First results from clinical sitings of a high production prototype xenon polarizer

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INTRODUCTION

Hyperpolarized xenon-129 (HXe) offers potential as a commercially-viable contrast agent for MRI. The counter-flow xenon production method has been scaled up in capacity and assembled into a portable package. This prototype polarizer with high-production capability was successfully relocated to two clinical sites and demonstrated at 1.5T and 3.0T with single and parallel coils on healthy volunteers and patients with various lung diseases.

The counter-flow hyperpolarized xenon production method was originally implemented at the University of New Hampshire as a large-footprint laboratory apparatus [1]. That early system utilized a 1.8 meter long glass polarizing column capable of production rates of one liter/hour at 50% polarization. Subsequent design improvements allowed incorporating that technology into a small automated package [2]. Another order of magnitude increase in the production rates of polarized xenon [3] was achieved by replacing the 2" diameter glass column with a 6"x6" square copper column with 16 separated internal channels provided, which allowed for heat dissipation from the newly-developed kilowatt wavelength narrowed CW laser. A first research prototype was built, which successfully demonstrated up to 15 liters per hour at polarizations exceeding 50%, and over 70% polarization at 2.5 liters per hour production. Being a research prototype, this high-power system was not designed with automation and mobility in mind, and also lacked a xenon separation and delivery system.

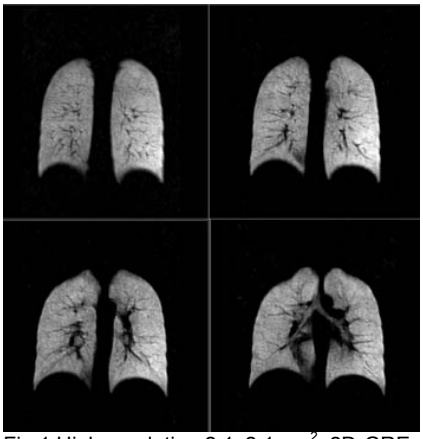

Fig.1 High resolution 2.1x2.1mm^2 2D-GRE HXe MRI (4 slices of 16 – 1cm thickness) of a healthy subject acquired with one liter HXe at the University of Virginia.

METHODS

We report here that this system was incorporated into a portable package and upgraded with xenon separation (freeze-out) and bag delivery subsystems. In nominal operation the system was producing at a rate of six liters/hour of hyperpolarized xenon. Thus for a batch of two liters the system would polarize for only 20 minutes. The HXe volume in one batch was limited by the capacity of the freeze-out, to 2.5 liters. Time constraints did not permit for optimization of the newly added components, causing lower polarization in the thawed xenon in the bag ranging from 20%-40% (later traced to strong magnetic gradients along the HXe output line).

The portable xenon polarizer prototype was relocated for collaborative imaging efforts to Boston, MA (for collaboration with Brigham and Women's Hospital) and to Charlottesville, VA (for collaboration with the University of Virginia). Efficiency improved over time to the point where two human subjects could be imaged daily, each subject undergoing two or more imaging sessions. Inhaled xenon volumes varied from 0.5 to 1.0 liters per breath-hold and were delivered following Xemed's IND and local approved IRB protocols. Human and animal imaging experiments could be performed on a daily basis for periods of two weeks with subject scheduling and data analysis breaks in between sessions. Imaging protocols were mostly exploratory and included high-resolution GRE ventilation images (Fig.1), XTC, CSSR, PAO2, ADC at short and long time, and direct dissolved state imaging. Details appear in other submissions to this conference.

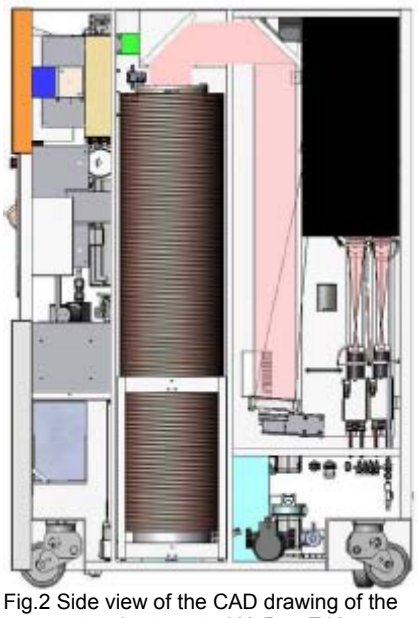

Fig.2 Side view of the CAD drawing of the compact and automated XeBox-E10 polarizer, available for collaborative research studies in 2010.

RESULTS

First high production xenon prototype polarizer was relocated at two different medical centers: MGH-BWH, Boston, and UVa, Charlottesville, for direct applications to human lung imaging. First results of lung imaging using hyperpolarized xenon demonstrated the capability of approaching resolutions previously attained only with helium-3 (Fig.1). Additionally, HXe offers a whole suite of protocols based on its high solubility in tissue and blood. Gained experience in operating the polarizer in a clinical setting helped in finalizing the design of the next polarizer XeBox-E10.

DISCUSSION

During clinical studies polarization performance of the flowing gas exceeded 50% as expected, however polarization in the bag at levels of 20-40% pointed to inadequate control of the large gradient fields created by the 0.3T freeze-out magnet box. Solutions to problems were found and will be implemented into the fully engineered system.

OUTLOOK

Starting from the prototyped technology and based on the experience gained by operating the polarizer in a clinical location, Xemed has designed its first engineered system XeBox-E10. The system is fully automated with minimal user interface consisting of start, stop, Tedlar bags attachment, and emergency shutdown switches. An on-board computer controls the polarizer, monitors operating parameters, and inventories produced xenon batches and their polarization. The polarizer is equipped with a rising dewar xenon freeze-out system, which minimizes polarization losses. Proprietary techniques and novel ideas were implemented to recover most of the xenon which flows through the system (~90%) with minimum polarization loss (~10%). A batch of up to two liters of MagniXene^{TM} can be produced and it can be delivered to as many as four bags. Each bag is individually recognized by the polarizer through a bar code reader. Gas delivery systems to the human subjects provided by Xemed simplify and standardize MagniXene^{TM} administration and dosing. Safety was a primary criterion in designing the hardware and software of the system. Key components which can pose a safety threat, such as the laser beam, are strictly monitored. The system will be assembled under an internal quality control system and will be certified under ISO9001 in the future.

Acknowledgments: NIH funding HL082013, HL087550, ES014005, HL078285, HL091578.

References

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