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Establishing an Accurate Gas Phase Reference Frequency to Quantify ^{129}Xe Chemical Shifts In Vivo

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Abstract

Purpose— ^{129}Xe interacts with biological media to exhibit chemical shifts exceeding 200 ppm that report on physiology and pathology. Extracting this functional information requires shifts to be measured precisely. Historically, shifts have been reported relative to the gas-phase resonance originating from pulmonary airspaces. However, this frequency is not fixed—it is affected by bulk magnetic susceptibility, as well as Xe- N_2 , Xe-Xe, and Xe- O_2 interactions. Here, we address this by introducing a robust method to determine the 0 ppm ^{129}Xe reference from in vivo data.

Methods—Respiratory-gated hyperpolarized ^{129}Xe spectra from the gas- and dissolved-phases were acquired in 4 mice at 2T from multiple axial slices within the thoracic cavity. Complex spectra were then fitted in the time domain to identify peaks.

Results—Gas-phase ^{129}Xe exhibited two distinct resonances corresponding to ^{129}Xe in conducting airways (varying from -0.6 ± 0.2 to $+1.3 \pm 0.3$ ppm) and alveoli (relatively stable, at -2.2 ± 0.1 ppm). Dissolved-phase ^{129}Xe exhibited five reproducible resonances in the thorax at 198.4 ± 0.4 , 195.5 ± 0.4 , 193.9 ± 0.2 , 191.3 ± 0.2 , and 190.7 ± 0.3 ppm.

Conclusion—The alveolar ^{129}Xe resonance exhibits a stable frequency across all mice. Therefore, it can provide a reliable in vivo reference frequency by which to characterize other spectroscopic shifts.

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¹An amagat is a practical unit of number density corresponding to 1 atm of ideal gas molecules at 0°C.

²Jameson expressed the ^{129}Xe chemical shift in xenon gas in terms of a chemical shielding constant, $\sigma = -0.548 \pm 0.004$ ppm/amagat. This can be related to the more conventional chemical shift of ppm/amagat by using the expression $B_{\text{eff}} = (1 - \sigma) B_0$. Thus, the negative shielding coefficient yields a positive xenon-induced chemical shift.

Keywords

Hyperpolarized ^{129}Xe spectroscopy; chemical shift; bulk magnetic susceptibility

Introduction

Hyperpolarized (HP) ^{129}Xe MR spectroscopy is emerging as a powerful in vivo probe of tissue composition, physiology, and pathology (1). This is enabled by three unique properties. First, ^{129}Xe is metabolically inert, but readily interacts with liquids, biological membranes, proteins, and lipid bilayers within living systems (2). Upon inhalation, it freely diffuses across the pulmonary-capillary barrier and dissolves in blood, to be transported to distal regions such as the heart, brain, and kidneys (3). Second, ^{129}Xe exhibits a wide range of chemical shifts—larger than any other biologically relevant NMR-sensitive nucleus. Furthermore, these shifts are sensitive to physiological variations, local tissue microenvironments, and xenon chemical exchange between them (2,4). Lastly, because the ^{129}Xe nuclear spin polarization can be enhanced by hyperpolarization (5), its frequency shifts can be detected from modest concentrations in distal tissues.

^{129}Xe chemical shifts have been extensively studied in vitro to examine the interaction of ^{129}Xe with cells and blood (4,6-10). With the advent of hyperpolarization, it has become possible to characterize shifts in mice (11-15), rats (3,8,16,17), and humans (18-21). Across these species, four ^{129}Xe resonances have been reported within the thorax: airspaces (−5 to 10 ppm); aqueous media (195-199 ppm); red blood cells (mouse: 199-200 ppm, rat: 210-213 ppm, human: 216-221 ppm); and adipose tissue (189-194 ppm). Beyond the thoracic cavity, dissolved ^{129}Xe has also been imaged in the lung, kidney, and brain, where similar chemical shifts have been reported (3,21-24).

