The Effect of Paramagnetic Agent on Relaxation and Mechanical Properties of Agar Hydrogel for Phantom in Magnetic Resonance Imaging

Y Dwihapsari*, N Maulidiyah, Darminto
Department of Physics, Institut Teknologi Sepuluh Nopember (ITS), Kampus ITS Sukolilo Surabaya 60111, Indonesia

*yanuritadh@physics.its.ac.id, yanuritadh@gmail.com

Abstract. Agar hydrogel is largely used in magnetic resonance imaging study as tissue mimicking phantom material for its cost-effectiveness and easy preparation. Spin-spin relaxation time, $T_2$ is one important parameter in Magnetic Resonance Imaging study. However, $T_2$ of agar sample is higher than those of human tissues. The addition of paramagnetic agent such as copper sulphate or CuSO$_4$ had been observed to match $T_2$-value of human tissues. In this study, the effect of CuSO$_4$ on relaxation and mechanical properties of agar is observed.

Keywords: hydrogel, agar, magnetic resonance imaging, mechanical properties, shear modulus, $T_2$, relaxation time, CuSO$_4$, phantom

1. Introduction
Agar hydrogel is largely used in magnetic resonance imaging study for tissue mimicking phantom material for its cost-effectiveness and easy preparation. In order to make a material eligible for tissue mimicking phantom material in Magnetic Resonance Imaging (MRI) study, the properties of material must serve some important parameters in MRI, such as spin-lattice relaxation time ($T_1$) and spin-spin relaxation time ($T_2$). $T_2$ refers to relaxation time of water protons which describes cumulative loss in phase coherence and results in signal decay from each voxel during MRI acquisition. The $T_2$-relaxation results from transient magnetic field due to molecular motion and depends on chemical exchange inside the material.

The increasing agar concentration results in lower $T_2$ although it is relatively high compared to $T_2$ of some human tissues [1]. The paramagnetic agent is normally added to get much lower $T_2$ and suitable with $T_2$ of corresponding tissues. The previous study showed that addition of paramagnetic agents, such as CuSO$_4$ and Mn(NO$_3$)$_2$ reduce $T_2$ along with increasing concentration of agar or other hydrogels [1, 2]. Several agar hydrogel studies have observed the mechanical properties of agar and showed that increasing agar concentration could increase the mechanical properties of agar hydrogel [3].

In this study the effect of concentration of agar and CuSO$_4$ on spin-spin relaxation time ($T_2$) and its shear modulus are discussed. The experiments of agar with various concentrations were measured ca. 2 h after gelation and scanned using MRI to obtain $T_2$. The shear modulus was observed using dynamic mechanical analyser (DMA) tool. The relation between shear modulus and $T_2$ is observed and plotted to explore their link to concentration of agar and CuSO$_4$. 

Content from this work may be used under the terms of the Creative Commons Attribution 3.0 licence. Any further distribution of this work must maintain attribution to the author(s) and the title of the work, journal citation and DOI.
Published under licence by IOP Publishing Ltd
2. Materials and methods
The solution of agar hydrogel was formed by mixing agar powder and 50 ml distilled water and boiled for 20 min to form 2.5, 5, and 7.5 w/v% of agar gel. The paramagnetic agent CuSO$_4$ was added to agar and distilled water to form concentration of 0.4 and 5.9 w/v% and boiled to form hydrogel. The solution was placed into plastic tube and cooled down to form hydrogel in room temperature. The samples were positioned in such a row and scanned after 2 – 4 h of preparation for measurement of spin-spin relaxation time $T_2$.

The MRI experiment to measure $T_2$ was performed using Carr-Purcell Meiboom Gill (CPMG) sequence in 1.5 T MRI scanner (Signa, General Electric, US) with spine gradient coil. Five slices were taken from each samples. The experiment was performed with parameters: field-of view (FOV) = 100 mm $\times$ 100 mm, matrix size = 64 $\times$ 64, repetition time (TR) = 1000 – 2000 ms, echo-time (TE) = 10 – 200 ms, and slice thickness = 5 mm. The image processing and analysis software, ImageJ was used to obtain signal intensity. $T_2$-value was obtained by fitting mean signal intensity into TE.

Each sample was cut into 5 mm x 5 mm x 1 mm plates for measurement of mechanical properties. The shear modulus of agar hydrogel was observed using DMA Mettler Toledo SDTA861 by varying force load from 1 to 20 N. The shear modulus was acquired by plotting and analysing stress-strain relation curve. The shear modulus of each sample was plotted against $T_2$ to obtain the relation between relaxation time and mechanical properties of agar hydrogel.

