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Assessment the Influencing Factors on MRS Signal Obtained from High Magnetic Field Strength (1.5T) MRI Scanners During the Application of Homemade Metabolite Phantom

Mahdi Saeedi-Moghadam[1], Majid Pouladian[2,3]*, Mehrzad Lotfi[4,5], and Reza Faghihi[6,7]

[1]*Department of Medical Radiation Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran*
[2]*Department of Biomedical Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran*
[3]*Research Center of Engineering in Medicine and Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran*
[4]*Medical Imaging Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*
[5]*Department of Radiology, Shiraz University of Medical Sciences, Shiraz, Iran*
[6]*Department of Nuclear Engineering, School of Mechanical Engineering, Shiraz University, Shiraz, Iran*
[7]*Radiation Research Center, School of Mechanical Engineering, Shiraz University, Shiraz, Iran*

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Purpose: This study aimed to present a protocol for constructing MRS phantoms that are supposed to be subjective of spectroscopy using 1.5T machines. Methods: As phantom containers, laboratory clear/amber glass bottles and an internally-designed Plexiglass and PVC cylinders were tested to evaluate the effect of phantom material and design on produced signals. HPLC and distilled-water were evaluated as solvent of metabolites. Finally, a protocol was suggested. Results: The results revealed that the physical walls of internally-designed phantom affect the WS and its baseline noise. The results also showed that even the amber-pigments inside the bottles can affect the MRS signal. Accordingly, the combination of HPLC-water inside clear-glass containers is suggested. Conclusion: The suggested protocol is as follows, apply clear-glass container as phantom body, do not build internal-structures using physical walls of glass or any other materials. Apply HPLC-water as solvent instead of distilled-water. Check the purity of chemical metabolites.

Keywords : MRS, phantom material, phantom structure

1. Introduction

Magnetic resonance spectroscopy (MRS) is a useful device that provides chemical information on tissues [1]. Using MRS, the concentration of different metabolites in the body's tissues are estimated and the results are presented as a spectrum of resonances along the x-axis in ppm and the resonance amplitudes in the y-axis with an arbitrary scale [2, 3].

Similar to all other imaging techniques some phantoms are designed to assess the accuracy of provided information by the scanner or to simulate a clinical situation, which is more important in the research area. MRS was first presented in 1982 by Brown *et al.* [4] and it was developed by Maudsley in 1983 [5]. One of the earliest MRS phantoms was built in 1989 by Hurd *et al.*, which was constructed by three 5 mm diameter-tubes containing a different concentration of Lactate (2.5, 5 and 10 mM) [6]. In 1998, an anthropomorphic 1H MRS head phantom was built by Rice *et al.* This phantom contained six glass spheres inside an outer sphere. Each sphere contained different metabolite components. The main sphere was made of glass, acrylic, and polystyrene internal structures [7]. Meanwhile, lots of other phantoms containing simple metabolic solutions were built [8-14].

Based on Task Group American Association of Physicists in Medicine (AAPM) #9, which is a reference for brain MRS data acquisition and processing [15], MR system manufactures should provide spherical phantoms with a diameter of 18-20 cm containing 1H metabolites, which are called test phantom. This phantom contains 12.5 mM N-Acetylaspartic acid (NAA), 10 mM Creatine (Cr), 3 mM Choline (Cho), 12.5 mM Glutamate (Glu), 7.5 mM Myo-inositol (M-Ins) and 5 mM lactate. These

*Corresponding author: Tel: +989121390336
e-mail: pouladian@srbiau.ac.ir

concentrations simulate brain metabolites. Because phantom does not contain many other metabolites, such as lipids and macromolecules, it results in a completely separated peak spectrum. There are also other phantoms that were built by researchers that contained more or less metabolites depending on the researchers' requirement [16, 17]. Designing and building new phantoms are still routine and efficient in new research situations to simulate the research condition.

Numerous phantoms that were built by manufactures or researchers show that phantom is a necessary device for evaluating the accuracy of system or for the investigation of a specific clinical situation. Most of the phantoms were described above, built of glass, acrylic, polyethylene, polystyrene or plastic and none described the process of phantom building or the sensitivity studies which are needed to build a phantom that can provide a suitable spectrum.

MRS is a sensitive device that can even sense the slightest impurities, which might exist in the chemical material. This issue can be even more important when the scanner device is a 1.5 T MRI machine since its signal to noise ratio (SNR) is less than 3 T scanner. The impurities inside the phantom structure can disturb the magnetic field, which can affect the signal and increase the noise. For the lower SNRs, these little changes can have a more important impact, especially on the metabolite signals in MRS that are several orders of magnitude smaller than water signal. Hence, for building a MRS phantom, performing some tests are essential, specifically where the scanner is a 1.5 T MRI.

According to the estimates of Electric Markets Research Foundation (EMRF), the number of 1.5 T MRI scanners in the world is 3.2 times more than 3T MRI machines. In a report in 2016 it declared that 55 % of MRI machines in the world are 1.5 T and only 17 % of them are 3T [18]. Therefore, it is necessary to have a protocol for building MRS phantoms that want to be used with a 1.5 T MRI.

