Improved Determination of Hyperpolarized ^{129}Xe T_1 in the Rat Brain

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Purpose

Due to high lipid solubility, absence of backgound signal in biological tissue, non-invasiveness and lack of radioactivity, hyperpolarized (HP) ^{129}Xe MRI has great potential as a tool for studying the brain, especially for the assessment of cerebral blood flow (CBF). The longitudinal relaxation time (T_1) of HP ^{129}Xe in brain is a critical parameter for the accurate determination of CBF values and tissue characterization using HP ^{129}Xe MRI. Although T_1 values have been reported for human, rat and mouse brain [1-4], the values are not consistent for any species and range from 3.6 to 26 seconds in the rat brain [1,4]. In this study, we reconciled discrepant measures of T_1 for HP ^{129}Xe in the rat brain by using two methods which have been corrected for errors introduced by low SNR measurments. Our methods produce highly consistent measures of T_1 and offer a resolution to the discrepancy between values of T_1 previously reported. Accurate assessment of T_1 in brain will allow rigorous measures of CBF and other applications to be made by HP ^{129}Xe MRI in future studies.

Methods

The MR measurements from rat brain were carried out on a Bruker Biospec 4.7T MRI system using a dual-tuned surface coil tuned to the ^{1}H and ^{129}Xe resonance frequencies (200 and 55.4 MHz, respectively). Four male Sprague-Dawley rats (175-230 g) were ventilated with alternate breaths of O_2 (2 sec) and HP ^{129}Xe (2 sec) via a computer-controlled gas delivery system. Experimental flip angle (θ=13.5±0.2 degree) was calibrated according to Patyal [5]. Two methods were used to measure the decay time constant (τ) during the washout of the ^{129}Xe signal. In the first (multi-pulse) method [6], 8 pulses were applied with a 2 sec. inter-pulse interval during the washout. The loss of HP ^{129}Xe magnetization due to each RF pulse was corrected for by a factor of $\cos^n\theta$. The decay time was obtained from the slope of the logarithm of the signal plotted against time. In the second (2 pulse) method, 2 pulses were applied with a variable inter-pulse interval (Δt) [4]. Eight scans were carried out using Δt values which ranged from 2s to 16s in 2s increments. The decay time was obtained from the slope of the logarithm of the ratio of the 2 signal amplitudes plotted against time interval. Decay time constants from both methods were used to calculate T_1 values in the brain using the a model based on the Kety-Schmidt equation [7], in which the decay time constant (τ) of HP ^{129}Xe in the brain during the washout is $\tau=1/(F/p+1/T_1)$, where F is cerebral blood flow, p is the partition coefficient for xenon in the rat brain, and T_1 is the longitudinal relaxation time constant in the rat brain [6].

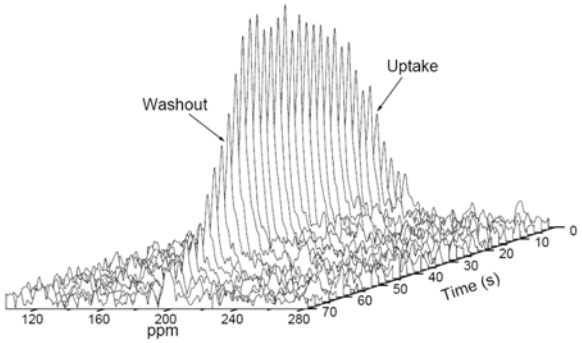

Fig. 1. MRS of HP ^{129}Xe from the rat brain *in vivo* obtained with a dynamic sequence during the uptake and washout of xenon.

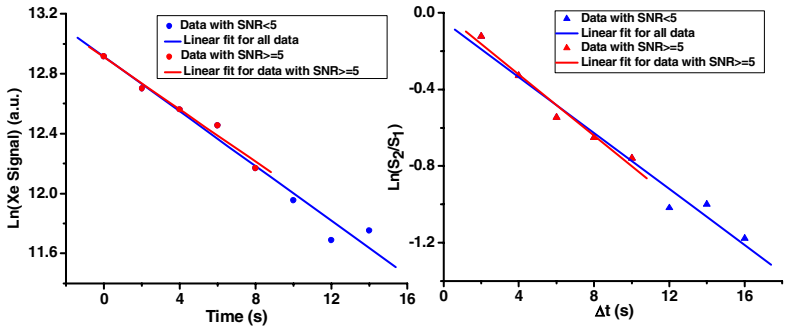

Fig. 2. Time-dependent decay of HP ^{129}Xe during washout in rat brain using **(a)** multi-pulse method and **(b)** 2-pulse method.

Results and Discussion

Figure 1 illustrates the dynamic, high SNR HP ^{129}Xe MRS in the rat brain during the uptake and washout of HP ^{129}Xe. **Figure 2a** shows the linear fits for all data points (blue) and only for the data with SNR≥ 5 (red) obtained using the multi-pulse scan. **Figure 2b** shows the linear fits for all data points (blue) and only for the data whose spectrum peaks from the second pulse, S_2 that have SNR≥ 5 (red). The two methods yielded inconsistent values of the decay time constants when all data points (conventional method) were used. The slope was again determined after discarding data points with an SNR less than 5 (improved method), which resulted in good agreement between the two methods. Table 1 shows the average T_1 of HP ^{129}Xe obtained from both methods using literature values of 106±7ml/100g/min for normal CBF in the rat, and of 1.015 for the partition coefficient of Xe in the brain [8]. T_1 values determined using these two methods differed significantly (about 5.6s) if all the data were fitted without accounting for the noise. However, if the effect of noise was minimized, the T_1's computed have a much smaller (about 1.5s) difference. These two approaches each have their own weaknesses. The 2-pulse method is more time consuming (at least 560s in the current protocol) since it needs 8 scans to collect a full data set. The polarization loss over this period results in low SNR values for the later data points. In contrast, the multi-pulse method acquires all the data it needs within a washout cycle. Its accuracy, however, depends heavily on the accuracy of the flip angle. Fortunately, the flip angles can be easily and quickly (obtained in less than 1s) calibrated.

Method	Multi-pulse method		2-pulse method	
	Ave. τ (s)	Ave. T_1(s)	Ave. τ(s)	Ave. T_1(s)
Conventional	10.2±0.8	12.4±1.2	13.7±0.9	18.0±1.6
Improved	11.8±0.9	14.9±1.4	12.7±1.3	16.4±2.2

Table 1. Average decay time τ and T_1 values obtained from the multi-pulse and 2-pulse method before (conventional method) and after (improved method) setting a threshold for SNR.

Conclusion

Due to high SNR signal and by incorporating an SNR threshold into two different approaches, the HP ^{129}Xe T_1 in the rat brain was determined as 14.9±1.4 and 16.4±2.2 s respectively, which are highly consistent (1.5s difference). Our data resolve the controversy of the HP ^{129}Xe T_1 in the rat brain, previously reported as ranging from 3.6 to 26 seconds.

References

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