In vivo observations of radiation damping effects from tissue-dissolved hyperpolarized 129Xe

Rosa Tamara Branca[1,2], Le Zhang[3], and Carlos Floyd[4]

[1]*Physics and Astronomy, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States,* [2]*Biomedical Research Imaging Center, Chapel Hill, NC, United States,* [3]*Material Science, University of North Carolina at Chapel Hill, NC, United States,* [4]*Physics and Astronomy, University of North Carolina at Chapel Hill, NC, United States*

Target Audience Pulmonary Hyperpolarized ^{129}Xe MRI;

Purpose Radiation damping(*1*) is a non-linear MR effect that can easily be observed from samples with high magnetization density like a test-tube of water in a high magnetic field. Because of the low gyromagnetic ratio, low polarizability, and low concentration achievable in *in vivo* settings, radiation damping has never been observed in *in vivo* hyperpolarized xenon experiments.

Here we report the first observations of radiation damping effects *in vivo* from hyperpolarized xenon dissolved in a tissue called brown adipose tissue (BAT)(*2*). These unexpected observations and simple SNR imaging measurements indicate a local xenon concentration of several mM. This concentration is orders of magnitude higher than the typical concentration of xenon expected in distal organs (~10^{-1}mM) upon inhalation of the gas and it requires a revision of the xenon uptake model to account for all the physiological changes that are known to occur during stimulation of brown adipose tissue thermogenesis.

Methods Radiation damping effects were observed at both 7T and 9.4T during experiments on HP 129Xe detection of BAT thermogenesis(*3, 4*). For these experiments, a single-tuned xenon surface coil (1cm in diameter) was placed above the interscapular BAT depots of anesthetized and tracheotomised obese mice. The animals were mechanically ventilated at a rate of 60 breaths/minute with a home-made HP-gas compatible ventilator, which delivered a mixture of oxygen and hyperpolarized xenon gas in a 25:75 volume ratio. Non-enriched 129Xe was hyperpolarized up to 12% by SEOP using a commercially available polarizer (Polarean Inc., NC). Spectroscopy data were acquired before and during stimulation of BAT thermogenesis (achieved by an intraperitoneal injection of norepinephrine in a dose of 1mg/kg) using adiabatic RF pulses with different flip angles (90°, 15 ° and 270°) and different repetition times (1s-60s). The signal intensity and the shape of the FID were then analyzed as function of the flip angle and repetition time. A modified version of the xenon uptake model was then utilized to determine the contribution of different physiological parameters to the enhanced tissue uptake.

Results Fig 1 shows the xenon signal as acquired from one of the obese animals analyzed before (a) and during (b-c) stimulation of brown fat thermogenesis. The FIDs and the spectral line-shape (1.c inset) present the characteristic radiation damping signature. The line-shape is highly distorted, while the non-exponential FID, acquired just after a single adiabatic RF excitation, has the characteristic hyperbolic secant-like envelope. Fig 1.d shows the normalized signal intensity of xenon dissolved in BAT as function of the repetition time, fitted to the xenon uptake model used in our experiments.

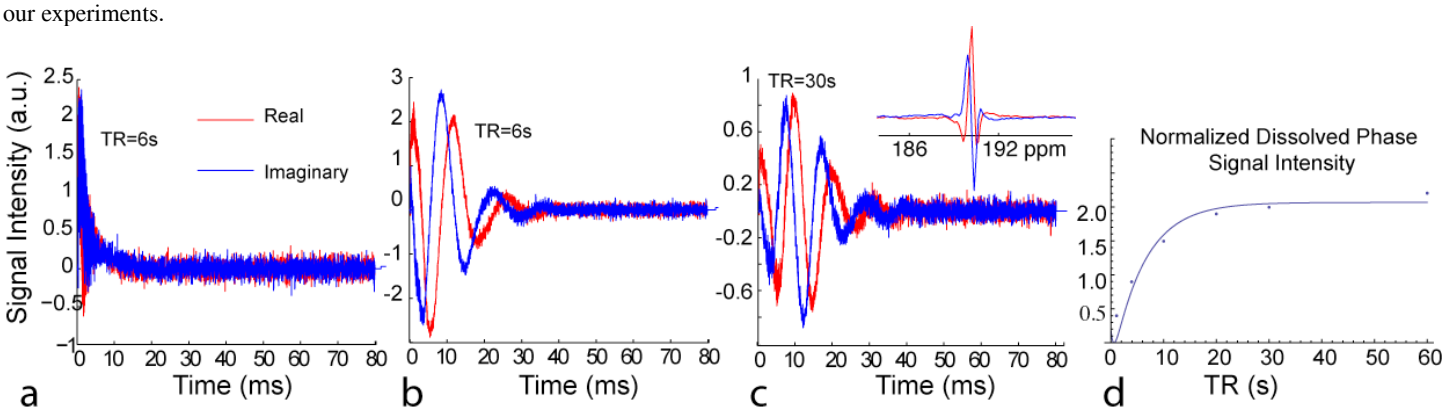

Figure 1 **a)** Un-localized FID as acquired from laser polarized xenon dissolved in tissue before and during stimulation of BAT thermogenesis. FID as acquired after an adiabatic excitation pulse using a repetition time of 6s. Imaging data show that the NMR signal, in this case, comes from all tissues covered by the sensitive region of the surface coil. b-c) FIDs acquired as in (a) during stimulation of BAT thermogenesis using the same repetition time (b), and a longer repetition time (c). The inset shows the distorted signal line-shape. Imaging data show that in this case the signal comes primarily from BAT. d) Xenon uptake curve as acquired in mice during stimulation of BAT thermogenesis fitted to a xenon uptake model that takes into account blood flow increase, changes in arterial-venous shunting, heart rate and cell permeability to BAT.

Discussion and Conclusion

We report the first observation of radiation damping *in vivo* from xenon dissolved in brown adipose tissue during stimulation of BAT thermogenesis. During stimulation of BAT thermogenesis, xenon uptake in BAT becomes orders of magnitude higher than the expected xenon uptake in distal organs, leading to the observation of radiation damping effects. This enhancement cannot be justified by a simple increase in blood flow to BAT that is known to occur during thermogenesis and other physiological changes need to be taken into account, such as changes in arterial-venous shunting, heart rate, and xenon tissue solubility.

References

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