In this study we first showed the difference of the MR spectrum provided by a 1.5 T and 3T machines to indicate the importance of removing factors that reduce signal quality. Then we introduced a protocol to construct MRS phantom that can provide a good signal by 1.5T MRI machine.

2. Methods

2.1. Assessing the necessity of this research

To assess the difference between spectrum provided by 1.5 T and 3 T scanners, a phantom was made of a 50 mL Polypropylene (PP) Falcon conical centrifuge tube comprising of 5 mM NAA, 10 mM Cr and 6 mM Cho solved in distilled water. A single voxel spectroscopy (SVS) was performed using the PRESS pulse sequence, TE of 144 ms, TR of 1500 ms and a voxel size of 3.38 cm^3 by a 1.5 T General Electric (GE) MRI and 3 T Siemens scanner. The results were compared to assess the outcome signals of 1.5 and 3 T MR scanners.

2.2. The prerequisite assessments for phantom construction

There are some measurements that are necessary to build a MRS phantom as follow: evaluating the accuracy of spectrum provided by the MRI machine, assessing the material of phantom container, and the water that is used to solve the metabolites and the purity of metabolites.

2.3. Evaluating the MRS spectrum

First of all, because of the need to check the spectrum of different components of the phantom, it is necessary to assure that the spectra produced by MRI machine are accurate and precise. For this step, the GE test phantom (Model 2152220, Milwaukee, WI, USA) was applied. It is a 2.7 L sphere containing 50 mM KH_2PO_4, 56 mM NaOH and 1 mL/L Magnevist. The metabolites are NAA, Cr, Cho, Glu and M-ins with the concentration of 12.5, 10, 3, 12.5 and 7.5, respectively [19]. All procedures in this study were performed using 1.5 T GE (Signa-HDXt) machine.

In order to assess the accuracy of spectrum created by MRS machine, a SVS was performed using the PRESS pulse sequence, TE of 144 ms, TR of 1500 ms and a voxel size of 8 cm^3. If the MRI machine provided the expected spectrum as the manufacturer suggested, other steps were followed and if there was an error in the spectrum of test phantom the error source was diagnosed and resolved before other measurements.

2.4. Evaluating the material of the phantom container

As phantom containers, laboratory clear and amber glass bottles, homogenous Plexiglass cylinder and internally designed Plexiglass and Polyvinyl chloride (PVC) cylinders were tested to evaluate the effect of phantom material and design on the produced signal. The internally designed phantoms were used to assess the effect of internal walls on the produced spectrum. The phantom containers that were used in this study are shown in Fig. 1.

All phantoms were filled with distilled water and a SVS was performed using the PRESS pulse sequence, TE of 144 ms, TR of 1500 ms and a voxel size of 8 cm^3. The spectra were assessed in terms of baseline noise and the

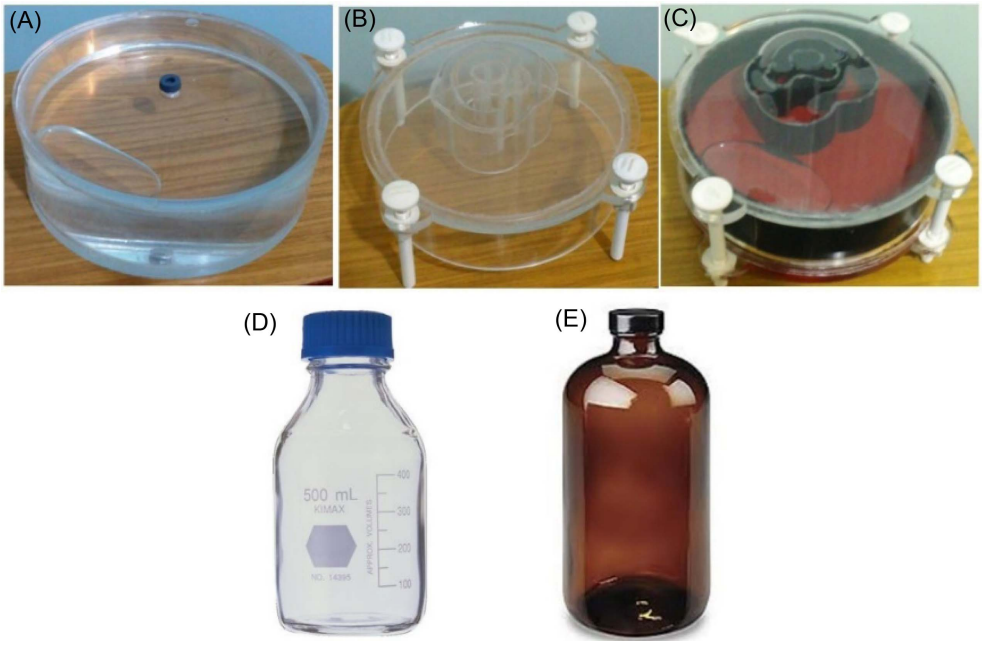


Fig. 1. (Color online) The phantom materials with and without internal design used to evaluate the effect of phantom material and design. (A) Homogenous Plexiglass cylindrical phantom without internal structure, (B) Plexiglass cylindrical phantom with internal structure, (C) PVC cylindrical phantom with internal structure, (D) clear laboratory glass bottle, (E) Amber laboratory glass bottle.

amplitude of water signal.