In vivo, dissolved-phase ^{129}Xe resonances exhibit interesting variations in amplitude, frequency, and linewidth. For example, in mouse models of lung cancer, the ^{129}Xe resonance in adipose tissue diminishes in size, subtly broadens, and also shifts downfield (25). Moreover, ^{129}Xe resonances in patients with idiopathic pulmonary fibrosis also undergo significant changes in amplitude, width, and frequency, which can be exploited to probe blood-oxygenation at the alveolar-capillary level (20). Therefore, as we seek to identify and characterize not only new ^{129}Xe resonances, but also the manner in which they shift with physiological or physical changes, we must develop a more accurate methodology.

Historically, ^{129}Xe chemical shifts have been reported by phasing the ^{129}Xe spectrum, identifying the frequencies at which peaks occur, and calculating shifts relative to the ^{129}Xe gas-phase resonance that arises from pulmonary airspaces. This standard practice has several shortcomings. First, rapid ^{129}Xe exchange between compartments leads to broad, overlapping resonances, making it challenging to accurately isolate contributions from individual components. Second, the accurate measurement of the ^{129}Xe gas-phase resonance, which is used as a reference frequency, is surprisingly challenging. By convention, this frequency should represent ^{129}Xe gas at zero pressure (2). Naturally, such signal is unobservable, and therefore signals are acquired at positive pressure and corrected using the known Xe-Xe interaction shift of $+0.548\pm0.004$ ppm/amagat^{1,2} (26). For in vivo

studies, collisions of ^{129}Xe with nitrogen and oxygen introduce additional shifts of $+0.209\pm0.020$ and $+0.939\pm0.009$ ppm/amagat (27-29). But, perhaps the greatest difficulty for in vivo studies is that the gas-phase ^{129}Xe reference originates mostly from airspaces inside the body, which was recognized by Wagshul (13) to be shifted by as much as -2 to -3 ppm from the true zero frequency by bulk magnetic susceptibility (BMS) effects. Given these confounding effects, previous reports of particular ^{129}Xe dissolved-phase chemical shifts have varied by as much as 2 to 3 ppm.

To minimize the variability in future reports of chemical shifts across different centers and between animals, we seek to introduce a robust methodology to identify ^{129}Xe resonances and their spectral parameters. We employ slice-selective spectroscopy to study the spatial variation of the gas-phase spectrum, and implement time domain-based curve-fitting to decompose the complex gas-phase signal into its alveolar and airway components. Using this tool, we establish a consistent 0 ppm reference and use these methods to identify five consistent peaks in the ^{129}Xe dissolved-phase spectrum arising from the mouse thorax.

Methods

^{129}Xe polarization and MR hardware

Natural abundance xenon gas (26% ^{129}Xe ; Spectra Gases Inc., Alpha, NJ) was polarized to $\sim 20\%$ using a commercial polarizer (Model 9800; Polarean Inc., Durham, NC). It was then dispensed in 150-mL volumes into a Tedlar bag (Jensen Inert Products, Coral Springs, FL), which was connected to a MR and HP gas-compatible constant volume ventilator (30). Studies were conducted on a 2T preclinical magnet (Oxford Instruments, Oxford, UK) controlled by a GE EXCITE 12.0 console, and using a quadrature dual-tuned ^{129}Xe - ^1H birdcage coil (m2m Imaging, Cleveland, OH).

In vitro ^{129}Xe spectroscopy

^{129}Xe spectra were acquired in two different phantoms: 1) a 20-ml tube containing initially pure N_2 gas (0.92 amagats), which was gradually replaced by pure ^{129}Xe (0.92 amagats) flowing at 16 ml/min; and 2) a 200-ml sealed glass tube containing 6.48 ± 0.92 amagats ^{129}Xe (thermally polarized), and 1.84 ± 0.92 amagats O_2 . Spectra were acquired from these phantoms with the following parameters: transmit/receive frequency on the gas-phase resonance, 30° $132\text{-}\mu\text{s}$ hardpulse, $\text{TR/TE} = 750/0.4$ ms, receiver bandwidth = 8.06 kHz, 2048 points, and $\text{NEX} = 101$.

