Hyperpolarized Xe-129 as a Non-invasive Biosensor to Characterize Atherosclerotic Plaques

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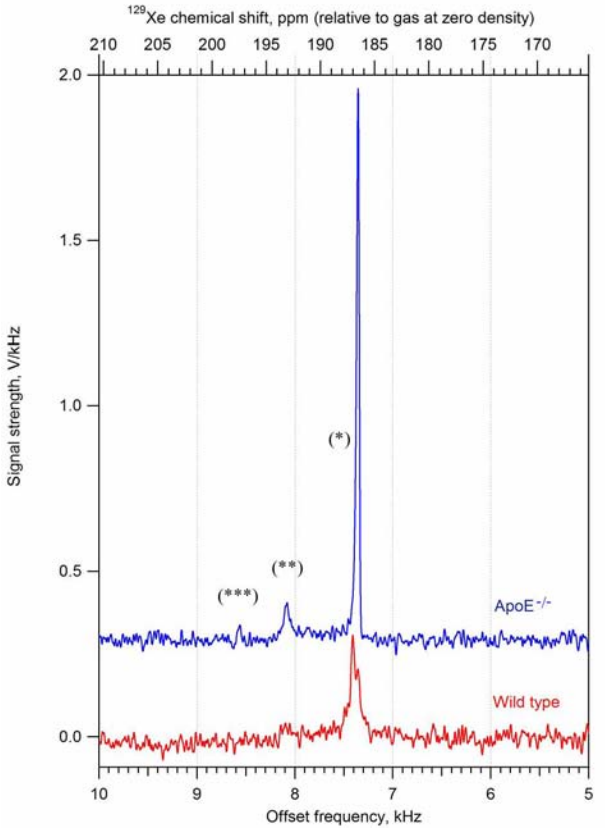
Due to its strong NMR signals, large range of chemical shifts and relaxation times, and high solubility in lipids, hyperpolarized Xe-129 gas is a particularly promising non-invasive biosensor for atherosclerosis diagnostics. In particular, Xe-129 chemical shift is very sensitive to the molecular environment in which the gas is dissolved. We propose to use this property of Xe-129 as a biosensor to identify plaque components, such as fibrous caps, lipid cores, and smooth muscle cells, and to correlate their spectral signatures with the known risk factors of sudden plaque rupture and thrombosis. In order to demonstrate that Xe-129 can provide this unique spectral information, we have recently carried out Xe-129 NMR experiments on mouse aorta tissues containing atherosclerotic plaques.

Figure 1 shows our preliminary results, in which atherosclerotic aorta tissues were harvested from two apolipoprotein E knockout (ApoE-/-) mice. Control samples were collected from three wild-type animals. In both cases, fat deposits external to the aorta were removed prior to harvesting the tissue. In the aortas of ApoE-/- animals, atherosclerotic deposits were clearly visible, as indicated by black arrows in the right panel of Fig. 1. The left panel shows the Xe-129 NMR spectra of hyperpolarized xenon gas dissolved in the tissues. The major peak, located at 186.5 ppm (*), is attributed to Xe-129 dissolved in D_2O. The ApoE-/- mouse tissues exhibit two extra peaks at 193 (**) and 197.5 ppm (***). Remarkably, we achieved a spectral linewidth of less than 0.6 ppm with our recent experimental improvements such as adopting a vertical sample geometry, and immersing samples in D_2O to eliminate the magnetic susceptibility mismatch at the tissue surfaces [1]. This narrow linewidth gives us a great advantage in spectral resolution compared to the recently reported Xe-129 spectroscopy in rat lungs (blood and tissue peaks were 17 ppm apart with ~7 ppm linewidth [2]). Signal-to-noise ratio in these experiments is not yet sufficient to establish a clear distinction between the two results: the fact that we used different batches of hyperpolarized xenon, as well as some difference in tuning of the NMR circuit might have affected the signal strength in the two experiments to a different degree. However, these data represent a big step forward towards accurate, verifiable characterization of atherosclerotic tissue types by Xe-129 NMR.



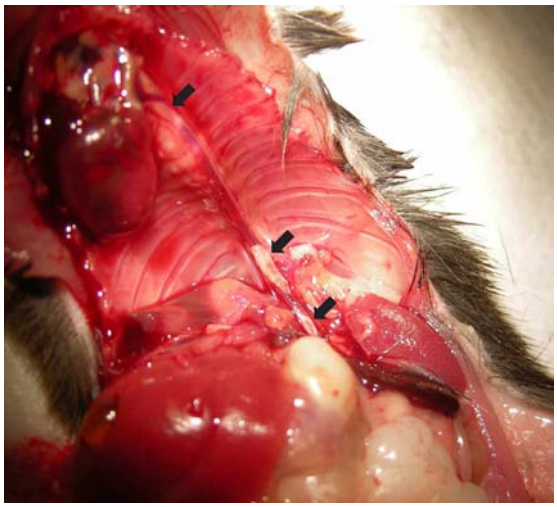


Fig.1 Ex-vivo hyperpolarized Xe-129 NMR spectra (left, top trace) from aortas of ApoE-/- mouse model (above, plaques indicated by arrows) and from wild-type controls (left, bottom trace), both at 22°C. Freshly harvested, sliced open aortas were mounted in the three-port NMR assembly of our Xe probe. Sample space was filled with D_2O. NMR spectra were recorded with 4 scans, over ~8 s. In addition to the peak of Xe in D_2O at 186.5 ppm (*), two other peaks appear: one at 193 ppm (**), and one at 197.5 ppm (***) in ApoE-/- tissues. Remarkably, the peak linewidths are very narrow (<0.6 ppm), making the discrimination of different signals based on their chemical shifts extremely promising.

[1] Kuzma *et al.*, abstract, 47th Experimental NMR Conference, Asilomar, California, 2006

[2] Abdeen *et al.*, Magn. Reson. Med. **56**, 255, 2006

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