

XENOVIEW HPX System

Category:

Best Medical Technology

Company Name:

Polarean

Product/Solution Name:

XENOVIEW HPX System

Compound/Tech Name:

Xe Xenon 129 hyperpolarized

Trade Name:

XENOVIEW

Corporate Name:

Polarean

Date of Approval:

2022-12-23

Indications:

XENOVIEW, prepared from the Xenon Xe 129 Gas Blend, is a hyperpolarized contrast agent indicated for use with MRI for evaluation of lung ventilation in adults and pediatric patients aged 12 years and older.

XENOVIEW has not been evaluated for use with lung perfusion imaging.

Therapeutic Areas:

Hyperpolarized MRI contrast agent for pulmonary care

General Information File Document upload:

Background information and need for drug / device:

Xenon Xe 129 hyperpolarized, tradename XENOVUE is the Drug component of a Drug-Device Combination Product. The Device components of this product are collectively called the HPX Hyperpolarization System and include the HPX Gas Handling Manifold, HPX Hyperpolarizer, HPX Polarization Measurement Station, and XENOVUE Dose Delivery Bag. XENOVUE in conjunction with the HPX System is a Drug-Device Combination Product approved by the FDA in December 2022. This MRI-based diagnostic imaging platform fulfills an unmet clinical need for patients with chronic and acute lung diseases by offering a non-invasive, non-radioactive means to provide a detailed, quantifiable image of gas distribution within the lung MRI scan, to provide greater diagnostic insight into both form and function. It provides pulmonologists, surgeons, cardiologists, transplant physicians, interventional pulmonologists, and other respiratory specialists with rapidly acquired regional maps of ventilation in their patients' lungs to assist them in managing their patient's disease. Specifically, this drug/device:

- May yield quantitative lung function information that improves staging and monitoring disease progression in the pulmonary diseases, such as asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), idiopathic pulmonary fibrosis (IPF), or Long-COVID.
- Could aid in the selection of patients with severe asthma that warrant the addition of expensive biologic therapy, and importantly provide an early indicator of response/non-response of therapy.
- In CF may enhance patient compliance with pharmacologic and non-pharmacologic treatment by showing ventilation defects that are not visible with traditional diagnostics such as FEV-1.
- Can identify regions of the lungs with higher or lower ventilation to better guide surgical resection or interventional pulmonology valve or stent placement.
- As a more sensitive measure of early decline in lung function than FEV-1 , it can provide an alert for early lung transplant rejection that may spur treatment that can prevent rejection of the transplanted lung;
- May provide a more sensitive functional measure of early or mild disease not visible with either spirometry or CT. In several obstructive lung diseases (Asthma, CF, COPD, BOS) the ability to more tightly monitor smaller changes in lung function before acute symptomatic decline could result in earlier intervention preventing later high cost options like ED visits or serial rehospitalization.

- In patients with Long-COVID symptoms, yet normal CT images, identifies poorly ventilated regions of the lung or impaired gas exchange. These images can better present the underlying pathology of Long-COVID enabling a longitudinal measure of lung function to assess persistence of the defects as treatments are tested.
- In adolescent patients aged 12-18, it is a more sensitive measure than spirometry because it is non-effort dependent, and therefore more repeatable with less variability, because it is a simple, single breath hold procedure.
- In COPD, studies report XENOVIEW MRI regional lung ventilation images provide diagnostic information that is otherwise not detected by spirometry or CT. 20% of COPD is frequently undiagnosed/misdiagnosed using traditional methods, despite their symptoms, exacerbations, and excess mortality compared to those without COPD. Identifying patients with early-stage COPD to engage in disease management is cost effective; leads to an improved quality of life with fewer exacerbations and ER presentations bringing down overall healthcare costs.