Animal preparation for MRI

Four BALB/c mice underwent in vivo MR studies, conducted under protocols approved by the Duke University Institutional Animal Care and Use Committee. Mice were anesthetized with a 75-mg/kg intraperitoneal dose of Nembutal, and supplemental doses of 20 mg/kg were used to maintain a stable heart rate and airway pressure waveform. Mice were perorally intubated with an 18-G catheter, and then ventilated with a constant-volume ventilator with these parameters: 0.2-ml tidal volume (20% O_2 ; 80% $\text{N}_2/\text{HP } ^{129}\text{Xe}$); 80 breaths/min, with each breath consisting of a 140-ms inspiration, 200-ms breath-hold, and 410-ms exhalation period. The animal was then placed supine on a cradle that fit into the ^{129}Xe - ^1H coil. During

acquisition, warm air was circulated through the magnet bore to maintain normal body temperature, and the animal's rectal temperature, ECG, and airway pressure were monitored.

In vivo ^{129}Xe gas-phase spectroscopy

Prior to ^{129}Xe spectroscopy, a ^1H localizer scan was employed to accurately center the lungs of the mouse in the bore. Using this positioning reference, HP ^{129}Xe gas-phase spectra were acquired from a 2-cm slice encompassing the entire thoracic cavity, as well as from 1-cm slices positioned sequentially from the base of the lung (−9 mm from center) to the trachea (+9 mm from center) in 1-mm increments. Spectra were acquired using the following parameters: slice-selective 90° flip by 1.2-ms 3-lobe sinc pulse (3.3 kHz BW resulting in $<1^\circ$ flip angle to the dissolved-phase (31)), TR/TE = 750/1.2 ms, 2048 points, receiver BW = 8.06 kHz, and NEX = 21. Each FID was acquired over a single breath and gated to commence at full-inspiration during the 200-ms breath-hold.

An identical study was conducted using HP ^3He as a control. Pure ^3He gas (Spectra Gases Inc., Alpha, NJ) was polarized to ~30% using a prototype polarizer (IGL9600.He, MITI, Durham, NC) and delivered as described for the ^{129}Xe studies. Because ^3He is insoluble in tissues, any shifts detected in ^3He spectra can be attributed entirely to BMS effects.

In vivo ^{129}Xe dissolved-phase spectroscopy

By increasing the transmit/receive frequency to +194 ppm above the gas-phase frequency, dissolved-phase ^{129}Xe spectra were also acquired from the thoracic cavity. The acquisition parameters were identical to those of the gas-phase studies, except that TR was progressively increased from 0.1 s to 8 s. This enabled studying how the spectrum evolved as xenon entered tissues progressively distal from the alveolar-capillary interface.

Processing of spectra

Complex spectra were processed using open-source software available for research use from www.civm.duhs.duke.edu/NmrSpectroscopy. The algorithm decomposes a free-induction decay (FID) into a series of additive Lorentzian components that are described by four parameters: amplitude (a_n), starting phase (ϕ_n), resonant frequency, and linewidth (w_n)

$$s_{\text{fit}}(t) = \sum_{n=0}^{n_{\text{components}}} a_n e^{i\phi_n} e^{2\pi i(f_0 - f_n)t} e^{-\pi w_n t} \quad [1]$$

These parameters were fitted to minimize the least squares error of the complex data using a trust-region-reflective algorithm (32). Additional components were included until the residual error between measured and fitted data became unpatterned. Because curve fitting was performed in the time domain, no linebroadening or zeropadding was needed. All spectral components were displayed in the frequency domain with their starting phases as acquired, as well as shifted to zero phase.

