

XeBox Xenon-129 Polarizer - Long Term Performance

Iulian C. Ruset¹, Jan Distelbrink¹, Jeff Ketel¹, Steve Ketel¹, Joe Jarvis¹, Igor Tsentlovich¹, F.W. Hersman^{1,2}

¹Xemed LLC, Durham, NH, USA

²University of New Hampshire, NH, USA

Design

- Xenon SEOP system based on high-flow low-pressure regime, operating at 140-150Celsius and driven by kilowatt laser system [Ruset04].
- Polarizing chamber upsized into a large copper column with multi-temperature functional zones (fig.1) [Hersman08]
- The hot lower section is immersed in a recirculated oil bath capable to hold temperature uniform by adding or removing heat. Column has a long Rubidium presaturator tube (fig.2,3).
- Large helicoidal shaped cryogenic freeze-out (fig.4) fully-automated allows for accumulation and dispense of xenon volumes up to 4 liters. Xenon is accumulated throughout the run uniformly.



Figure 1: Copper column



Figure 2: Rubidium presaturator in glass.



Figure 3: Rubidium presaturator in metal hose.

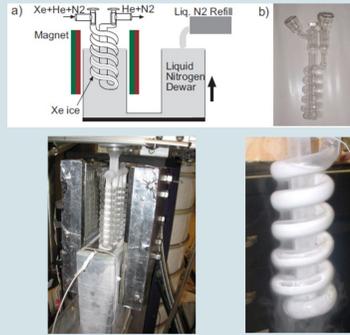


Figure 4: Freeze-out system schematic, glass accumulator, magnet, and frozen xenon at dispense.

Implementation and Results

- XeBox xenon polarizer is a compact system, fully automated, and ready for large scale clinical use (fig. 5, 6).
- Operator just have to chose batch size on the touch screen panel, attach, and detach the bags.
- Can produce up to 4 bags or 4 liters of xenon per batch (fig. 7)
- Xenon production rates of “slow” (3 liters/hour), “medium” (4.5 liters/hour) and “fast” (6 liters/hour) and polarizations reported by customers exceeding 50% (in the bag).



Figure 5: XeBox polarizer with panels removed, showing modular design.



Figure 6: XeBox polarizer with panels on, as being delivered to the clinical research site., showing modular design.



Figure 7: Xenon dispense box (arrow points at location inside polarizer) with examples of Tedlar bags.

- Performance from one of our systems delivered to University of Pennsylvania is presented in Figure 8.
- System has produced about 2,750 liters of xenon over the last five years in cca. 1700 batches, mostly “medium” flow, with dispensed polarizations of typically over 45%.
- Record polarization of 55% reported by Lakehead University from a similar system for “slow” flow rates.

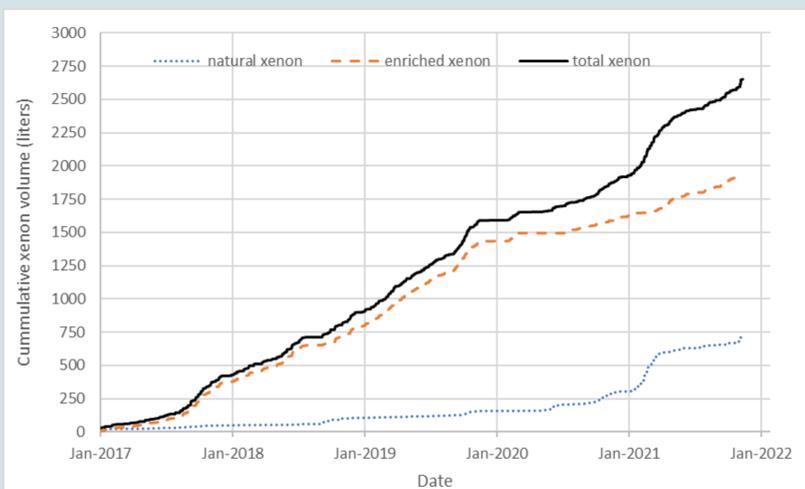


Figure 8: Xenon production at University of Pennsylvania, showing total, enriched, and natural xenon usage over the last five years.

Applications

- Xemed’s XeBox produces MagniXene® (hyperpolarized xenon-129 gas) used as a contrast agent for lung MRI.
- Regulatory support to investigators (collaborators, customers) under FDA IND regulatory oversight since 2005.

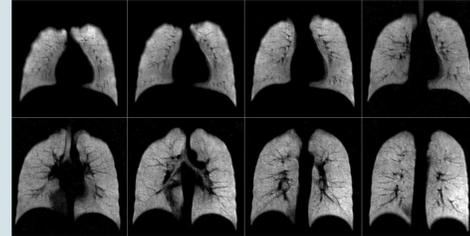


Figure 9: Healthy human subject imaged at University of Virginia with MagniXene: FLASH spin density acquisition, 2.1 x 2.1 x 10 mm3, acceleration factor 2.