Background File Document upload:

N/A

History of the development of the solution/product:

Hyperpolarization technology, the mechanism which allows XENOVIEW to be visualized on an MRI scan, has been studied since the 1950s. Hyperpolarization enhances the magnetization of xenon by a factor of 5-6 enabling it to be viewed. Spin exchange optical pumping (SEOP), the specific method of hyperpolarization was discovered in 1960 and was studied through the 1980s. The first scan of hyperpolarized xenon-129 was in February 1993. In 1994, the first biological studies using hyperpolarized xenon-129 in mouse lungs occurred. A paper from July 1994 stated \"as xenon is rapidly and safely transferred from the lungs to the blood and thence other tissues,... images of the circulatory system, the brain and other vital organs can be obtained.\" During this time hyperpolarized gas production using SEOP was rapidly being studied to scale up production of the hyperpolarized gas.

In 1995, the first hyperpolarized gas image of the lungs ex vivo, in creature, was captured. A year later in 1996, the first image of hyperpolarized gas in a human lung was captured. Within the same year hyperpolarized gas MRI was translated from a deceased mouse to a human. In 1997, the first human hyperpolarized MRI, using xenon-129, was acquired. Over the next few years as the demand for hyperpolarized gas was on the rise scientists worked to build a polarizer system that could increase

output.

Hyperpolarized xenon-129 phase 1 trials began in 2006. Phase 1/2 trials continued between 2006-2008. In 2012, Polarean was founded and started selling HPX systems for research use. During this same time frame the phase 3 trials were beginning.

The new drug application (NDA) for XENOVIEW (Xenon Xe 129 hyperpolarized) was originally submitted on October 5, 2020. A year later, for this NDA review cycle a Complete Response (CR) was issued. The NDA was resubmitted on March 30, 2022, to address approvability issues identified in the CR letter dated October 5, 2021. A major amendment consisting of product quality information was submitted on September 27, 2022, which extended the review period by three months.

On December 23, 2022 the NDA multi-disciplinary review and evaluation was complete resulting in approval for XENOVIEW, the first hyperpolarized MRI contrast agent.

Post-approval, in February 2023, the FDA grants a New Chemical Entity designation for XENOVIEW (xenon Xe 129 hyperpolarized) providing a five-year market exclusivity period.

On May 11, 2023 the first clinical scan using XENOVIEW was conducted at Cincinnati Children's Hospital Medical Center.

Research of xenon 129 is on going and further trials are planned to expand the indication of XENOVIEW.

Development File Document upload:

N/A

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:

Improving human condition with XENOVIEW:

Current FDA indication is for ventilation imaging which refers to the imaging of the hyperpolarized xenon-129 in the pulmonary airways. This can help observe obstructive diseases such as COPD, asthma, and CF. There is no current solution that provides a direct measure of regional lung ventilation, images the smallest airways (Generation 23-25, aka the silent zone on PFTs), is a radiation-free procedure, and is effort independent. XENOVIEW is a diagnostic test that affects health outcomes through changes in disease management brought about by physician actions taken in response to test results. Such actions may include decisions to treat or withhold treatment, to

choose one treatment modality over another, or to choose a different dose or duration of the same treatment. XENOVIEW informs treatment options for patients with confirmed or suspect respiratory disease allowing monitoring of a novel treatment for difficult to treat diseases such as Long COVID-19, interstitial lung disease, or patients with both asthma and COPD. This new chemical entity, hyperpolarized MRI contrast agent, leads to improved treatment of lung abnormalities in disease, by causing physicians to prescribe a different, more appropriate treatment than they would have prescribed without access to the test results. XENOVIEW brings the added patient benefit being not effort dependent unlike patients who have difficulty with spirometry or PFTs lending their diagnostic reliability suspect.