Results

In vitro ^{129}Xe spectroscopy

Figure 1A shows the change in resonant frequency of dynamic ^{129}Xe gas-phase spectra recorded from a tube containing a Xe-N₂ mixture transitioning from pure N₂ to pure ^{129}Xe , as HP ^{129}Xe constantly flowed through the tube. The resonant frequency recorded at 100% ^{129}Xe concentration—after correcting for the Xe-Xe shift of $+0.548\pm0.004$ ppm/amagat—served as the true 0 ppm reference frequency. Using this reference, the chemical shift of highly diluted ^{129}Xe in N₂ gas was measured to be 0.22 ± 0.02 ppm, consistent with the Xe-N₂ shift of 0.209 ± 0.020 ppm/amagat reported by Jameson (28,29). Figure 1B additionally illustrates the effect of the Xe-O₂ shift in the high-pressure thermal phantom. Using the zero reference just described, its resonant frequency was measured at $+5.77\pm0.02$ ppm, which is within the error of the $+5.3\pm1.4$ ppm shift calculated using the known gas densities of 6.48 ± 0.92 amagats of ^{129}Xe , and 1.84 ± 0.92 amagats of O₂. Thus, by subtracting 5.77 ppm from the measured frequency of this phantom, the 0 ppm reference was calculated on a scan-by-scan basis. (Note: this reference value is not affected by the uncertainty in this phantom's internal gas densities because true zero is derived from the flowing atmospheric phantom.) The thermal phantom ^{129}Xe frequency was measured ~2 hours prior to the mouse scans, and this time difference could potentially introduce an error in chemical shifts depending on the stability of the 2T field. However, we determined that field only drifted by -5.79 Hz/day or -0.24 ppm/day, thus introducing an error of up to 0.02 ppm, which while negligible relative to the statistical errors across the cohort (>0.1 ppm), has been incorporated.

In vivo ^{129}Xe gas-phase spectroscopy

Figure 2B illustrates the variation of the lineshape of the in vivo gas-phase ^{129}Xe spectrum at different axial positions within the thoracic cavity. Spectra from the most inferior slices exhibited a dominant single resonance at ~ -2 ppm. As the slice was translated toward the center of the lung, a second distinct resonance grew at ~ 0 ppm. At the superior-most portions of lung, where the trachea dominates, the resonance exhibits a frequency exceeding 0 ppm.

These visually apparent features could be assessed more quantitatively by using curve fitting to decompose the complex spectrum into individual resonances (Figure 2C). From the entire thoracic cavity (2-cm slice), two resonances were found: 0.3 ± 0.5 ppm and -2.2 ± 0.1 ppm. However, spectra from 1-cm slices at different axial locations in the lung (Figure 2D) showed differences in the relative amplitudes and frequencies of the two peaks. At the center of the lung, two approximately equal-sized resonances were seen at -0.6 ± 0.2 ppm and -2.2 ± 0.1 ppm. In superior slices, the downfield resonance dominated in amplitude and increased in frequency, ultimately to $+1.3\pm0.3$ ppm in the trachea. In contrast, near the base of the lung, only the upfield resonance remained. Its frequency was consistently measured at -2.2 ± 0.1 ppm across all mice and all spatial locations. All measurements represent the mean $\pm$ standard error across all mice.

In vivo ^{129}Xe dissolved-phase spectroscopy

Having a robust 0 ppm reference led us to more thoroughly investigate numerous dissolved-phase ^{129}Xe resonances in the thorax and accurately report their chemical shifts. These are illustrated in Figure 3 as a function of increasing ^{129}Xe replenishment times. Individual resonances were extracted by curve fitting as shown in Figure 3B, and their evolution with replenishment time is seen in Figure 3C. At the lowest TR of 100 ms, the ^{129}Xe distribution was confined to the gas-exchange region and exhibited two broad resonances at 197.4 ± 0.9 and 193.0 ± 0.7 ppm. As TR increased, additional peaks developed as ^{129}Xe reached downstream compartments. At the longest TR (8 s), five robust peaks were identified at 198.4 ± 0.4 , 195.5 ± 0.4 , 193.9 ± 0.2 , 191.3 ± 0.2 , and 190.7 ± 0.3 ppm.

