$H_2{}^{17}O$ AS A T2 CONTRAST AGENT WITH RELAXIVITY SENSITIVE TO TISSUE METABOLIC STATUS

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Introduction

There are a broad range of MRI methods to monitor tissue metabolic status, relying on intrinsic contrast mechanisms (T_1 and T_2 weighted imaging), tissue biophysical properties (diffusion imaging), or the introduction of exogenous agents (contrast agents, isotopic labels). We present a novel method to monitor perturbed metabolic status via a T_2 contrast agent with relaxivity modulated by tissue pH and phosphate concentration. Scalar coupling interactions between ^{17}O and covalently bonded protons reduce the T_2 of protons in $H_2{}^{17}O$ (1), this relaxivity effect is transmitted to bulk water protons by proton exchange. As water proton exchange rate is sensitive to pH and phosphate concentration, $H_2{}^{17}O$ can be used as a contrast agent capable of distinguishing between tissue with near-neutral pH and low phosphate content (normal) and tissue with acidic pH and elevated phosphate content (ischemic). We administered $H_2{}^{17}O$ to mice to elevate the ^{17}O enrichment of body water to ~1.5%, then compared the T_2 of brain water protons under normal *in vivo* and *post mortem* conditions.

Experimental

Female CD1 mice were administered 70% ^{17}O-enriched water (16 g/kg body weight) to produce an approximately 1.5% ^{17}O enrichment of body water (assuming a body water content of ~70%). Labeled water equilibrated with body water for two hours prior to MR imaging. Animals were anesthetized with isoflurane (2% in O_2). MR data were acquired on a 4.7 T, 30cm diameter horizontal bore magnet and spectrometer (AMRIS, UF). T_2 measurements were made with a multi-slice multi-echo sequence (TE = 20 ms, 10 echoes per repetition, TR = 3000 ms). Global hypoxia was initiated by exchanging the anesthetic carrier gas with nitrogen. Image acquisition was repeated after failure of heart function.

Results and Discussion

Figure 1A&B shows T_2 maps generated from multi-slice multi-echo images acquired from a control mouse (no $H_2{}^{17}O$). *Post mortem* T_2 values show little change from *in vivo* values, with a mean T_2 of 59.2 ± 3.9 and 59.1 ± 3.8 ms for *in vivo* and *post mortem* brain respectively. Figure 1C&D shows T_2 maps from a mouse administered $H_2{}^{17}O$ to a body water enrichment of ~1.5%. *In vivo* T_2 values are approximately 15-20% lower than in control mice due to the presence of $H_2{}^{17}O$, mean brain T_2 was 54.1 ± 2.6 ms. *Post mortem* T_2 values were elevated compared to *in vivo* values with a mean T_2 of 57.7 ± 2.4 ms. The change in T_2 between *in vivo* and *post mortem* brain is assigned to a decrease in $H_2{}^{17}O$ relaxivity, resulting from an increase in water proton exchange rate caused by a change in tissue pH and phosphate content.

Conclusions

$H_2{}^{17}O$ can act as a "smart" contrast agent with relaxivity sensitive to tissue metabolic status. Furthermore, as the exogenous contrast agent is isotopically labeled water, the method is as minimally invasive as is possible.

Acknowledgements and References

1) Meiboom, S., J Chem Phys, **34**, 375-388 (1961). Funded by NIH grant P41 RR16105 and the National High Magnetic Field Laboratory. Thanks to Jim Rocca for useful discussions and to Barbara Beck and Raquel Torres for technical support.

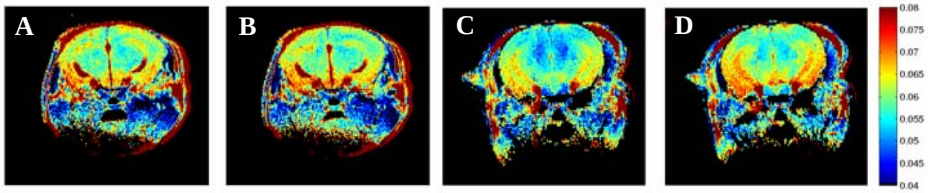

Figure 1
T_2 maps of mouse brain water protons in control (A, B) and $H_2{}^{17}O$-enriched (C, D) under normal *in vivo* conditions (A, C) and during global ischemia (B, D). Water proton T_2 values are shorter in $H_2{}^{17}O$ enriched mice, and $H_2{}^{17}O$ relaxivity is greater in normoxic conditions than following ischemia.