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Mixture and dissolution of laser polarized noble gases: Spectroscopic and imaging applications

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1. Introduction

Despite their importance for natural sciences and medicine conventional NMR methods suffer from a notorious lack of sensitivity that still limits their power and applicability. This fundamental insensitivity originates from the minuscule size of nuclear magnetic moments, which results in an exceedingly small equilibrium nuclear spin polarization even in high magnetic fields. This situation can be overcome by the creation of hyperpolarized states, that is, by the generation of metastable states with extremely high polarization. The most common examples are laser polarization (LP) of noble gases via optical pumping [1,2], dynamic nuclear polarization (DNP) via unpaired electrons [3,4] and parahydrogen-induced polarization (PHIP) via chemical association of a molecule with parahydrogen [5–7]. In this article we focus on different applications of hyperpolarized gases. Two methods are used to achieve optical pumping of nuclear spins of noble gases: Spin exchange optical pumping (SEOP) [8–10] and metastability exchange (MEOP) [11–13]. Both methods share the same basic principle in which angular momentum is transferred from laser photons to electron spins [14] and finally via magnetic coupling (hyperfine interaction) to nuclear spins [8,15], thereby temporarily enhancing the nuclear spin polarization in these systems by four to five orders of magnitude. State of the art polarizers can produce up to 70% polarization on ^{3}He [16,17] and 50–60% on ^{129}Xe. Taking into account the lower (spin) density and gyromagnetic ratios of gases signal to noise ratio (SNR) enhancements of two to three orders of magnitude are reached for ^{3}He and up to two for ^{129}Xe, compared to an equal volume of water at a typical field of 7 T. Thus, even for radio frequency (rf) pulses with tip angles in the range of 5°, very good SNR can be obtained and with a single batch of gas a large number of acquisitions can be performed for example in an MRI experiment [16,18,19].

The very different characteristics of helium and xenon have led to a very wide range of applications of LP gases, where the major impact of ^{3}He has been on imaging of the lung cavity. Helium is a perfectly inert noble gas that can be inhaled in large quantities without any severe adverse effects, as the solubility in blood is negligible rendering LP–^{3}He the ideal contrast agent for *in vivo* lung imaging [20–22]. Xenon, on the other hand, can be dissolved in liquids (e.g. blood) which might complicate the images but also provides a tool for the simultaneous measurement of the gas and tissue space of the lung. A drawback of MRI with LP gases, however, is the very high diffusion coefficient of gases, which is up to five orders of magnitude higher than in liquids. The rapid Brownian motion strongly attenuates the NMR signal in the presence of static field gradients which severely restricts the achievable spatial resolution [23]. Nevertheless, in the case of lung MRI the presence of restrictions imposed by the alveoli dramatically reduces the mean free path that a gas molecule can travel during an experiment. Depending on their size, such small structures will result in a much lower apparent diffusion coefficient (ADC) and this in turn will generate a contrast in MRI which depends on the cavity sizes. For gases in general, the determination of diffusion coefficients in restricted media has been successfully employed to probe the microscopic structure and functionality in lungs [19,24,25] and time dependent diffusion coefficient measurements were shown to give structural information on porous media [26–28].

The typical strategy to reduce the influence of diffusion, by applying a burst of 180°-pulses [29] in a CPMG-type sequence, is problematic in the non-equilibrium state of hyperpolarization. Firstly, imperfections in the rf-homogeneity might cause additional depolarization. Secondly, the application of such a sequence is debatable, due to the very strict limits of rf-irradiation at high fields in clinical practice. Therefore, rapid data acquisition with gradient echoes is the common approach used to minimize the influence of diffusion on the MRI-signal. Of course, the timing of sequences is constrained by technical and safety limits for the gradient strength and rise time. This typically requires echo times $TE > 0.5$ ms, i.e. a mean diffusive path length of around half a millimeter for ^{3}He. Fortunately, this effect is less dramatic as the mean path length is restricted by the size of the cavities of the lung. The essential parameters which control the influence of diffusion on the MRI-signal are the sequence timing, the gradient strength and the diffusion coefficient. While the gradient strength and timing is predefined by the field of view and spatial resolution, additional delays in the sequence and the diffusion coefficient can be varied to optimize the contrast for specific structural elements [23,30]. As temperature and pressure are not variables in most clinical applications, at first sight, the diffusion coefficient of hyperpolarized ^{3}He does not appear to be a variable that can be changed intentionally. Such control can, however, be achieved by mixing ^{3}He with inert buffer gases of different molecular mass. The first part of this article describes our latest achievements on controlling the diffusion coefficient of LP–^{3}He by admixture with buffer gases as a means of generating different contrast in MRI [31–34]. Additionally we show how the rapid spatial diffusion