Discussion

The positional dependence of the two gas-phase peaks within the thoracic cavity suggests that the -2.2 ppm peak arises from ^{129}Xe in alveolar airspaces, and the variable downfield peak arises from ^{129}Xe in conducting airways. This -2.2 ppm shift for alveolar ^{129}Xe signal is consistent with an empirical estimate of -2.46 ppm that factors in the BMS shift for ^{129}Xe in a sphere, and positive shifts caused by Xe-Xe and Xe-O₂ interactions. The susceptibility shift in an alveolus—modeled as a sphere—is given by $\chi_e/3$ (13,33), where χ_e is external susceptibility of the lung parenchyma (estimated as pure water = -9.06 ppm (34)). This leads to a suggested shift of -3.02 ppm. However, under our experimental conditions, the alveoli contained 80% xenon and 20% O₂ at approximately 0.9 amagats, which contributed an additional downfield shift of $0.39 \pm 0.17 = +0.56$ ppm.

Alveolar ^{129}Xe signal intensity and frequency have been previously reported to also be affected by inflation level (13,35). To investigate this effect, gas-phase ^{129}Xe spectra were acquired from the thoracic cavity (2-cm slice) at full-inspiration and at 3 different times during exhalation. The alveolar resonance was extracted from these spectra and its frequency was correlated with its intensity, which served as a surrogate for inflation. As illustrated in Figure 4, the frequency of this peak decreased linearly from full inspiration to lower inflation levels ($r = -0.99$), and ultimately shifted by -0.09 ppm at end-expiration.

This change in alveolar ^{129}Xe frequency is smaller, but in the same direction as the -0.3 ppm shift between the two stages of the breathing cycle in the ^3He spectral frequency reported by Chen in guinea pigs (35). The larger shift shown by Chen may be a function of species or tidal volume. Such inflation-dependent shifts in the gas-phase alveolar ^{129}Xe peak were also reported by Wagshul in free-breathing mice to be 0 to -0.4 ppm in one mouse, while no inflation effects were noted in another mouse suspected of shallow breathing (13). Despite modest differences in the magnitude of reported shifts, all three studies suggest the alveolar ^{129}Xe resonant frequency becomes more negative at end-expiration. That effect is attributable to the way in which lung inflation alters the volume-weighted average susceptibility of the gas and parenchymal tissue phases (33).

While the relatively stable alveolar ^{129}Xe resonant frequency can be explained by BMS effects arising from a spherical geometry, the airway resonance is somewhat more enigmatic.

The variations in the airway peak frequency are also attributable to BMS effects, but arise from a cylindrical geometry that depends on orientation. Such BMS shifts are expressed by

$$\delta_{\text{cylinder}} = \frac{(\chi_i - \chi_e)}{6} (3\cos^2\theta - 1) + \frac{1}{3}\chi_e \quad [2]$$

where θ is the angle between the cylinder axis and B_0 direction, and χ_i and χ_e represent the susceptibilities inside and outside it (33). We again assume $\chi_i = 0$ ppm, and $\chi_e = -9.06$ ppm and thus, depending on the orientation of an airway relative to B_0 , BMS shifts in cylinders range from 0 (parallel to B_0) to $\chi_e/2$ (orthogonal). Thus, the lineshape of the airway component of the gas-phase ^{129}Xe spectrum is likely derived from weighted contributions of airways at various orientations. In our slice-selective spectra, the base of the lung did not exhibit any detectable airway ^{129}Xe signal, which we attribute to this region containing acini that contribute little signal relative to alveolar ^{129}Xe . As the slice moves from lung base to apex, an increasingly dominant and higher-frequency airway resonance is observed, consistent with more airway contributions and progressive alignment of the larger airways with B_0 . Ultimately, the highest frequency airway peak was observed in the superior-most slice containing the trachea, which was roughly parallel to B_0 . However, its resonant frequency of +1.3 ppm cannot be explained within the framework of cylindrical BMS shifts, which for diamagnetic tissues predicts only shifts <0 ppm.