2.5. Evaluating the solvent water

Water is the usual solvent in MRS phantoms. In this study the distilled water and high performance (or high pressure) liquid chromatography (HPLC) water was assessed inside the clear and amber glass bottles. The SVS with the same parameters (TE of 144 ms, TR of 1500 ms and a voxel size of 8 cm^3) were performed.

2.6. Evaluating the Purity of metabolites

If the provided spectra were different from the expected spectra, the first thing to do was to check the metabolites. The metabolites of a MRS phantom should be from a reliable chemical company. If they are provided from a mediator the purity and accuracy of the metabolites should be checked by performing a spectroscopic imaging or performing mass spectroscopy or nuclear magnetic resonance (NMR) assessments. This study provided three examples of assessing metabolite materials of NAA, Cho, and Cr using the MRS imaging, mass spectroscopy, and NMR.

3. Results

The results of SVS of Falcon tube phantom using 1.5 and 3T MRI scanner is shown in Fig. 2.

The MRS signal provided by GE MRI in comparison to

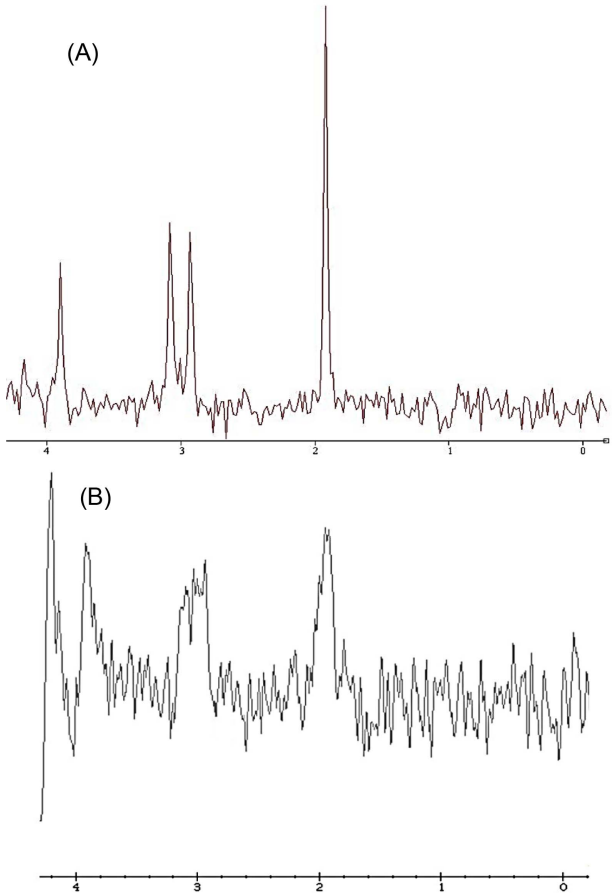


Fig. 2. (Color online) Spectrum of Falcon tube phantom provided by (A) 3T MR scanner and (B) 1.5 T MR scanner.

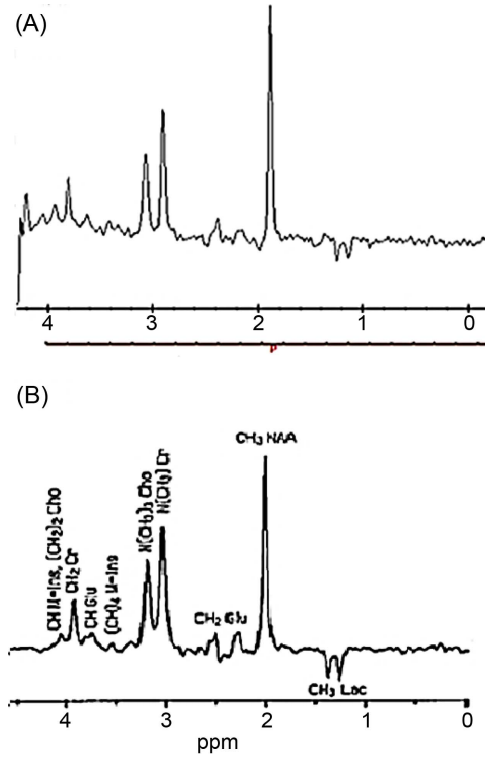


Fig. 3. (A) GE standard phantom spectrum. (B) the expected spectrum predicted by AAPM #9. The MRS parameters were PRESS pulse sequence, TE of 144 ms, TR of 1500 ms and voxel size of 8 cm^3.

the expected signal is shown in Fig. 3. The expected MRS signal of test phantom was predicted by AAPM #9.

