# The first observation of 17O MRI in normal rats at 21.1 T

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## Synopsis

**The capability of $^{17}O$ MRI in a rat head was evaluated at the high magnetic field of 21.1 T (NHMFL, Tallahassee). The results demonstrated that $^{17}O$ MR relaxation times are dependent on the magnetic field strength which correlates with experimental observations for sodium. Well separated MR peaks of $^{17}O$ water and 6-$^{17}O$ glucose provided the time courses of water distribution and glucose consumption in vivo. 3D $^{17}O$ MRI is possible with a resolution of 1 mm$^3$ in normal rats. $^{17}O$ MRI is a promising tool for future tumor detection and evaluation of tumor glucose consumption rates.**

## Introduction

The natural abundance $^{17}O$ MR signal in vivo ranks third after proton and sodium. For the same acquisition interval, the $^{17}O$ signal is 3 times less than sodium [1]. Thus, the capability of the $^{17}O$ MRI for in vivo studies at the magnetic field of 21.1 T (NHMFL, Tallahassee) is a promising tool. It is already expected that the increased magnetic field can bring a gain in scan time or in imaging resolution. However, the ultra-high magnetic field can also change $^{17}O$ MR relaxation times, which will be demonstrated below. The main goal of this study is to explore the capability of $^{17}O$ in vivo MRI at 21.1 T and present the results of using labeled $^{17}O$ glucose and $^{17}O$ water as the first steps for future tumor detection based on the Warburg effect.

## Methods

The MR experiments were performed on a 21.1 T magnet using Bruker MRI Avance III console (PV 5.1). The MR frequency for $^{17}O$ was 121.65 MHz. The in vivo RF probe has a double tuned $^{17}O/^{1}H$ *volume* RF coil with an internal diameter of 33 mm, covering the whole rat head. Duration of the 90 RF pulse for $^{17}O$ in vivo was 165 µs. The $^{17}O$ MR relaxation times $T_1$ and $T_2$ were measured using 180°-t-90° or 90°-t-180° pulse sequences respectively using 256 steps, NA = 16. Both data were fitted by a single exponential function. 3D MR rat head imaging scans were performed using a modified Bruker UTE pulse sequence with voxel of 1 mL, matrix 64x64x64, FOV=64x64x64 mm, TR = 15 ms, TE = 0.2 ms, NA = 16 for natural $^{17}O$ abundance or NA=1 after $^{17}O$ enrichments. Scan time in the last case was 1.5 min. The time course of $^{17}O$ MR signal was investigated after IV tail injections of 1 mL PBS solution containing 17% enriched $H_2{}^{17}O$ or 1.5 ml of PBS with 500 mg of 6-$^{17}O$ 47% enriched D-glucose. The in vivo experiments were performed using 3 male Fisher 344 rats (~ 200 g). All animal experiments were conducted according to the protocols approved by The Florida State University ACUC.

# Results and Discussion

The relaxation times $T_1$ and $T_2$ at 21.1 T are presented in comparison to the previous data of others at a lower magnetic field [2, 3] (Fig. 1). It was found that $T_2$ of $^{17}O$ in a rat head was 2.07 ± 0.03 ms (n = 3), which is much less than the 3.03 ms found earlier at 9.4 T [2]. The corresponding $T_1$ relaxation time at 21.1 T was 5.35 ± 0.09 ms (n=3), which is a bit higher than at 9.4 T and close to 16.4 T [3]. Additionally, the $^{17}O$ MR relaxation times in 0.45% saline solution, are both larger at 21.1 T ($T_1$ = 7.6 ± 0.24 ms, $T_2$ = 6.5 ± 0.2 ms) than at 9.4 T ($T_1$= 6.5 ms, $T_2$=4.1 ms) [2]. Thus, the $^{17}O$ MR relaxation mechanism is dependent on the strength of the magnetic field, as was also observed for sodium [4, 5]. 3D MRI of $^{17}O$ in a rat head can be acquired with a resolution of 1x1x1 mm with a scan time of 1.5 min after an IV injection of 1 ml of 17% enriched $H_2{}^{17}O$ (Fig. 2). The image acquired one minute after $^{17}O$ water injection demonstrated the increased perfusion of the rat brain and cortical areas. The $^{17}O$ water signal decreased after the injection due to its distribution inside the rat body with the exponential decay time of 11 ± 0.4min (n=2). Injection of the 6-$^{17}O$ labeled glucose yielded in 1.5 minutes a separate MR peak of glucose well separated from the $^{17}O$ water signal (Fig. 3). The glucose peak, after the initial bolus passage, was slowly decreasing as a result of glucose metabolism (Fig 3). The exponential glucose breakdown time was 48.2 ± 1.9 min (n=2). At the same time the rate of increase for the $^{17}O$ MR water peak was ~ 1.5 times less.

# Conclusion

The results demonstrate that $^{17}O$ MR relaxation times are dependent on the strength of the magnetic field which correlates with the earlier observations for sodium. The well separated $^{17}O$ MR signals of glucose and water at the ultra-high magnetic field and the corresponding time courses provided separate rates of water distribution and glucose consumption in the rat head. 3D $^{17}O$ MRI is possible with a resolution of 1 $mm^3$ in the rat head. Thus, enriched oxygen MRI can be a promising tool for future tumor detection based on the Warburg hypothesis and for evaluating the rates of glucose metabolism in tumors.