XENOVIEW directs treatment decisions. It is an unbiased, quantitative measure compared to the patient's own lung, not a calculation taken from a population based standard as in PFTs. XENOVIEW is safe for longitudinal measurement of treatment effect; each subsequent XENOVIEW MRI lung ventilation examination is again compared to the patient's lung prior low ventilation percentage and image at Time (0) to increments of hours, months, or years. Comparing the XENOVIEW scan for lung ventilation to the patient's own lung for each imaging encounter detects the subtle differences that cannot be captured by spirometry for PFTs. Spirometry uses calculations based on age, race, height, national averages. Such calculations are gross estimates of not able to report a quantitative lung ventilation defect. XENOVIEW provides an objective quantified measure specific to the individual patient. This procedure has the potential to remove health disparities and improves equality in healthcare outcomes of chronic diseases where marginalized populations have little options for unbiased lung ventilation evaluation. Objective measures of a patient's individual low ventilation percentage reduces inequities in healthcare; race is not an element to quantify low ventilation percentage guiding informed treatment options that can be longitudinally followed.

The first clinical scan at Cincinnati's Children Hospital was a 19 year old male who had better than 'normal' lung ventilation according to a PFT that measured a FEV1 of 112%. The patient was still experiencing symptoms and they were trying to decide a treatment plan. Upon further investigation they did a XENOVIEW scan and discovered there were still abnormalities in the lung and he should definitely remain on his therapy. XENOVIEW improves patient outcomes by discovering earlier or milder disease and giving the complete picture of a patients regional lung ventilation. FEV1 is a global value that compares a patients value to other patients with the same demographics. XENOVIEW is personalized to the patients own thoracic cavity.

Clinical Trials:

Another benefit is as an endpoint in clinical trials. Less variation in the low ventilation percentage resulting in smaller sample size required for a normal population. There is also no limit on the amount of procedures making longitudinal studies more feasible

whether its 15 minutes or 5 years apart.

Future Research:

The inherent properties of xenon provide the ability to image the gas exchange pathway of inhaled oxygen. After xenon is inhaled and enters the alveolar space it diffuses across the alveolar-capillary membrane where it undergoes a phase shift in its resonant frequency. Xenon then passes into blood vessels where it enters the red blood cells where it undergoes another phase shift. The xenon in each of the three mentioned compartments (air space, barrier, and red blood cell) can be differentiated. Researchers can use this technology to measure ventilation, barrier uptake, and red blood cell transfer allowing them to analyze a wider range of pulmonary diseases. For example, in idiopathic pulmonary fibrosis patients, hyperpolarized xenon-129 can be used to evaluate the fibrotic thickening of the interstitial barrier tissue and alveolar collapse. This technology helps visualize and study the effects of anti-fibrotic drugs. There are also studies ongoing that have found Long-Covid patients who have normal ventilation but still feel out of breath. Using hyperpolarized xenon-129 it has been found that there are abnormalities in their gas exchange which previously could not be explained.

Another benefit of hyperpolarized xenon-129 that is being utilized in research is the ability to help diagnose and evaluate pulmonary hypertension and other cardiopulmonary diseases. Pulmonary hemodynamics can be studied by looking at the cardiac oscillations. It has been found that different disease states have different regional heterogeneity of the cardiac oscillations.

Innovation File Document upload:

N/A

Please provide appropriate references (PubMed, Abstract, Website):

Using hyperpolarized ¹²⁹Xe gas-exchange MRI to model the regional airspace, membrane, and capillary contributions to diffusing capacity
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8354826/>

Hyperpolarized ¹²⁹Xe MRI of the Human Lung
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3558952/>

New developments in imaging Idiopathic Pulmonary Fibrosis with hyperpolarized Xenon MRI
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6392051/>

Pulmonary xenon-129 MRI: new opportunities to unravel enigmas in respiratory

medicine

<https://erj.ersjournals.com/content/55/2/1901987>

A TWO-CENTER ANALYSIS OF HYPERPOLARIZED ^{129}Xe LUNG MRI IN STABLE PEDIATRIC CYSTIC FIBROSIS: POTENTIAL AS A BIOMARKER FOR MULTI-SITE TRIALS