The results of the material of phantom containers (Plexiglass with and without internal structure and PVC with internal structure) is shown in Figs. 4. The results of the combination of water and containers is shown in Fig. 5.

A MRS was performed for the solution of each metabolite in HPLC water separately. If the spectra were not as the expected spectra, mass spectroscopy and NMR was performed to assess the validity of metabolites. The results of MRS is shown in Fig. 6.

The spectrum of Cho was as it was expected, but the NAA and Cr spectra were not as they were expected. Hence, the metabolites were sent to the laboratory for mass spectrometry and NMR tests. The results of these tests are shown in Figs. 7-8.

Cr and NAA metabolites were purchased again and assessed using MRS. Figure 9 shows the results of Cr and NAA MRS.

4. Discussion

Designing and constructing the phantoms to evaluate accuracy and precision of a clinical and research device can be very helpful in controlling their performance and

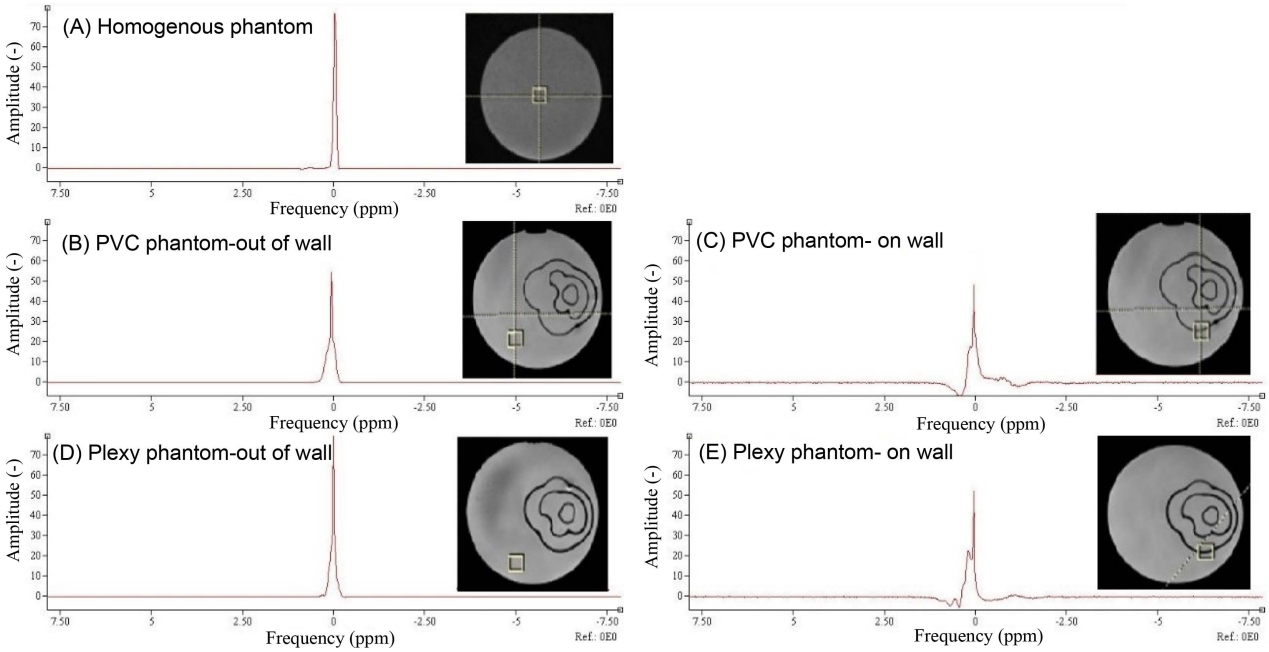
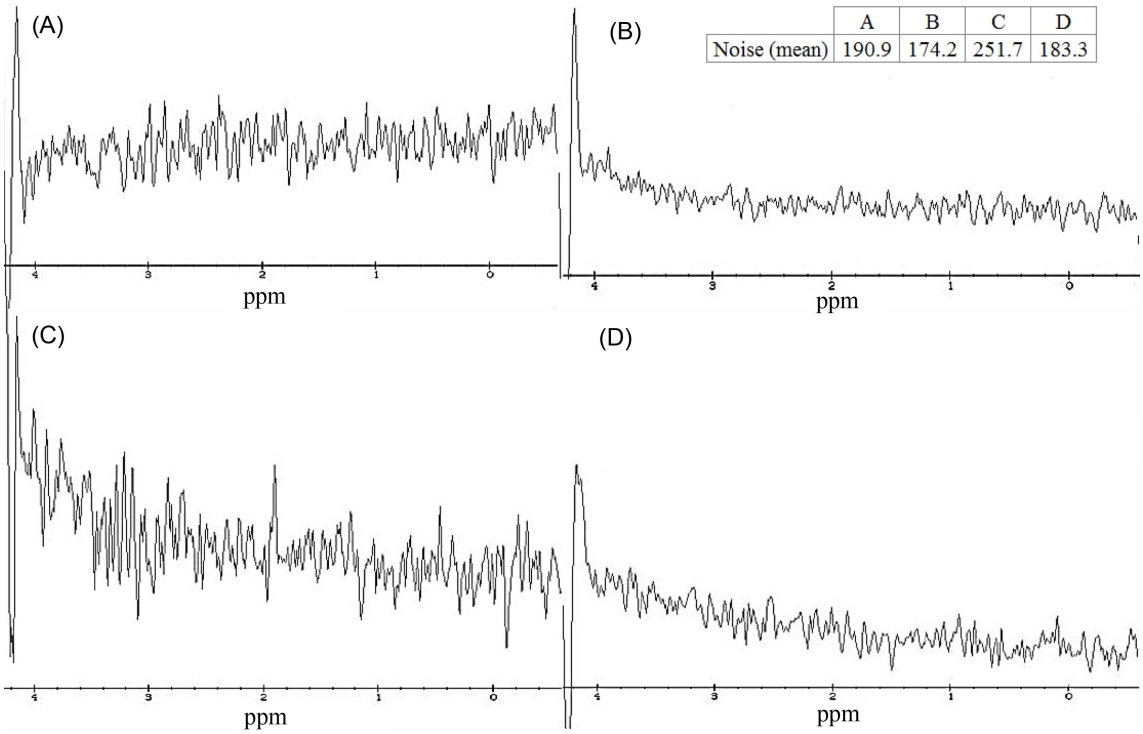