# Acknowledgements

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# References

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# Figures

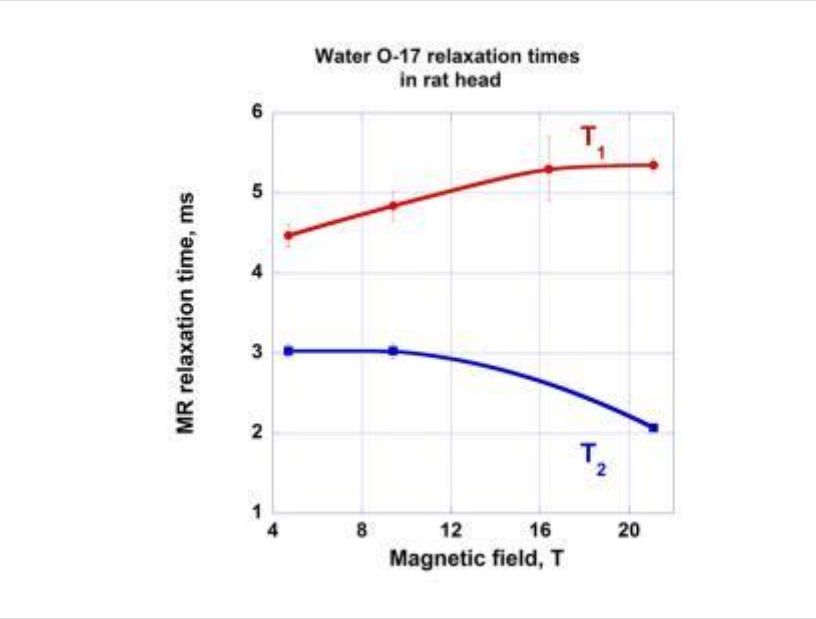


Fig. 1. Magnetic field strength dependence of $^{17}O$ MR relaxation times in a rat head. The data at 21.1 T is presented relative to the lower field data of others [2, 3]. Note the decrease of the $T_2$ relaxation time at the high magnetic field.

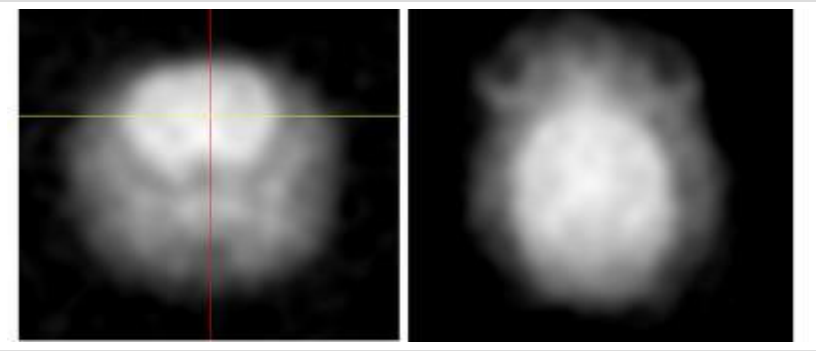

Fig. 2. $^{17}O$ 3D MRI of rat head 1 min after injection of 17% enriched $H_2{}^{17}O$. Scan time was 1.5 min, resolution 1x1x1 mm. Note the increased perfusion in all areas of the rat brain and in the cortical areas.

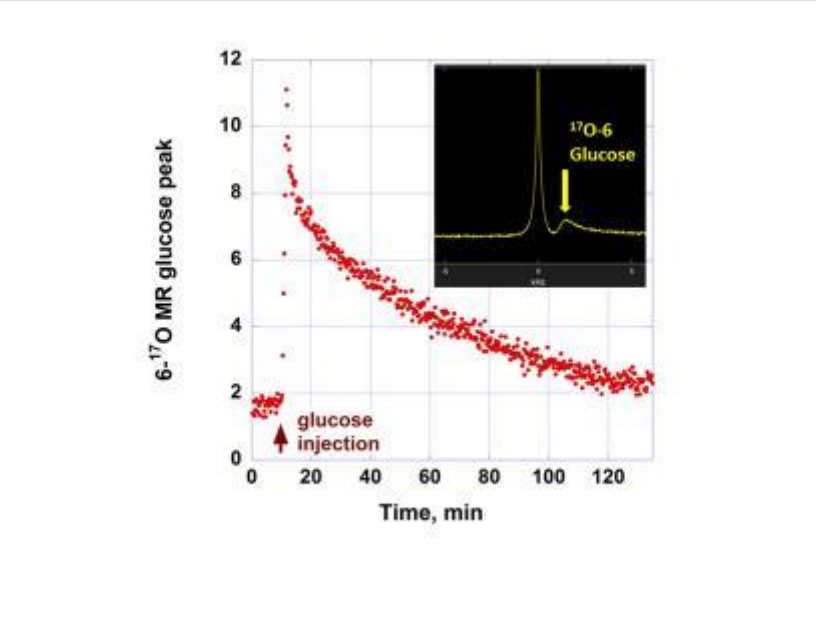


Fig. 3. The time course of metabolic $^{17}O$ MR glucose signal decrease in a rat head after IV injection of the $^{17}O$ labeled glucose. Each point represents a 6-$^{17}O$ glucose MR peak with a step of 15 s. The insert demonstrates one of such peaks, when the glucose MR signal is maximum. The MR peak of 6-$^{17}O$ glucose is at -12.3 ppm relative to $^{17}O$ water peak. Glucose signal in the rat head after the initial quick bolus passage was fitted reasonably well by the exponential function with a decay time of 48.2 ± 1.9 min (n=2).