Modeling Hyperpolarized ^{129}Xe Bolus Passage for Quantification of Pulmonary Blood Flow

H. E. Möller[1,2], Z. I. Cleveland[2], L. W. Hedlund[2], J. Nouls[2], M. Freeman[2,3], Y. Qi[2], and B. Driehuys[2]

[1]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2]Center for In Vivo Microscopy, Duke University Medical Center, Durham, NC, United States, [3]Graduate Program in Medical Physics, Duke University, Durham, NC, United States

Introduction: In previous work, we have shown that spatially resolved information on pulmonary perfusion can be obtained by imaging with intravenous injection of hyperpolarized (HP) ^{129}Xe dissolved in saline (Fig. 1) [1]. Further work has demonstrated a potential of for absolute quantification [2] by fitting signal curves recorded during bolus injection to a simple model based on the Kety theory of diffusible tracers (Fig. 2) [3]. However, careful analysis showed that such fits required using an effective flip angle α_{eff} that was considerably smaller than the value obtained from a separate flip-angle calibration scan. Similar observations were reported from brain perfusion experiments employing HP ^{129}Xe inhalation [4]. Here, we demonstrate that such effects can be addressed by a refined model that accounts for bolus delay and dispersion effects.

Methods: Three Sprague-Dawley rats (male, 316-342g; Charles River, Wilmington, MA) were prepared according to an IACUC-approved protocol including anesthesia by IP injections of pentobarbital/butorphanol and ventilation on a constant-volume ventilator [5]. HP ^{129}Xe, enriched to 83% (Spectra Gases, Alpha, NJ) was produced in batches of ≈120 mL at P≈10% using a prototype commercial polarizer (model 9800, MITI, Durham, NC). ^{129}Xe MR experiments used a 23.6MHz quadrature birdcage coil in a 2T, horizontal, 30cm clear-bore magnet (Oxford Instruments, Oxford, UK) and GE Excite console (GE Healthcare, Milwaukee, WI). HP ^{129}Xe was dissolved in 30-40mL of half-concentrated saline and shaken for ≈20 s. Subsequently, 5 mL of the fluid was withdrawn into a syringe and injected over a period of 15 s into the rat's tail vein while respiration was suspended. A total of 32 experiments with repetitive spectroscopic acquisitions for 30 s (α 3-33°, *TR* 125-250ms) were performed to study dynamics of the HP ^{129}Xe resonances.

To model signal dynamics we assumed constant injection starting at $t = 0$ and ending at $t = t_B$ and treated HP ^{129}Xe as a diffusible tracer considering an arterial input depending on pulmonary perfusion, Q, and ^{129}Xe exchange between the vascular and alveolar compartments, determined by the Ostwald solubility, L. Contributions to signal loss arise from relaxation and transport described by an apparent relaxation rate, $1/T_{1app} = QL/V_A + 1/T_{1A}$, and from repetitive RF pulsing described by cos α. Delayed arrival of HP ^{129}Xe in the gas-exchange region at time $t = t_0$ was considered by convolution of the ideal bolus profile with a δ-function, whereas dispersion effects were modeled by convolution of the delayed profile with an exponential transport function $h(t) = \tau^{-1} e^{-t/\tau}$ with time constant τ [6]. The final model function (Box 1) is a sum of two terms: The first term is equivalent to the solution for an ideal bolus, whereas the second term accounts for dispersion.

$$S(j) = \begin{cases} 0 & \text{if} \quad (j-1)T_R \le t_0 \\ \Delta S\left[(1-E_1)\dfrac{1-C^{j-t_0-1}}{1-C} - \varphi\,\varepsilon_\tau^{\,j}\,(1-\zeta^{j-t_0-1})\right] & \text{if} \quad t_0 < (j-1)T_R \le t_0 + t_B \\ \Delta S\left\{(1-E_1)\dfrac{1-C^{t_B}}{1-C}C^{j-t_0-t_B-1} - \varphi\,\varepsilon_\tau^{\,j}\left[1-\zeta^{j-t_0-1} - \varepsilon_B(1-\zeta^{j-t_0+t_B-1})\right]\right\} & \text{if} \quad (j-1)T_R > t_0 + t_B \end{cases}$$

$$E_1 = \exp(-T_R/T_{1app})\,,\ \varepsilon_\tau = \exp(-T_R/\tau)\,,$$
$$\varepsilon_0 = \exp(t_0/\tau)\,,\ \varepsilon_B = \exp(t_B/\tau)\,,$$
$$C = E_1\cos\alpha\,,\ \zeta = C/\varepsilon_\tau\,,$$
$$\varphi = \frac{\tau}{T_{1app}-\tau}\varepsilon_0\frac{E_1-\varepsilon_\tau}{\varepsilon_\tau - C}\,.$$

Box 1. Analytical model function of the signal recorded with the jth RF pulse.

