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T2* Relaxation of Agar Gel With and Without The Presence of Tumor-Like Structure as Obtained from Resting State Fmri Sequence Protocol

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Abstract. The objective of this study was to determine the change in signal-to-noise ratio (SNR) as a function of TE of agar gel phantom with and without the presence of tumor-like structure, using a resting state fMRI sequence protocol. The phantoms were prepared using a conventional method. Citrus hystrix DC (kaffir lime) was used to mimic tumor and was submerged in the agar gel. The phantoms were scanned using a 3T-MRI system. An rsfMRI sequence protocol (TR = 2000 ms; TE = 51 ms – 115 ms) was used in obtaining the SNR at several TEs. In addition, a standard MRI phantom as control was also scanned using the same sequence protocol. For the prepared phantoms, the SNR was obtained from several 7-mm diameter ROIs at a distance 2, 4 and 6 cm from the centre of the image and was averaged. For the standard MRI phantom, similar ROI diameter was used for SNR determination but for three different slice thicknesses; 3, 5 and 10 mm. The MRI, agar gel and agar gel with kaffir lime phantoms show T2* relaxation that fits the exponential equation $\text{SNR} \propto e^{-\frac{TE}{T2*}}$. The average T2* for the standard MRI phantom is 86.7 ± 0.1 ms. The average T2* for agar gel phantom is 70.1 ± 0.1 ms while T2* is shortened to an average of 54.8 ± 0.1 ms for agar gel phantom with kaffir lime. This indicates an increase in local magnetic field inhomogeneity in the vicinity of the tumor. The relaxation is thus faster causing a drop in the magnetic resonance signal intensity. The agar gel and agar gel with tumor mimicking phantom are suitable for a long TE rsfMRI scans.

1. Introduction

Resting state fMRI (rsfMRI) is an fMRI experiment conducted on patients while they are at rest to investigate, among others, the functionality of the default mode network (DMN) [1]. The output from rsfMRI is very much depends on the sequence protocol in particular the time to echo (TE) and the transversal relaxation of a tissue (T2*). The amount of T2* weighting that is seen in an image depends on TE [2], thus making it an important controlling parameter in obtaining sufficient amount of signal from an fMRI experiment.

T2* value of a substance or tissue can be determined from the SNR vs. TE plot and the equation $\text{SNR} \propto e^{-\frac{TE}{T2*}}$ [3]. The exponential curve can be fitted to the equation to determine T2*. By knowing the value of T2*, a suitable TE for an fMRI experiment or QC can be chosen. Conventional, suitable...
TE is about the T2* of tissue or substance. Newly developed phantom would also be possibly tested and investigated.

This study implemented T2* determination on MRI phantom, agar gel phantom and agar gel phantom with the presence of tumor-like structure represented by fresh *Citrus hystrix* DC (kaffir lime). Consistency of the SNR value by using the TE determined in the present study will be the main focus of our subsequent study.

2. Methodology

2.1 Preparation of agar gel phantom

An amount of 50 g dry agar gel powder (Merck) and 10 g preservative thimerosal powder (Fisher Scientific) were mixed with 1000 ml distilled water in a 1-l container at 5% concentration. Magnetic stirring technique was used to homogenize the solution for 30 minutes, while the solution was increasingly heated on the hot plate. The solution complete transformation from the sol state to molecular state was indicated by the change in its color from murky to crystal clear, which occurred at its boiling temperature of 100°C. The solution was continued to be heated for 10 minutes to ensure a complete transformation and subsequently poured into a cylindrical plastic container (12 cm diameter and 12 cm height) and was let to gradually cool down to room temperature to form the jelly phantom structure. For the phantom that contained tumor-like structure, a fresh *Citrus hystrix* DC (kaffir lime) was submerged into the solution. Its position is controlled so that it will be at the center of the plastic container longitudinally and axially as the solution hardened.

2.2 Magnetic resonance imaging scans

Magnetic resonance imaging (MRI) scans on the phantoms were conducted in the Department of Radiology, Hospital Canselor Tuanku Muhriz using a 3-T Siemens Magnetom Verio MRI system. The phantom was placed vertically at the iso-centre of the magnet bore inside the head coil, which was used to deliver the radiofrequency (RF) pulses. The resting state functional MRI (rsfMRI) protocol implementing gradient echo – echo planar imaging (GRE-EPI) sequence was used to obtain axial T2* weighted images of the phantoms at TR = 2000 ms and several TE values (TE = 51, 55, 61, 65, 71, 75, 81, 85, 91, 95, 101, 105, 111 and 115 ms). Other imaging parameters are number of slice = 29, field of view (FOV) = 200 × 200 mm, flip angle (α) = 90°, matrix size = 64 × 64, slice gap = 1 mm. For comparisons and validation, resting state fMRI protocols were also implemented on a standard MRI phantom using the above parameters but for different slice thickness; 3 mm, 5 mm and 10 mm.

