European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

Assessing 129Xe Multi-Breath Washout MRI Response to Elexacaftor/Tezacaftor/Ivacaftor Intervention in Pediatric CF

Lay Title:

Assessing novel modulator therapy in children with cystic fibrosis using xenon gas MRI during multiple-breath washout

Authors:

Faiyza Alam[1,2], Samal Munidasa[1,2], Brandon Zanette[2], Sharon Braganza[2], Daniel Li[2], Renee Jensen[3], Marie-Pier Dumas[3,4], Felix Ratjen[2,3] Giles Santyr[1,2].

Affiliations:

1. Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada.
2. Translational Medicine Program, The Hospital for Sick Children, Toronto, ON, Canada.
3. Division of Respiratory Medicine, The Hospital for Sick Children, Toronto, ON, Canada.
4. Clinical Epidemiology & Health Care Research, University of Toronto, Toronto, ON, Canada.

What was your research question?

After inhaling xenon gas, its washout from the lungs after multiple breaths can be imaged with magnetic resonance imaging (MRI) to measure ventilation. Does multiple-breath washout xenon MRI show improvement in regional ventilation one month after elexacaftor/tezacaftor/ivacaftor (ETI) therapy? How does this compare to clinical lung function measures like spirometry?

Why is this important?

Since CF worsens over time, sensitive tools are important to quickly assess how well a treatment is working so that people with CF can find better therapies. Clinical pulmonary function tests like spirometry which provide an at-the-mouth average of lung function (i.e. whole lung) are insensitive to early CF lung disease especially in children. This makes it difficult for pulmonary function tests to assess the effectiveness of new treatments such as ETI, particularly in children. Imaging the washout of xenon gas using MRI produces a picture of lung function, providing regional information which may be more sensitive to treatment effects.

What did you do?

Cystic Fibrosis Research News

12 children with CF (aged 15.3±2 years) were recruited for a baseline visit (within 1 week prior to starting the ETI therapy) and then completed a second visit 1 month following ETI therapy. At each visit, the children completed at-the-mouth pulmonary function tests such as spirometry, as well as xenon MRI, including multiple-breath washout imaging. In this latter technique, the children breathed in a single bag of xenon gas, then were coached to exhale the gas with multiple breaths. After each exhale, the lungs were imaged using MRI and compared with at-the-mouth pulmonary function tests.

What did you find?

Multiple-breath washout xenon MRI was able to show significant improvements in ventilation in these children with CF after 1 month of ETI therapy, which agreed with at-the-mouth pulmonary function tests such as spirometry. Improvement in specific regions of the lungs was detectable due to the visual image provided by the technique, making multiple-breath washout xenon MRI complementary to at-the-mouth pulmonary function tests.

What does this mean and reasons for caution?

These results suggest that this multiple-breath washout xenon MRI technique, which assesses lung function regionally (i.e. by providing an image of ventilation across the lung) can be used in clinical trials to assess lung function over time and are complementary to at-the-mouth pulmonary function tests. While this study offers promising preliminary evidence that xenon MRI adds new regional information in the context of CF treatment response, this study is limited by the small sample size (12 participants) so the clinical utility of this approach is not clear at this time.

What's next?

At-the-mouth methods like spirometry show that people with CF on ETI therapy have sustained improvements at two years. Does the regional information provided by multiple-breath xenon MRI tell the same story, or different? To answer this, these participants will be followed up to three years using multiple-breath washout xenon MRI.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/39353741/

cfresearchnews@gmail.com