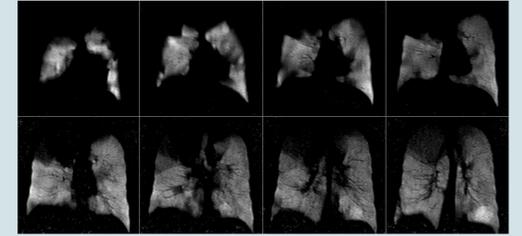


Figure 10: COPD human subject imaged at University of Virginia with MagniXene: FLASH spin density acquisition, 3.1 x 3.1 x 15 mm3, acceleration factor 3.

- Xemed is pursuing regulatory FDA approval in collaboration with academic clinical research sites.
- Two confirmatory clinical trials completed in 2015 at University of Virginia for “delineation of regions of normal and abnormal ventilation” (figure 9 and 10)
- Recently published a phase 2 double-blinded study (subjects, data analysis) enrolled 30 severe asthma patients prescribed for bronchial thermoplasty (BT) treatment at Washington University in St. Louis [Hall20].
- HXe MRI can identify the most involved airways of severe asthmatics and prioritize them for treatment by Bronchial Thermoplasty (BT)
- HXe MRI guided BT shows clinically significant improvement from baseline in a single treatment session as measured by AQLQ (primary endpoint).
- HXe MRI data analysis showed that single guided BT is superior to single unguided BT and similar in ventilation improvement to standard 3 session BT
- Additionally, subjects in the guided group had only one severe exacerbation vs six in the unguided group, and less than half the incidence of asthma related AE/SAEs.

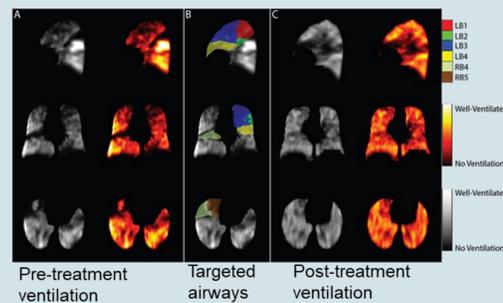


Figure 11: Example of a set of images from one subject participating in the guided BT clinical trial.

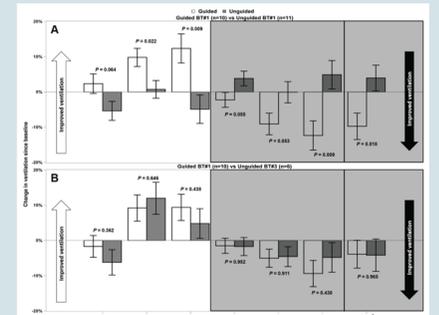


Figure 12: HXe MRI data analysis showed that a single guided BT is superior to a single unguided BT and similar in ventilation improvement to standard 3 session BT

Outlook

- New Atomic Line Filter (ALF) laser spectral narrowing technology recently developed
- Allows implementation of many kilowatt laser power
- ALF laser used for HeliBox helium-3 polarizer reached 85% polarization in a large 2L polarizing cell [Anderson20]. Highly polarized helium-3 can be used for most fragile patients (neonates, infants)
- Technology to be implemented at 2.4 and 3.6kW power in xenon polarizers allowing for exploring new polarizer designs, higher performance, and cost reduction.
- New phase 2 clinical trial using MagniXene to be started at University of Pennsylvania for studying targeted radiation therapy in lung cancer patients.

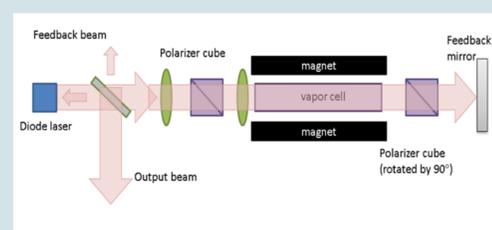


Figure 13: Design of new Atomic Line Filter for spectral narrowing for diode laser arrays using a reference birefringent Rb vapor cell [Hersman18].

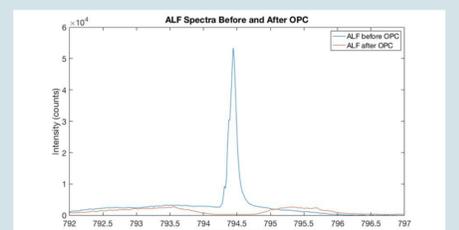


Figure 14: Example of ALF narrowed spectrum. Spectrum after the cell Optical Pumped Cell (OPC) shows all the narrowed peak is absorbed within the cell.

References

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