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Elexacaftor/tezacaftor/ivacaftor reduces trapped gas in children with cystic fibrosis

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Background: Mucus plugging, one of the features of early cystic fibrosis (CF) pathophysiology, can lead to poorly ventilated areas in the lung that are incompletely emptied during tidal breathing. The volume of gas retained within these lung units is referred to as trapped gas and can be assessed using different modalities such as multiple-breath washout (MBW) and functional imaging. During MBW, the volume of trapped gas (VTG) can be quantified by adding a series of inspiratory capacity breaths at the end of a standard nitrogen (N_2) MBW test to recruit lung regions that release residual N_2 [1]. VTG has been shown to be high in CF, but it is unknown whether VTG captures changes after elexacaftor/tezacaftor/ivacaftor.

Methods: This is a single-center add-on study of participants enrolled in one of two ongoing studies: the multi-center HyperPOlarized Imaging of New Therapies (HyPOINT, NCT04259970) study and a SickKids-based observational study of participants initiated on CF transmembrane conductance regulator (CFTR)-modulator treatment. In this study protocol, the following tests were performed at baseline and 1 month after start of elexacaftor/tezacaftor/ivacaftor. N_2 MBW was performed using the ExhalyzerD MBW device and Spiroware 3.3.1 software (EcoMedics, Duernten, Switzerland). Lung clearance index (LCI) and VTG were reported, with VTG expressed as percentage of forced vital capacity measured using spirometry (VTG/FVC%). Hyperpolarized ^{129}xenon magnetic resonance imaging (Xe-MRI) and free-breathing MRI were also performed at each visit for participants enrolled in the HyPOINT study. Using the Phase Resolved FUnctional Lung (PREFUL) method, fractional ventilation (FV) maps were determined from free-breathing images [2]. Ventilation defect percentage (VDP) was calculated from Xe-MRI ventilation images (VDP_{Xe}) based on a threshold of 60% of the mean ventilation signal and FV maps (VDP_{FV}) using k-means clustering [2]. Statistical analysis included Wilcoxon rank sign test for before and after comparisons and Spearman test for correlations.

Results: Ten participants (median age 16.2, range 13.5–18.6), have completed MBW at both visits; recruitment is ongoing. At baseline, median LCI was 9.66 (range 6.22–16.08) and percentage predicted forced expiratory volume in 1 second (FEV_1pp) was 73% (43–95%). Across the two visits, median LCI decreased from 9.66 (interquartile range (IQR) 7.43–11.39) to 7.73 (IQR 6.51–8.91) ($p = 0.04$), and FEV_1pp increased from 72% (IQR 66–80%) to 88% (IQR 78–99%). VTG/FVC% decreased from 3.47% (IQR 2.40–6.23%) to 1.36% (IQR 0.89–3.61%) ($p < 0.01$). Relative difference in VTG/FVC% correlated with relative change in VDP_{Xe} ($r = 0.71$, $p = 0.05$, Figure 1A) and with VDP_{FV} ($r = 0.86$, $p < 0.01$, Figure 1B).

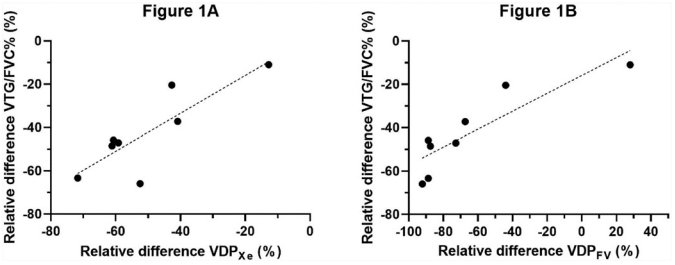

Figure 1. Correlation between relative difference in volume of trapped gas expressed as percentage of forced vital capacity measured using spirometry (VTG/FVC%) and A) relative difference in ventilation defect percentage (VDP) calculated from ^{129}xenon magnetic resonance imaging ventilation images and B) relative difference in VDP fractional ventilation maps

Conclusions: Trapped gas, measured according to VTG/FVC% during MBW, decreases after initiation of highly effective CFTR modulator therapy and correlates well with changes measured using functional MRI.

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References

[1] Gustafsson PM, Johansson HJ, Dahlbäck GO. Pneumotachographic nitrogen washout method for measurement of the volume of trapped gas in the lungs. *Pediatr Pulmonol* 1994;17(4):258–68.

[2] Couch MJ, Munidasa S, Rayment JH, Voskrebenzev A, Seethamraju RT, Vogel-Claussen J, *et al.* Comparison of functional free-breathing pulmonary 1H and hyperpolarized 129Xe magnetic resonance imaging in pediatric cystic fibrosis. *Acad Radiol* 2021;28(8):e209–218.

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Acceptability and usability of a soft, flexible, wearable device for cough detection in children with cystic fibrosis

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Background: Cough is a common symptom in cystic fibrosis (CF), and an increase in cough is an important sign of worsening lung disease and pulmonary exacerbation, the most common cause of hospitalization in people with CF. Objective monitoring of cough could be an important outcome measure for clinical trials, especially in children too young to perform pulmonary function tests. There are no accurate, objective methods of quantifying the frequency, severity, and duration of cough. Devices that have been tested to measure cough are neither highly reliable nor user friendly. We developed a mechano-acoustic sensor (MAS): a 4.8-cm- × 2.8-cm- (1 inch) long, thin, lightweight, stretchable, wireless device that adheres easily and securely to the skin surface and is worn at the base of the neck. The device was validated in adults being monitored for COVID-19. This study evaluated usability and acceptability to children and their parents.

Methods: In Cohort 1, a small, flexible, fully wireless accelerometer-based MAS was applied to the suprasternal notch of children with CF using gentle adhesives. Participants were asked to perform activities that included forced coughs while sitting, lying down, and performing activities such as jumping or jogging and other pharyngolaryngeal activities such as swallowing, speaking, and throat clearing. The sessions were an average of about 30 minutes long. In Cohort 2, participants were asked to test the device for a longer period of wearable time (4–6 hours) in various settings, including outpatient clinics, inpatient rooms, and outside clinic and at-home environments. Upon completion, all participants from both cohorts