30 ± 8.19          | 48.38 ± 8.03          |
| 7      | (2.5%, 75%)                      | 25.28 ± 3.82          | 27.02 ± 4.33          | 27.57 ± 3.02          |
| 8      | (5%, 75%)                        | 16.96 ± 2.07          | 15.23 ± 2.12          | 17.53 ± 1.84          |
| 9      | (7.5%, 75%)                      | 16.51 ± 2.01          | 14.56 ± 1.71          | 17.08 ± 1.27          |
acquisition and instrumental setting, $T_2$ quantification could provide more information about properties inside samples. The quantification could also be used for measurement of the effectiveness of contrast agent for increasing image contrast in MRI scanning.

Acknowledgments
This work was funded by Institut Teknologi Sepuluh Nopember (ITS) and Kementerian Riset dan Teknologi / Badan Riset dan Inovasi Nasional.

References
[1] Deoni S 2011 Methods Mol Biol 711 65
[2] Baudrexel S, Nurnberger L, Rub U, et al 2010 Neuroimage 51 512
[3] Rugg-Gunn FJ, Boulby PA, Symms MR, Barker GJ, Duncan JS 2005 Neurology 64 318
[4] Townsend TN, Bernasconi N, Pike GB, Bernasconi A 2004 Neuroimage 23 318
[5] Meiboom S and Gill D 1958 Rev Sci Instrum 29 688
[6] Bloch F 1946 Phys Rev 70 4604
[7] Clark PR and St Pierre TG 2000 Magn Res Imaging 18 431
[8] Carneiro AAO, Vilela GR, de Araujo DB, Baffa O 2006 Braz J Phys 36 9
[9] Young IR, Clarke GJ, Bailes DR, Pennock JM, Doyle FH, Bydder GM 1981 J Comput Tomogr 5 543
[10] Buxton RB, Edelman RR, Rosen BR, Wismer GL, Brady TJ 1987 J Comput Assist Tomogr 11 7
[11] Mitchell MD, Kundel HL, Axel L, Joseph PM 1986 Magn Res Imaging 4 263
[12] Dwihapsari Y, Maulidiyah N, Darminto 2018 IOP Conf Series: Mat Sci Eng 395 012025
[13] Majumdar S, Orphanoudakis SC, Gmitro A, O’Donnell M, Gore JC 1986 Magn Reson Med 3 397
[14] Majumdar S, Orphanoudakis SC, Gmitro A, O’Donnell M, Gore JC 1986 Magn Reson Med 3 562
[15] Lee MJ, Kim MJ, Yoon CS, Song SY, Park K, Kim WS 2011 Korean J Radiol. 12 358