Fig. 4. (Color online) (A) Water signal without water suppression in the center of homogenous Plexiglass phantom. (B) Water signal without water suppression in the region outside the wall material in PVC phantom. (C) Water signal without water suppression in the region that include wall material in PVC phantom. (D) Water signal without water suppression in the region outside the wall material in Plexyglass phantom. (E) Water signal without water suppression in the region that include wall material in Plexyglass phantom. All peak's amplitudes were normalized to 100.



	A	B	C	D
Noise (mean)	190.9	174.2	251.7	183.3

Fig. 5. (A) Baseline noise of HPLC water in the amber bottle. (B) Baseline noise of HPLC water in clear bottle. (C) baseline noise of distilled water in the amber bottle. (D) Baseline noise of distilled water in clear bottle. Noise values are shown in the upper right of the figure.

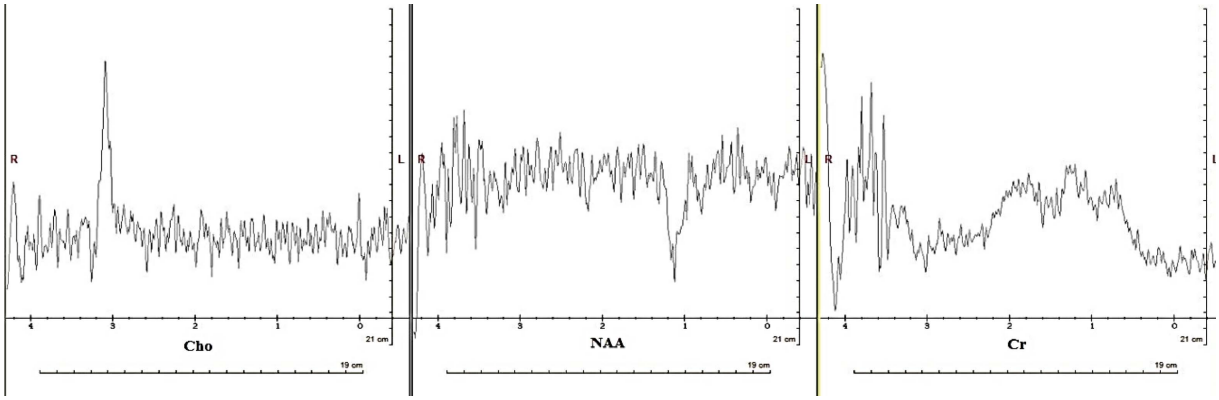


Fig. 6. MRS spectra of Cho, NAA, and Cr using 1.5 T MRI machine, the pulse sequence of PRESS and TE of 144 ms.

efficiency, especially those that are very sensitive to different variables.

MRS by nature is a very sensitive tool since it should be able to detect metabolites signals, which their concentration is thousand times less than water or fat signals. So that a few impurities can change the result of spectrometry and because of this, it is important to create a phantom that has the least interfering impurities. Using a 1.5 T scanner that SNR is less than 3 T MRI, existence of impurities can worsen the effect.

A goal of this study was to show the differences between the provided signals from a MRS phantom by 1.5 and 3 T scanners to indicate the necessity to introduce a protocol for construction the MRS phantom.