3. Results and discussion
Spin-spin relation time $T_2$ from various concentration of agar and mixture of agar and CuSO$_4$ is shown in Table 1. The result shows the decreasing $T_2$ as agar concentration increases, even less with addition of CuSO$_4$. The value of $T_2$ in our experiment is comparable to $T_2$-value from other experiments [1] and adjustable to $T_2$ of human tissue from other studies which range between 30 – 100 ms at 1.5 T [4 - 6]. The small reduction of $T_2$ due to increasing agar concentration shows the effectiveness of increasing CuSO$_4$ concentration for reducing $T_2$ value. As shown in Table 1, the addition of CuSO$_4$ affects $T_2$-value for the same agar concentration. The reduction of $T_2$ as a result of increasing CuSO$_4$ concentration is up to 50% for 0.4% and only 40% for 5.9 w/v% of CuSO$_4$. It shows that the addition of CuSO$_4$ yields the maximum reduction in particular range of concentration.

The results in this study are relevant with results from other study which found linear reduction in $T_2$ when agar and CuSO$_4$ concentration are increased [1, 2]. The linear reduction of $T_2$ found in the study is useful in predicting the concentration of paramagnetic agents needed for preparation of tissue-mimicking phantom materials.

| Sample | CuSO$_4$ concentration (w/v%) | Agar concentration (w/v%) | $T_2$ (ms) | SD |
|--------|-------------------------------|--------------------------|------------|----|
| 1      | 0                             | 2.5                      | 116.705    | 4.119 |
| 2      | 0.4                           | 2.5                      | 51.493     | 2.770 |
| 3      | 5.9                           | 2.5                      | 32.798     | 4.630 |
| 4      | 0                             | 5                        | 102.271    | 18.818 |
| 5      | 0.4                           | 5                        | 50.025     | 2.538 |
| 6      | 5.9                           | 5                        | 24.149     | 2.899 |
| 7      | 0                             | 7.5                      | 90.799     | 44.139 |
| 8      | 0.4                           | 7.5                      | 46.211     | 2.415 |
| 9      | 5.9                           | 7.5                      | 23.998     | 2.604 |

The addition of CuSO$_4$ concentration give insignificant contribution to shear modulus in the same agar concentration as described in Table 2. In the experiment of shear modulus, data from 2.5% agar...
concentration was excluded due to broken sample during testing. The significant increase was found in higher agar concentration and showed that shear modulus is significantly dependent on agar concentration.

**Table 2.** Shear modulus of various concentration of agar and mixture of agar and CuSO$_4$. Agar 2.5w/v% was excluded due to broken sample during testing.

| Sample | CuSO$_4$ concentration (w/v%) | Agar concentration (w/v%) | Shear modulus (kPa) |
|--------|-----------------------------|--------------------------|---------------------|
| 1      | 0                           | 5                        | 178.225             |
| 2      | 0.4                         | 5                        | 150.180             |
| 3      | 5.9                         | 5                        | 131.475             |
| 4      | 0                           | 7.5                      | 380.449             |
| 5      | 0.4                         | 7.5                      | 365.749             |
| 6      | 5.9                         | 7.5                      | 302.882             |

The link between $T_2$ and shear modulus of agar hydrogel is shown in Figure 1. The addition of CuSO$_4$ significantly reduces $T_2$ but insignificantly affects shear modulus. On the contrary, increasing agar concentration significantly increases shear modulus but gives little effect to $T_2$-value. The linear relation is found between $T_2$ and shear modulus and the fitting shows that the slope depends on agar concentration and can be determined with more variation of agar concentration.

![Figure 1](image.png)

**Figure 1.** Shear modulus vs $T_2$ of agar and mixture of agar and CuSO$_4$. 1) Agar + CuSO$_4$ 0%, 2) Agar + CuSO$_4$ 0.4%, 3) Agar + CuSO$_4$ 5.9%. The result from agar 2.5% was excluded in this plot.

4. Conclusion
The effect of adding paramagnetic agent, in our study CuSO$_4$ to agar hydrogel had been observed. The results show that addition of CuSO$_4$ results in significant reduction in $T_2$-value but insignificant increase in shear modulus of agar hydrogel. The shear modulus is linearly related to $T_2$-value along with increasing concentration of agar and CuSO$_4$. The study works for limited concentration of agar
and more variation of agar and CuSO$_4$ concentration is needed to observe the link between T$_2$ and shear modulus in agar hydrogel.

5. References

[1] Mitchell MD, Kundel HL, Axel L, Joseph PM 1986 *Magn Reson Imaging* 4(3) 263-266
[2] Hellerbach A, Schuster V, Jansen A, Sommer J 2013 *Plos One* 8(8) 1 - 8
[3] Ahearne M, Yang Y, El Haj AJ, Then KY, & Liu K-K 2005 *J. of the Royal Society Interface* 2(5) 455–463
[4] Sled JG, Pike GB 2001 *Magn Reson Med* 46 923–932
[5] Gold GE, Han E, Stainsby J, Wright GA, Brittain J, Beaulieu C 2004 *Am J Neuroradiol* 183 343–350
[6] Pell GS, Briellmann RS, Waites AB, Abbott DF, Jackson GD 2004 *Neuroimage* 21 707–713

Acknowledgments

ITS is highly acknowledged for funding Research Grant Penelitian Pemula ITS 2017. Authors wish to thank Prof Suminar Pratapa and Nur Aini Fauziyah for discussion and assistance on DMA measurement.