2.3 SNR determination

The middle slice obtained from each measurement (or each TE) of the phantoms was chosen for SNR evaluation [4]. Three circular shaped regions of interest (ROIs) were drawn on the phantom image and the average signal intensity ($I_p$) was measured from the three ROIs. The intensity of the background noise ($I_b$) and its standard deviation ($\sigma_b$) were measured from a large ROI drawn outside the phantom image. For a good averaging, each signal intensity measurement was done three times. The SNR were than calculated from $\text{SNR} = (I_p - I_b)/\sigma_b$. This procedure was repeated for all TEs. For the standard MRI phantom, this SNR determination was done for three different slice thickness; 3 mm, 5 mm and 10 mm for validation purpose. For the agar gel phantom, SNR was determined at three different radii (2, 4 and 6 cm) from the center of the phantom image.

2.4 T2* determination

The T2* value for the standard MRI phantom and for each of the agar gel phantom was then determined from the SNR vs. TE plot from which the equation $\text{SNR} \propto e^{-TE/T2*}$ was fitted with the experimental data using Microsoft Excel trend line function. The equation of the trend line will then be compared to $\text{SNR} \propto e^{-TE/T2*}$ to determine the T2* value of the standard MRI and agar gel phantoms.
3. Results

Figure 1 shows the exponential decrease of SNR as a function of TE for the standard MRI phantom. The exponential model has been fitted as closely as possible to the experimental data as indicated by the trend line and the respective equation. Generally, SNR increases with slice thickness at all TEs but decreases with the increase in TE for a fixed thickness. By comparing the exponential equations with \( \text{SNR} \propto e^{\frac{TE}{T2^*}} \), it can be shown that T2* values are 76.9 \( \pm \) 0.1 ms, 83.3 \( \pm \) 0.1 ms and 100.0 \( \pm \) 0.1 ms for slice thicknesses 3 mm, 5 mm and 10 mm, respectively. Thus, the average T2* for the standard MRI phantom is 86.7 \( \pm \) 0.1 ms, slightly larger than its standard manufactured value which is 80 ms. These results validate the technique to be used for agar gel phantom.

Likewise, Figure 2 shows a similar trend of exponential SNR decrease as a function of TE for agar gel phantom. The trend line for each plot shows a good fit of the exponential model to the experimental data. SNR is about the same for 2 cm and 4 cm distances at all TEs, but decreases markedly at 6 cm. The trend line equations obtained for each plot indicated T2* values of 66.7 \( \pm \) 0.1 ms, 66.7 \( \pm \) 0.1 ms and 76.9 \( \pm \) 0.1 ms for radial distance of 2 cm, 4 cm and 6 cm, respectively. An average T2* value for agar gel phantom is 70.1 \( \pm \) 0.1 ms.

![Figure 1](image.png)

**Figure 1.** The plots of SNR vs. TE for the standard MRI phantom at different slice thicknesses; ○: 3 mm, □: 5 mm and Δ: 10 mm
Figure 2. The plots of SNR vs. TE for the agar gel phantom at different radial locations; ○: 2 cm, □: 4 cm and △: 6 cm from the center of the phantom.

Figure 3. The plots of SNR vs. TE for the agar gel phantom in the presence of tumor-like structure at different radial locations; ○: 2 cm, □: 4 cm and △: 6 cm from the center of the phantom.

Figure 3 is the behavior of SNR similar to that shown in Figure 2 but in the presence of kaffir lime as tumor like structure, being longitudinally and axially submerged in the agar gel phantom. Similar change in SNR with distance can be observed. The T2* values determined from fitting the exponential model to the experimental data are 58.8 ± 0.1 ms, 55.6 ± 0.1 ms and 50.0 ± 0.1 ms for radial distances of 2 cm, 4 cm and 6 cm, respectively. The average T2* of the agar gel phantom in the presence of kaffir lime is 54.8 ± 0.1 ms which is lower than that obtained in the absence of the tumor like structure.
Figure 4 shows another way of evaluating the change of SNR with TE, hence determination of T2* value. The plots are the ln of the average of SNR of Figure 1, Figure 2 and Figure 3 as a function of TE. For comparisons, it can be seen from the slope of the lines that a faster exponential decrease is indicated by a higher slope which is shown by the agar gel phantom with kaffir lime, while the MRI standard phantom has a slower relaxation. Obviously, the presence of tumor like structure has the effect of decreasing the T2* value of the agar gel. From the slopes, it can be shown that T2* values for the phantoms under study are 88.5 ± 0.1 ms, 69.0 ± 0.1 ms and 55.9 ± 0.1 ms for the standard MRI, agar gel and agar gel with kaffir lime, respectively, which are about the same with that obtained from the exponential equations.