Figure 2 shows that the signal of a Falcon tube phantom provided by 3 T scanner had a good resolution, the peaks were narrow and well separated, but the provided spectrum using 1.5 T scanner had wide and poorly separated peaks. To exclude Falcon tube walls from the spectroscopic volume, a small volume size (3.38 cm^3) had been chosen. This small size explains the baseline noise, which can be seen in both 1.5 and 3 T images. The baseline

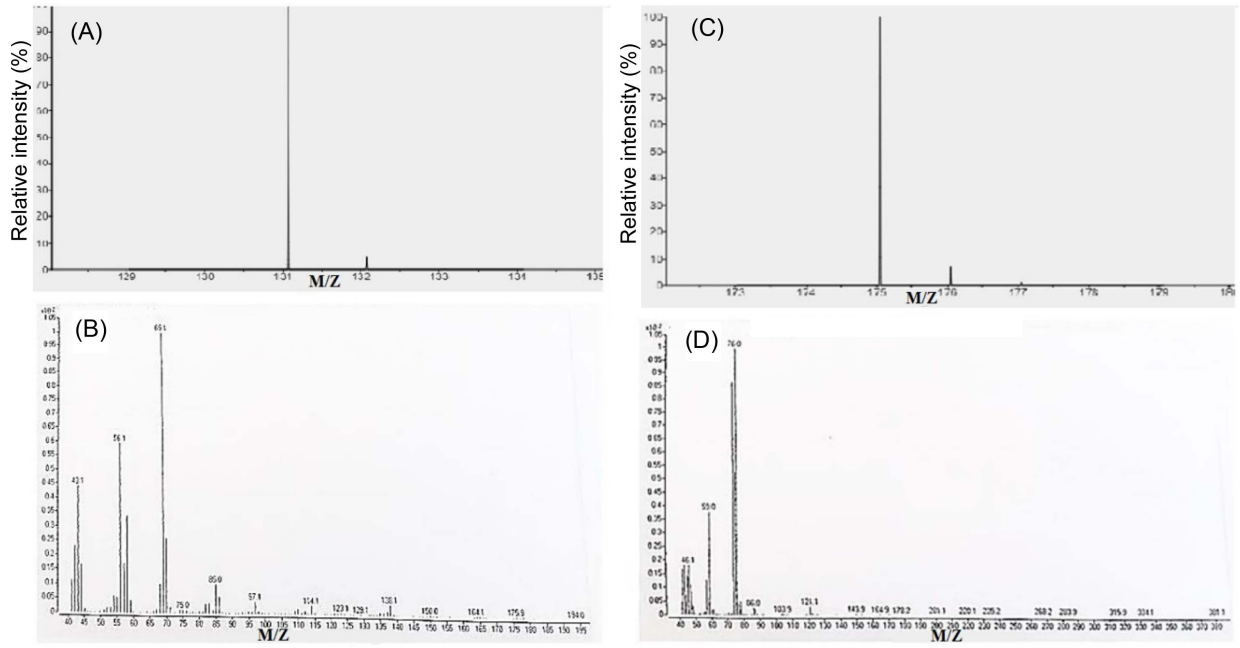


Fig. 7. (A) The expected result of Cr mass spectrometry. (B) The Results of the mass spectrometry of Cr. (C) The expected result of NAA mass spectrometry. (D) The Results of the mass spectrometry of NAA.

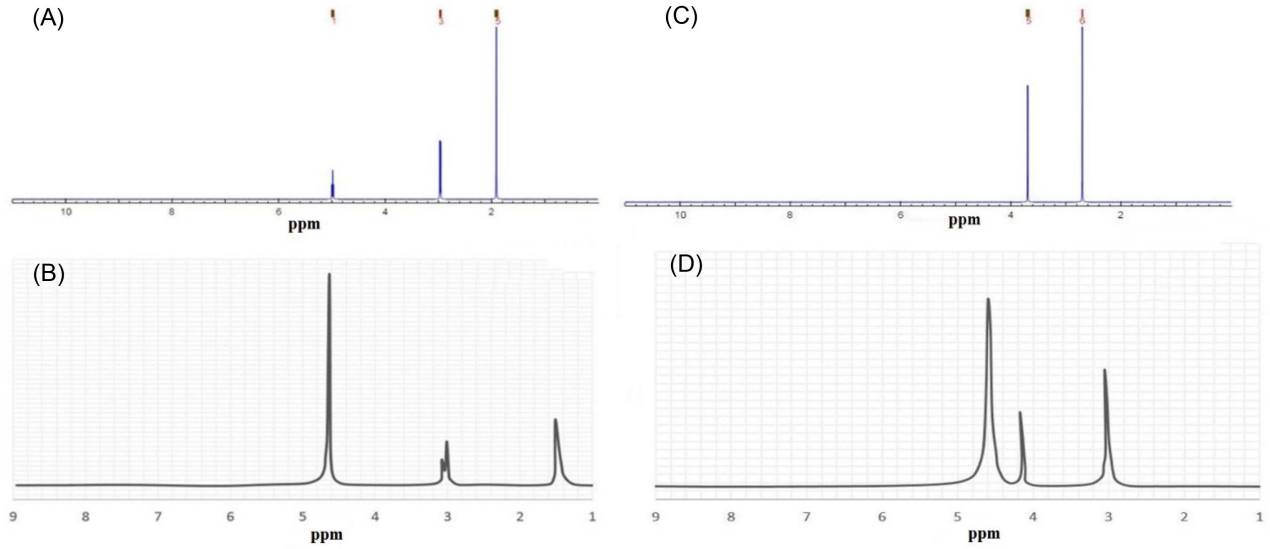


Fig. 8. (Color online) (A) the expected result of NAA NMR. (B) The Results of the NMR of NAA. (C) The expected result of Cr NMR. (D) The Results of the NMR of Cr.

