Deuterium prolonged relaxation reveals the macromolecular content in MRI

Chin-Tien Lu\(^1\), Chih-Ching Lai\(^1\), Sheng-Min Huang\(^1\), and Fu-Nien Wang\(^1\)

\(^1\)Department of Biomedical Engineering and Environmental Sciences, National Tsing Hua University, Hsinchu, Taiwan

Introduction. Recently, the deuterium oxide (D\(_2\)O) has been used as a negative contrast agent for perfusion imaging by indirectly monitoring the infused deuterium via the conventional proton imaging. [1] It is also noticed that the H/D isotope exchange effect of deuterium can prolong the T\(_1\) and T\(_2\) relaxation of protonium. In this study, we aimed to further investigate the contrast mechanism in an environment with organic macromolecules. The interaction of macromolecules, such as bovine serum albumin (BSA), has been reported to change the relaxivity of Gd-based contrast agent. [2] Since the H/D isotopes will also exchange on the macromolecules [3], it is anticipated that the relaxivity provided by deuterium would be also altered. Therefore, the T\(_1\) and T\(_2\) of H\(_2\)O/HDO/D\(_2\)O solution phantoms with various BSA concentrations were measured by a MRI scanner to investigate the macromolecular effect.

Materials and methods. All experiments were conducted on a 4.7T Bruker Biospec 47/40 MRI scanner with protonium RF coils. The BSA (Sigma-aldrich, USA) was dissolved into H\(_2\)O/HDO/D\(_2\)O solutions to five concentrations: 0%, 5%, 10%, 15% and 20% in 1-ml tubes. Five different H\(_2\)O/HDO/D\(_2\)O solutions are formulated by diluting 0, 10, 20, 30, 40 and 50% of D\(_2\)O (99.8%, Cambridge Isotopes, USA) with deionized H\(_2\)O, and then placed into a 50-ml centrifuge filled with deionized H\(_2\)O. T\(_1\) and T\(_2\) of phantoms were measured through IR-EPI and MSME sequences, respectively. The imaging parameters for IR-EPI were as follows: TE/TR= 54/20000ms, Matrix size= 128x128, TI= 50 to 3650ms with intervals of 600ms; MSME sequence: TE/TR= 15/2000ms, echo= 15 to 225ms with intervals of 15ms. In this study, D\(_2\)O relaxivity r\(_1\) and r\(_2\) (unit: mM\(^{-1}\)sec\(^{-1}\)) of all BSA phantoms were measured as r\(_{1,2}\) = r\(_{(0)}_{1,2}\) + r\(_{1,2}\) \([\text{D}_2\text{O}]\), where r\(_{1,2}\) (unit: s\(^{-1}\)) are reciprocals of the T\(_1,2\) and r\(_{(0)}_{1,2}\) denotes the relaxation of BSA solutions without the influence of D\(_2\)O. All acquired data were processed by Matlab script.

Results. Fig 1. (a)(b) R\(_1\) and R\(_2\) relaxation rates of BSA phantoms as a function of D\(_2\)O concentration. (c)(d) The r\(_1\) and r\(_2\) relaxivities of D\(_2\)O as a function of BSA concentration. It is noted that the r\(_2\) has a negative slope with BSA in (d).

Discussion and Conclusion. In previous report, the negative relaxivity of D\(_2\)O on protonium imaging is attributed to the isotope exchange effect. Because of the less interference from deuterium than protonium, the protonium on the HDO molecule has longer relaxation times. In this study, we further found that this contrast mechanism is sensitive to the macromolecular content in the environment. This mechanism is still not clear, and further study is needed. It is speculated to be related to the change of bound water and the H/D isotope exchange on the macromolecule. In NMR studies, the H/D isotope exchange effect on spectroscopy has been used to investigate misfold proteins, which are abnormally aggregated in brain of patients with Alzheimer’s disease. [3] In our results, we demonstrate that T\(_1\) and T\(_2\) relaxation can provide information of the macromolecules. Therefore, we may use the T\(_1\) and T\(_2\) image contrast of MRI to extract molecular information after administration of D\(_2\)O contrast agent in vivo. Furthermore, it is possible to utilize the T\(_1\) change for calibrating regional D\(_2\)O concentration, and then use the T\(_2\) change for quantification of the effect of macromolecules. In conclusion, we demonstrated that employing D\(_2\)O as a contrast agent for protonium MRI is potentially valuable for future MR molecular imaging.