Results and Discussion: Experimental signal curves and fits to the model function are shown in Fig. 3. While the accuracy of T_{1app} is improved for small flip angles, the influence from dispersion effects increases for larger flip angles. Combined fits of all curves recorded in a 316g rat yielded τ = 2.6 ± 0.3 sec, which agrees reasonably well transit times in the rat lung [7] and T_{1app} = 14.4 ± 0.3 sec. Assuming an alveolar volume of V_A=6.6 mL obtained from allometric scaling laws [7] and an alveolar relaxation time T_{1A} = 19.6 sec [8] leads to Q = 47 ± 4 ml/min for global lung perfusion, which is of the expected order of the cardiac output (74 mL/min [7]). Hence, accounting for bolus dispersion by an exponential transport function leads to quantification of pulmonary perfusion from HP ^{129}Xe injection studies without the assumption of unreasonably small effective flip angles.

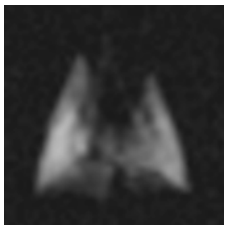

Fig. 1. HP ^{129}Xe perfusion image acquired during 16 sec with a GRE sequence (α 15°, TR 250 msec, bandwidth 4 kHz, matrix 64×64, FOV 7.5 cm) starting 5 sec after injection onset.

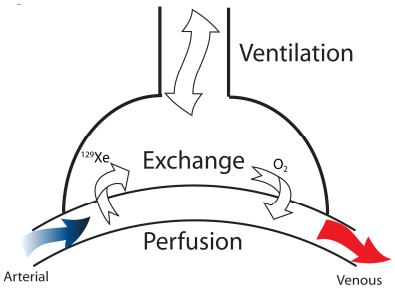

Fig. 2. Following IV injection, the bolus is transported to the lungs, where HP ^{129}Xe is excreted from the capillaries into the alveolar space. Both compartments are easily distinguished by their specific chemical shift.

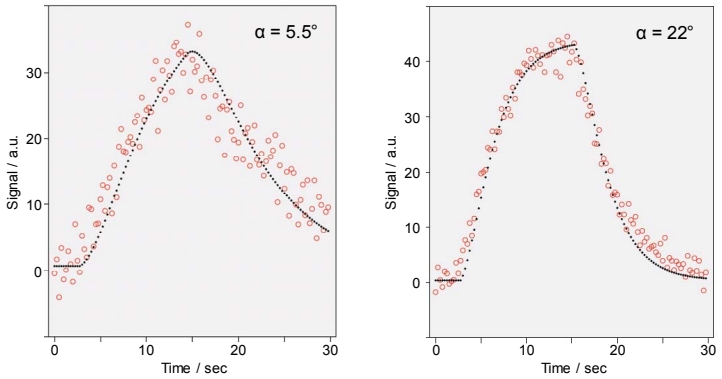

Fig. 2 Gas-phase signal amplitudes recorded with flip angles of 5.5° and 22° and *TR* of 250 ms (red circles) and results from non-linear least-squares fits (black dots).

References: [1] B Driehuys et al. *Radiology* 2009; **252**: 386. [2] H.E. Möller et al. *Proc. ISMRM* 2008; **16**: 1775. [3] S.S. Kety. Pharmacol. Rev. 1951; 3: 1. [4] W. Kilian et al. Magn. Reson. Med. 2004; 51:843. [5] J. Nouls et al. submitted. [6] M. Schmitt et al. Magn. Reson. Med. 2002; 47: 787. [7] R.G. Presson et al. *J. Appl. Physiol.* 1997; **83**: 543. [7] W.R. Stahl, *Adv. Biol. Med. Phys.* 1963; **9**: 355. [8] H. E. Möller et al. *Magn. Reson. Med.* 2002; **47**: 1029.

Acknowledgments: Center for In Vivo Microscopy (NIH/NCRR P41 RR005959).