noise in 1.5 T image is obviously more than the 3 T image. The higher SNR of 3 T MRI scanner allows higher quality data acquisition, which in turn permit easier and better quantification of provided data from smaller voxel size [20]. Moreover, the small impurities existed in the phantom structure, such as PP container led to poorly resolved and broad signal in 1.5 T spectroscopy. There are some impurities in the material of PP Falcon containers that might differ from brand to brand that can affect the spectroscopic signals [21]. These impurities might disturb the magnetic field homogeneity, which in turn disturb the signal provided by MR scanner. Since the SNR of the 1.5 T is less than 3 T scanner the effect of magnetic field disturbance can be more obvious, especially when the confounding factors are near the volume of interest (VOI) where it might not be completely shimmed [22].

Therefore, it can be concluded that the phantoms that

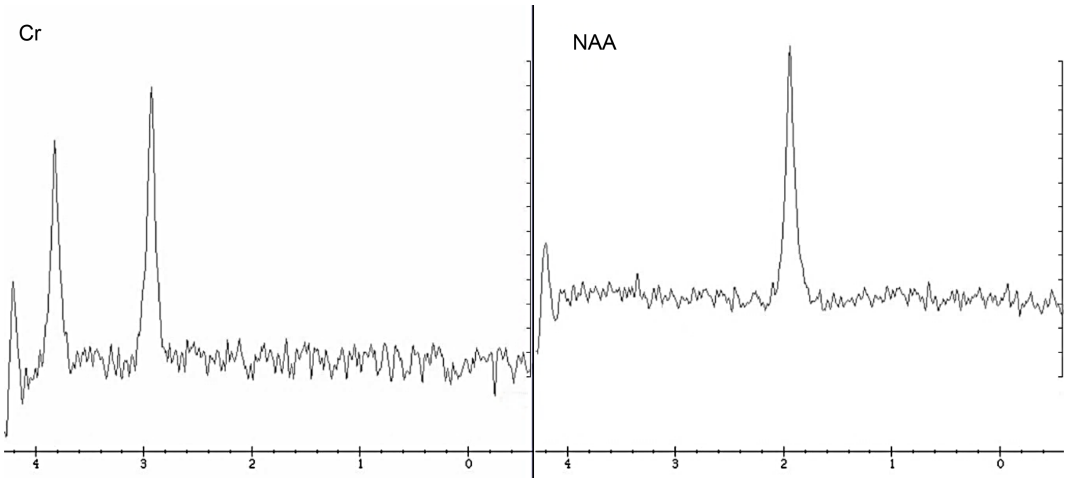


Fig. 9. MRS spectra of NAA and Cr using 1.5 T MRI machine, the pulse sequence of PRESS and TE of 144 ms.

provide good spectrums in the ultrahigh magnetic field (≥ 3 T) MRI scanners might not necessarily lead to the same results in the 1.5 T scanners. To obtain a proper result by 1.5 T MRIs, more considerations should be taken into account. One other goal of this study was to introduce a protocol for building MRS phantom that can provide good spectrum using 1.5 T MRI scanner.

According to Fig. 3, the signal provided by our 1.5 T GE MRI scanner from a test phantom was in good agreement with the expected signal provided by AAPM. It was a good assurance that our system had an acceptable performance.

The results presented in Fig. 4 and Table 1 revealed that the water signal provided from the central region of Plexiglass phantom without internal structure had the greatest amplitude, while the water signal in Plexiglass and PVC phantoms in the region out of the walls had decreased amplitudes in comparison to homogenous phantom, 15.09 and 34.30 %, respectively.

The water signal in the regions of phantom walls had even a more reduced amplitude. One reason can be simply because the wall occupied some volume of the spectroscopic voxel and so that less water molecules were presented in the voxel, which in turn produced a lower amplitude signal. The results of the area under the curve also prove that the water signal in these cases are less than homogenous phantom or when the voxel is out of the wall region (Table 1). The other reason can be the effect of impurities existed in Plexiglass and PVC phantom. The wall material can produce susceptibility and partial volume artifacts in the signal, which can affect the signal shape and make it broad [23].

Polymers like Polyethylene and Plexiglass materials produced by different brands and companies can contain some impurities, such as A1, As, Au, Br, C1, Co, Cr, Cu, Fe, Hg, K, La, Mn, Mo, Na, Sb, Sc, Sm, V, and Zn [24]. Depending on method of Plexiglass manufacturing the amount of impurities can vary [25, 26]. The PVC materials also have some mixed metal, tin, lead and organic additives as stabilizers and plasticizers [26, 27]. The impurities in PVC is more than Plexiglass. The susceptibility of PVC is –1.8 ppm so it can even shift the water frequency [28]. The water peak in this study using PVC phantom shifted from 4.7 ppm to the 4.76 ppm.