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7054852/>

Imaging lung perfusion

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404706/>

^{129}Xe MRI as a measure of clinical disease severity for pediatric asthma

<https://pubmed.ncbi.nlm.nih.gov/33227317/>

Is hyperpolarised gas magnetic resonance imaging a valid and reliable tool to detect lung health in cystic fibrosis patients? a cosmin systematic review

<https://pubmed.ncbi.nlm.nih.gov/33454201/>

Regional Gas Exchange Measured by ^{129}Xe Magnetic Resonance Imaging Before and After Combination Bronchodilators Treatment in Chronic Obstructive Pulmonary Disease

<https://pubmed.ncbi.nlm.nih.gov/33960534/>

Hyperpolarized ^{129}Xe MRI and Spectroscopy of Gas-Exchange Abnormalities in Nonspecific Interstitial Pneumonia

<https://pubmed.ncbi.nlm.nih.gov/34313473/>

Dregely, I, JP Mugler, 3rd, IC Ruset, TA Altes, JF Mata, GW Miller, J Ketel, S Ketel, J Distelbrink, FW Hersman, and K Ruppert, 2011, Hyperpolarized Xenon- 129 gas-exchange imaging of lung microstructure: first case studies in subjects with obstructive lung disease, *J Magn Reson Imaging*, 33(5):1052-1062.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3081140/>

Ebner, L, M He, RS Virgincar, T Heacock, SS Kaushik, MS Freemann, HP McAdams, M Kraft, and B Driehuys, 2017, Hyperpolarized ^{129}Xe Magnetic Resonance Imaging to Quantify Regional Ventilation Differences in Mild to Moderate Asthma: A Prospective Comparison Between Semiautomated Ventilation Defect Percentage Calculation and Pulmonary Function Tests, *Invest Radiol*, 52(2):120-127.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5488725/>

Kirby, M, S Svenningsen, A Owrangi, A Wheatley, A Farag, A Ouriadov, GE Santyr, R Etemad-Rezai, HO Coxson, DG McCormack, and G Parraga, 2012, Hyperpolarized ^3He and ^{129}Xe MR imaging in healthy volunteers and patients with chronic obstructive pulmonary disease, *Radiology*, 265(2):600-610.

<https://pubmed.ncbi.nlm.nih.gov/22952383/>

Patz, S, I Muradian, MI Hrovat, IC Ruset, G Topulos, SD Covrig, E Frederick, H Hatabu, FW Hersman, and JP Butler, 2008, Human pulmonary imaging and spectroscopy with hyperpolarized ^{129}Xe at 0.2T, *Acad Radiol*, 15(6):713-727.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2475597/>

Rao, MR, NJ Stewart, PD Griffiths, G Norquay, and JM Wild, 2018, Imaging Human Brain Perfusion with Inhaled Hyperpolarized (^{129}Xe) MR Imaging, *Radiology*, 286(2):659-665.
<https://pubmed.ncbi.nlm.nih.gov/28858563/>

Rayment, JH, MJ Couch, N McDonald, N Kanhere, D Manson, G Santyr, and F Ratjen, 2019, Hyperpolarised (^{129}Xe) magnetic resonance imaging to monitor treatment response in children with cystic fibrosis, *Eur Respir J*, 53(5).
<https://erj.ersjournals.com/content/53/5/1802188>

Thomen, RP, LL Walkup, DJ Roach, ZI Cleveland, JP Clancy, and JC Woods, 2017, Hyperpolarized (^{129}Xe) for investigation of mild cystic fibrosis lung disease in pediatric patients, *J Cyst Fibros*, 16(2):275-282.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5274600/>

Wang, JM, SH Robertson, Z Wang, M He, RS Virgincar, GM Schrank, RM Smigla, TG O'Riordan, J Sundry, L Ebner, CR Rackley, P McAdams, and B Driehuys, 2018, Using hyperpolarized (^{129}Xe) MRI to quantify regional gas transfer in idiopathic pulmonary fibrosis, *Thorax*, 73(1):21-28.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5897768/>

References File Document upload:

N/A