One additional mechanism that could shift the gas-phase ^{129}Xe frequency would be provided by the bulk magnetic moment of hyperpolarized ^{129}Xe in airways. Such a shift should depend on both ^{129}Xe polarization and the geometry in which it is confined. These effects can be estimated by considering the additional magnetic field provided by the magnetization M in the trachea, which we consider as a cylinder aligned with B_0 . For this geometry, the total field is given by

$$B = H + 4\pi M \quad [3]$$

where H is the applied magnetic field, and M can be expressed as

$$M = [^{129}\text{Xe}] \hbar \gamma_{Xe} P_{^{129}\text{Xe}} \quad [4]$$

where $[^{129}\text{Xe}]$ is the density of ^{129}Xe atoms, and $P_{^{129}\text{Xe}}$ is their polarization. Assuming $[^{129}\text{Xe}] = 0.57$ amagats and $P_{^{129}\text{Xe}} = 20\%$, this creates a magnetization-related field $B = -0.179$ mG, which leads to an absolute frequency shift of -0.21 Hz. Although this is independent of the applied field strength, at 2T, it would correspond to a shift of only -0.009 ppm. Thus, bulk magnetization effects have a minor influence on gas-phase ^{129}Xe relative to the larger BMS-induced shifts. Moreover, if such magnetization effects played a major role,

they would be even more evident in the spectra of ^3He , which has a nearly 3-fold larger magnetic moment and is isotopically pure.

To test this hypothesis, HP ^3He spectra were recorded from identical spatial positions within the mouse thorax (Figure 5B). In the absence of an accurate 0-ppm reference ^3He frequency, these spectra were displayed by aligning the most upfield ^3He resonance with the constant -2.2 ppm alveolar peak in the ^{129}Xe spectrum. ^3He spectra exhibited similar location-specific frequency shifts and intensities, with no discernible differences caused by its larger bulk magnetic moment. Furthermore, given its insolubility, this confirms that for both ^{129}Xe and ^3He , the shifts are caused exclusively by BMS effects, and not by chemical interaction or solvent shielding effects. Although the magnitude of the downfield ^{129}Xe frequency shift in major airways is unexpectedly large, the range of shifts found here agree with previous literature reports of in vivo ^{129}Xe spectra in mice (13), in vivo ^3He spectra in guinea pigs (35), ex vivo ^1H spectra in rat lungs (36), and in vitro ^{23}Na spectra in cylindrical phantoms aligned at different orientations relative to B_0 (34).

Although we have used a thermal phantom scan to calculate the frequency reference for each ^{129}Xe study, our work clearly illustrates that the alveolar ^{129}Xe peak is reproducibly found within mice at -2.2 ppm and is relatively insensitive to inflation. Thus, in the absence of a phantom measurement, this robust alveolar gas peak can serve as a useful in vivo reference frequency. However, to use this signal, the spectrum should be carefully decomposed into separate alveolar and airway components. We note that our work here does benefit from the highly homogeneous magnetic field over the ~2-cm extent of the mouse lung and must be validated for other species.