To assess the peak broadening the FWTM was evaluated, since the peak broadening happened lower than the half

Table 1. The area under the peak for the water signal, the amplitude of water peak, the mean of the noise, SNR and Full width at tenth maximum (FWTM) for the water signal provided in each container.

Phantom type Parameters Location of voxel	Area under the curve	Peak amplitude	Noise (mean)	SNR	FWTM
homogenous Plexiglass phantom	5.86×10^7	9.01×10^6	230.81	3.90×10^4	0.10
Plexiglass phantom- out of wall	4.89×10^7	7.65×10^6	302.24	2.53×10^4	0.16
PVC phantom-out of wall	5.48×10^7	5.92×10^6	333.32	1.78×10^4	0.23
Plexiglass phantom-on wall	3.25×10^5	3.23×10^4	117.01	2.76×10^2	0.19
PVC phantom-on wall	4.49×10^5	3.00×10^4	116.08	2.59×10^2	0.25

amplitude of the peak. According to Table 1, the narrowest peak was from the center of the homogenous and the widest peak was from the PVC phantom when the voxel was on the inner wall of the phantom. Shortly, the FWTM of the water peaks using Plexiglass and PVC phantom when the voxel was on the wall were more, or the peaks were broader in comparison to the situation when the voxel was outside of the inner walls of phantom, which can also be the effect of the wall impurities.

The baseline noise of the water signal in all phantoms were assessed by the mean of noise. The results show that the baseline noise in the center of homogenous Plexiglass phantom (230.81) was less than the baseline noise of the signals out of the wall region of internally designed phantoms (302.24 and 333.33). These results revealed that the homogenous Plexiglass phantom could provide a better water signal with less baseline noise. Hence, it can be concluded that the internal walls of internally designed phantom affect the water signal and its baseline noise so that as far as it is possible, application of internal walls in phantom should be avoided. Application of gelatin-based phantom can be very helpful in situations when the internal structure is unavoidable.

Figure 5 shows the baseline noise of distilled and HPLC water signal in different containers. Figure 5-A and 5-C are the water signals in amber containers, which show more baseline noise in comparison to clear glass containers (Figs. 5-B and 5-D). This result simply shows that even the amber pigments inside the bottles can affect the MRS signal. The Amber pigments contain iron oxide [29, 30] that can disturb the magnetic field, and so that affect the signal and increase the noise. According to Fig. 5, the least baseline noise belonged to HPLC water inside clear glass containers. HPLC water is an ultrapure water, free from organic and inorganic impurities and also free from the contaminations that might exist in distilled water. Clear laboratory glass bottles are made of SCHOTT DURAN® or borosilicate 3.3, which is not contaminated by Fe, Cr, Mn, Zn, Pb or other heavy metal ions [31], hence, they are free from the elements that can disturb the magnetic field. Glasses which contain iron oxide or lead are not suitable for this application because of their magnetic susceptibility [28].

Figure 6 shows the MRS signal of each metabolite. The MRS signal of Cho was as it was expected. It should have a peak in ppm of 3.2, and it has a peak in the expected ppm. However, NAA should have a peak in ppm of 2 and Cr should have 2 peaks in ppms of 3.0 and 3.9 [32], but there are not the peaks in the expected ppms. Consequently, the purity of Cho was verified, while NAA and Cr were sent to a lab for more tests for such things as mass spectrometry and NMR. Figure 7 that shows the results of mass spectroscopy and Fig. 8 that shows the results of NMR revealed that Cr and NAA had problems and new metabolites should be bought. After providing the new metabolites of NAA and Cr a MRS imaging with the same parameters was performed. Figure 9 shows expected spectra of Cr and NAA.

These results revealed that if the metabolites were provided from a mediator and the signal was not that it was expected, they should be checked before being applied in the phantom because there might be some problems. Although these problems are so rare, but it happened during this study. The metabolites were bought from a mediator and later on it was determined that they are fake or there might have been some packaging problems.

5. Conclusion

According to the results of this study, the 1.5 T MRI scanners are more sensitive to the little impurities that might exist in phantom structures in comparison to 3 T scanners. The number of 1.5 T MRI scanners in the world is more than 3 T scanners and many clinical or research centers are equipped with this magnetic field strength. Therefore, it is suggested that if the researchers intend to build a MRS phantom, which is going to be subjected to spectroscopy using a 1.5 T scanner, it is better to use this protocol.

The protocol is as follows, 1. apply clear glass or high pure plexiglass container as a phantom body, 2. do not build internal structures using physical walls of glass or any other materials. If it is essential to internally design the phantom, use gelatin-base phantoms and provide the internal designs using Porcine or agar gelatin that are routinely used to produce MRI phantoms. 3. apply HPLC water as a solvent instead of natural or distilled water. 4. Check the purity of chemical metabolites by MRS, mass spectrometry or NMR if it is necessary.

Conflict of Interest

There is no conflict of interest.

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