4. Discussion

Studies on other gelling materials as an alternative to agar gel for MRI phantom fabrication has been done [5–7] to investigate their homogeneity, gel stability, reproducibility and time consumption in preparation. Two important quantities of interest are the T1 and T2 relaxation times, which were obtained from their respective curves. In Hellerbach et al. [5], it is shown that Carbomer-980 and Carbopol-974P were two promising novel phantom materials. These gelling agents are readily available, inexpensive and easy to handle given that thermal treatment is not required. In Christoffersson et al. [6] it is shown that The T1 and T2 values of the gel can be varied independently by changing the relative amounts of magnetic additives (nickel) and agarose. In addition, a novel tissue-equivalent MRI phantom based on carrageenan gel was fabricated [7]. Carrageenan gel is an ideal solidifying agent for making large, strong and flexible phantoms in a wide variety of shapes. In this study, agar gel was used as opposed to gelling materials in [5–7] due to its flexibility, availability and cheaper cost.

The SNR obtained from the standard MRI phantom, agar gel and agar gel in the presence of kaffir lime mimicking phantom follows an exponential decrease as a function of TE. As TE increases, more signals are lost due to the duration of spin-spin interactions that are allowed to occur. All hydrogen spins in the MRI and agar gel phantoms are subjected to the same constant external magnetic field (of 3T in this study). However, despite the homogeneity of the 3-T magnetic field upon the application of shimming, spin-spin interactions caused by local magnetic field inhomogeneity of a material or tissue still persist. Protons will still be experiencing differences in their local magnetic fields caused by differences in their surroundings. Some protons precess faster than the other. A larger difference
between the fastest and the lowest precession frequency of the protons indicates a larger inhomogeneity and will enhance a larger amount of spin-spin interaction, hence, a shorter $T_2^*$. $T_2^*$ relaxation is slower (or longer $T_2^*$) for the standard MRI phantom. The standard MRI phantom is fluid in nature and has smaller molecules and higher mobility causing a longer $T_2^*$, which is $86.7 \pm 0.1$ ms on average as compared to $70.1 \pm 0.1$ ms for agar gel and $54.8 \pm 0.1$ ms for agar gel in the presence of kaffir lime. Materials with higher mobility, such as fluid will increase local magnetic field homogeneity causing a small difference between the precessional frequencies among the protons. On the contrary, gelling materials such as agar gel contains larger molecules thus will create a larger local magnetic field inhomogeneity that will cause spin-spin interaction to complete in a shorter duration. This is more prominent in the presence of kaffir lime. Kaffir lime has caused disturbance in the local field homogeneity of the field distribution in the gel phantom resulting in a faster drop in SNR as a function of TE.

The three highest chemical compounds in kaffir lime peel oil are Sabinene (4-methylene-1-(1-methylethyl)bicyclo[3.1.0]hexane), Limonene (1-Methyl-4-(1-methylethenyl)-cyclohexene) and $\beta$-Pinene (6,6-Dimethyl-2-methylidenebicyclo[3.1.1]heptane) [8] all with chemical formula of $C_{10}H_{16}$ which contained about 71.8% of its total content as determined by gas chromatography (GC) and gas chromatography–mass spectrometry (GC-MS) [8]. It is believed that an abundant amount of hydrogen atom in kaffir lime has caused disturbance in the distribution of magnetic field lines in the agar gel surrounding the kaffir lime which in turn introducing magnetic field inhomogeneity that has caused a decrease in $T_2^*$ value of the phantom.

5. Conclusion
Due to the local inhomogeneity of the magnetic field introduced by the gelling materials, the $T_2^*$ values are shortened and the effect is larger in the presence of kaffir lime. This could be due to the increasing number of hydrogen atom resulting in a higher degree of field inhomogeneity. The fabricated phantoms are suitable to be used with long TEs resting state fMRI protocols.

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