Introduction. Recent advances in low temperature DNP methods for producing hyperpolarized \(^{13}\)C for MRI applications [1,2] have generated broad interest due to a potential extension to other NMR-active nuclei. Currently, spin-exchange optical pumping (SEOP) is the dominant method for producing hyperpolarized \(^{129}\)Xe. In this work, we utilize \(^{129}\)Xe DNP as an alternative polarization technique [3,4] for in-vivo lung MRI. The greatest advantage of this approach is its potential for producing significantly larger sample volumes compared to the SEOP process. Unlike traditional dissolution DNP (where all of the active ingredients are soluble and in liquid form), creating a solid sample consisting of a very heavy gaseous atom that is well integrated within the polarizing matrix is not trivial. The addition of a glass-forming medium is necessary to achieve high DNP efficiency. Such additives not only serve to uniformly disperse the polarizing agent within the matrix, but they also prevent \(^{129}\)Xe crystallization. However, spontaneous formation of \(^{129}\)Xe-rich domains due to poor sample mixing has been shown to significantly impede \(^{129}\)Xe DNP enhancements, as the propagation of polarization appears to be stunted at the \(^{129}\)Xe cluster boundary. Here, we introduce a new apparatus for creating homogeneously mixed solid (\(^{129}\)Xe/1-propanol/trityl radical) samples and explore the potential use of \(^{129}\)Xe NMR parameters to probe the heterogeneity of these samples.

Methods and Results. All \(^{129}\)Xe DNP experiments were performed at a magnetic field of 4.997 T using a home-built spectrometer based on an Oxford TMR7/88/15 Teslatron MR superconducting magnet [3]. The integrated DNP/NMR capabilities and the liquid helium cryostat allows for routine DNP-enhanced \(^{129}\)Xe NMR measurements between 1.43 and 1.60 K. An external vacuum pump is used to achieve cryogenic temperatures, while a high power 140 GHz microwave generator (with a 70 mW microwave amplifier) is used as our irradiation source. The acidic form of the Finland (trityl) radical provides unpaired electrons for DNP. A schematic description of our newly developed sample preparation manifold is provided in Figure 1; the primary components are indicated in numeric succession. Firstly, the appropriate amount of radical concentration is weighed and dissolved in a predefined amount of glassing agent (1-propanol). After being transferred to a 5 mm (o.d.) medium wall NMR tube, miniature magnetic stirrers are added. Once mounted on the manifold, the mixture is carefully degassed using an oil-free vacuum pump to remove both air and oxygen from the mixture. After the pressure chamber is filled with 14.7 psi of nitrogen gas, the radical/1-propanol mixture is loaded with about 25 cm\(^3\) of \(^{129}\)Xe gas (as indicated by the syringe) at STP. Isolated from the internal syringe, the primary function of the pressure chamber is to compress the loaded \(^{129}\)Xe gas to the appropriate pressure required for condensation (~64 psi at 201 K). A gas cylinder of nitrogen is used to maintain the necessary overpressure, while an ethanol/solid-CO\(_2\) bath is employed to reduce the sample temperature and reduce the vapor pressure. The sample is stirred for 3-5 min as the appropriate amount of \(^{129}\)Xe is condensed into the radical-doped glassing agent—an adjustable external magnetic stirring plate is used to control the stirring frequency. When the appropriate amount of \(^{129}\)Xe is condensed, the magnets are extracted from the liquid \(^{129}\)Xe/1-propanol/trityl radical mixture and the sample is quickly frozen by immersion in liquid nitrogen. Once DNP samples are prepared, they are immediately placed into the spectrometer.

Figure 2: \(^{129}\)Xe NMR parameters (chemical shift and line width) act as local self-reporting probes of sample homogeneity within the solid-state mixtures. The breadth of the FWHM is the first indication of the sample condition. Better mixing typically results in more narrow line widths. More heterogeneous icy matrices lead to larger \(D_{\text{DNP}}\) (splitting between \(\nu^+\) and \(\nu^-\)) and slightly higher \(^{129}\)Xe NMR frequencies. The \(D_{\text{DNP}}\) of a “well mixed sample” ranges from 90-108 MHz, indicating that the solid-effect is the prominent DNP mechanism. The average polarization is improved by a factor of 2 compared to previous sample preparation techniques under similar experimental conditions (~10% polarization). Warming the sample to above 60 K tends to lead to improvements in the observed \(^{129}\)Xe spectral parameters upon re-cooling. The reduced line width is often accompanied by an upfield shift in the \(^{129}\)Xe NMR frequency.

Conclusions. As previously suggested, engineering a more efficient loading apparatus with an improved cooling scheme leads to improved DNP enhancement in solid-state \(^{129}\)Xe/1-propanol/trityl radical samples. Results suggest that \(^{129}\)Xe NMR parameters provide valuable information on the mixing conditions of the sample; the effective line width being the initial measure of the homogeneity. Trityl-induced \(^{129}\)Xe contact shifts are of particular interest for the ongoing efforts focused on elucidating these phenomena.

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