NMR signals from hyperpolarized Xe-129 dissolved in atherosclerotic plaques

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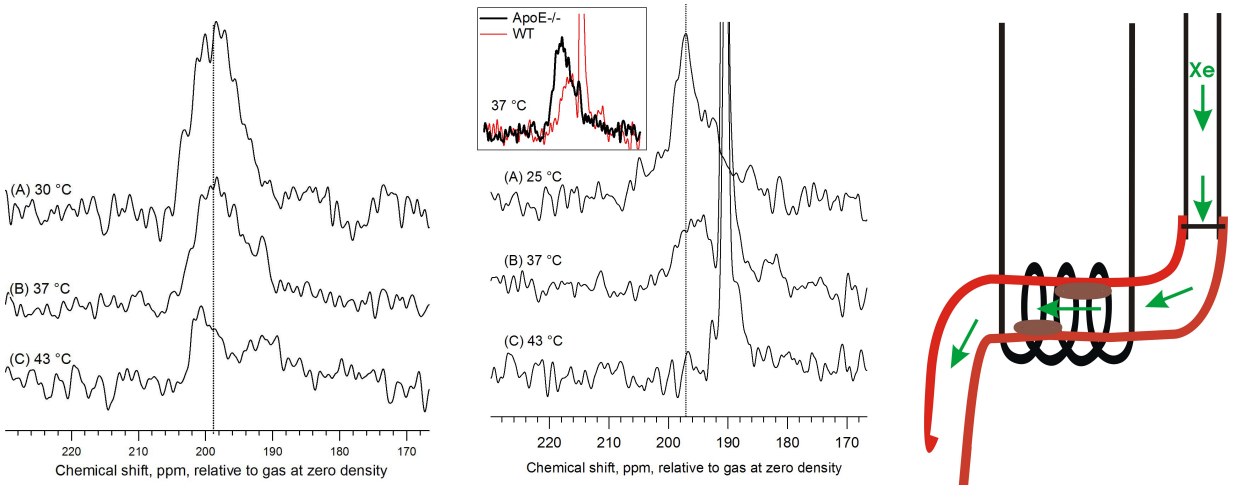
We report the first confirmed NMR signals from hyperpolarized Xenon-129 (HP Xe-129) dissolved in atherosclerotic plaques of mouse aortas. HP Xe-129 has a broad range of properties that make it a biosensor of choice to characterize biological systems. These properties include high sensitivity to molecular environments, high solubility in biological tissues, and several orders of magnitude increase in NMR signal intensity by optical pumping. Exploring the use of these advantages for atherosclerosis diagnostics, we have performed ex-vivo NMR on excised mouse aortas. For the first time, we have detected characteristic signals from HP Xe-129 dissolved in the atherosclerotic plaques. The animal model used was the apolipoprotein E-deficient (ApoE-/-) mouse which features high levels of plasma cholesterol and spontaneous development of atherosclerotic lesions resembling human disease [1]. At 57 weeks of age, plaques are clearly visible inside the aorta walls [2].

Figure 1(*a*,*b*) shows our NMR results. The schematic of our experimental setup is shown in Fig. 1*c*. To increase the sensitivity, a 4-turn microcoil of 1.5 mm diameter and 3 mm length was used. The excised mouse aortas were first cannulated with a gauge-20 polyethylene tubing though which HP Xe gas was supplied during data acquisition. The aortas were placed in the coil, and the plaques of interest were positioned in the middle of the coil (Fig. 1*c*). As shown in Fig. 1*a*, the ApoE-/- spectra consist of two components. The component on the left (downfield) has negligible temperature dependence while the component on the right (upfield) progressively shifts upfield with increased temperature. As a result, two distinct peaks (200 ppm and 192 ppm, respectively) appear at 43 °C. In comparison, the most pronounced observation in the wild-type control spectra in Fig. 1*b* is the absence of the temperature-independent component at 200 ppm (the large spikes at 190 ppm (truncated) come from HP Xe-129 dissolved in H_2O inside the NMR tube). The single Xe-129 peak (besides the peak from H_2O) from the healthy aorta displays a temperature dependence in a similar way to that of the upfield spectral component in ApoE-/- mice. To facilitate comparison, in the inset of Fig. 1*b* we overlay the spectra from the ApoE-/- and control mice, both at 37 °C. It can be seen that the ApoE-/- aorta spectrum contains a significant amount of additional intensity at higher chemical shifts.

Based on the above observations, we attribute the temperature-independent spectral component to the atherosclerotic plaques while the temperature-dependent component to the unaffected regions of aorta walls. Our observation of the characteristic plaque signal represents a big step forward in utilizing HP Xe-129 for atherosclerosis diagnostics.



a. ApoE-/- *b. Wild-type control* *c. Experimental setup*

Figure 1: (*a*) The NMR spectra of HP Xe-129 dissolved in the atherosclerotic mouse aortas consist of two components. The left (downfield) component, which is attributed to atherosclerotic plaques, shows negligible temperature dependence. The right (upfield) component, which progressively shifts upfield with temperature, is attributed to the healthy aortic tissues; (*b*) The corresponding spectra from wild-type control mouse have only one component from the healthy tissues, which is temperature dependent. (The large spikes at 190 ppm (truncated) come from HP Xe-129 in H_2O residuals inside the NMR tube); (*c*) The schematic of our experimental setup (see text for details).

References

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