In addition to evaluating gas-phase frequency shifts, Lorentzian linewidths were also measured in the trachea and lung compartments. For reference, the linewidth over the 10-cm thermal phantom was 6 Hz. However, over 1-cm slices within the lung, the linewidths of both the alveolar and airway peaks were 50 ± 7 Hz. This width implies a lower limit for $T2^*$ of 7 ± 1 ms, which is shorter than that observed in guinea pig lungs (37) and human lungs (38). This may be attributable to a denser airway and tissue architecture in the mouse lung. The estimated $T2^*$ in the trachea slice was somewhat longer at 15 ± 5 ms. These relatively short $T2^*$ values in the mouse point to the advantages of imaging with radial sampling (39).

The refined precision of the 0 ppm reference, combined with curve fitting of complex FIDs, has enabled us to more accurately identify and characterize the dissolved-phase ^{129}Xe resonances in the mouse thorax. Based on their signal dynamics, and the limited available literature, we can postulate the origins of these peaks. We suggest that the 198.4 ppm peak originates from blood (13,40), and the 195.5 and 193.9 ppm peaks from aqueous media (pulmonary-capillary barrier tissue, plasma, and possibly the myocardium). The remaining upfield peaks at <192 ppm, which only appear at long ^{129}Xe replenishment times, arise from the slowly perfused and distal epicardial fat (3). With the exception of the two fat peaks, which could not be distinctly separated across the cohort, all the other peaks exhibited distinct frequencies ($P < 0.01$ for all pairwise comparisons using the Tukey-Kramer test).

Conclusion

We have characterized the variability of the gas-phase ^{129}Xe frequency in mice using slice-selective spectroscopy and decomposition of the complex FID, to establish a robust method for setting an accurate 0 ppm reference using in vivo data. This framework also enabled five dissolved-phase resonances to be identified and their spectral parameters accurately measured. Our decomposition technique and accurate referencing methodology should facilitate standardized comparison across sites and aid in advancing the use of ^{129}Xe spectroscopy to detect pathology.

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Figure 1.

(A) Evolution of the ^{129}Xe resonant frequency in a phantom containing a Xe- N_2 mixture transitioning from highly diluted ^{129}Xe in N_2 gas to pure ^{129}Xe . The 0 ppm reference frequency at zero pressure was estimated from the ^{129}Xe resonant frequency at 100% xenon concentration by compensating for the Xe-Xe shift of $+0.548 \pm 0.004$ ppm/amagat (arrow). This yielded a starting shift for highly diluted ^{129}Xe in N_2 of $+0.22 \pm 0.02$ ppm (dotted line). (B) Phased Lorentzian fits of ^{129}Xe spectra from both phantoms show that the high-density thermal phantom is shifted downfield from the low-density one.

Figure 2.

(A) Slice selection: 2-cm slice encompassing the entire mouse thoracic cavity, and 1-cm axial slices ranging from the base of the lung to the trachea. (B) Magnitude spectra from 1-cm slices in 2-mm increments show the evolution of spectral structure. (C) Fitting spectra arising from the entire thorax revealed the presence of two resonances. (D) Comparing fits from different positions revealed that the upfield resonance consistently appeared at -2.2 ± 0.1 ppm, whereas the downfield resonance exhibited a location-dependent frequency ranging from -0.6 ± 0.2 to $+1.3 \pm 0.3$ ppm.

Figure 3.

(A) ^{129}Xe dissolved-phase spectra (real, phased) at different ^{129}Xe replenishment times. (B, C) Fitting revealed 2 broad peaks at the shortest replenishment time, while the spectrum became richer as TR increased and allowed xenon to dissolve into new microenvironments; at the longest TR of 8 s, 5 robust peaks were identified.

Figure 4. Change in frequency of the alveolar ^{129}Xe resonance versus its peak intensity shows a small linear dependence on inflation.

Figure 5. Hyperpolarized ^{129}Xe and ^3He spectra (magnitude) from 1-cm slices at different spatial positions within the thoracic cavity (see Figure 1A for slice positions). ^3He exhibits similar location-specific frequency shifts and intensities as ^{129}Xe , which confirm that these shifts are caused by bulk magnetic susceptibility effects.