

were measured. LCI was measured using an Exhalizer D MBW device (EcoMedics, Duernten, Switzerland; Spiroware 3.3.1). MBW Xe-MRI was performed as previously described [3], with the ^{129}Xe dose (10% of total lung capacity) was topped with nitrogen to a volume of 1/6th total lung clearance. CoV_{FV} was calculated by comparing the average value of FV in one voxel to that of its nearest neighbors through image kernel convolution and taking the standard deviation over the mean. The Wilcoxon signed-rank test was used to determine significant changes between visits. Correlations between absolute differences in mean FV and CoV_{FV} and LCI were tested with a Spearman correlation.

Results: Xe-MRI (breath = 1), FV, and CoV_{FV} maps for three representative subjects are shown in Figure 1A. The following values are averages from the maps. Median (IQR) CoV_{FV} was significantly ($p = 0.03$) lower at 1 month (median 0.07, interquartile range [IQR] 0.06–0.08) than at baseline (median 0.10, IQR 0.08–0.14). Absolute changes in CoV_{FV} between visits were found to significantly ($p = 0.003$) and highly ($r = 0.96$) correlate with absolute changes in LCI (Figure 1B). Median FV did not change significantly ($p = .16$) between baseline (0.36, IQR 0.33–0.40) and 1 month (0.41, IQR 0.40–0.44) or correlate significantly with LCI ($r = -0.61$, $p = 0.17$).

Conclusions: CoV_{FV} detected improvements in ventilation homogeneity 1 month after ELX/TEZ/IVA treatment. Absolute changes in CoV_{FV} correlated with LCI. The ongoing study will help clarify the relationship between this novel measure and other imaging outcomes in capturing treatment response.

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178

Toward targeted exhaled breath analysis for young children in cystic fibrosis care to detect bacteria in the lungs

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Background: Children with cystic fibrosis (CF) are prone to bacterial infections, which can be associated with lung function decline. Consequently, detection of bacteria plays an important role in CF care, but culture-dependent diagnosis of such infections is a challenge in children because of limited sample availability and quality. Exhaled breath analysis measuring volatile organic compounds (VOCs) might be a promising noninvasive, culture-independent tool to identify bacteria. Several explorative studies have suggested that VOCs can differentiate

between bacterial species, although these results are not always consistent. The next step for exhaled biomarkers would be to move from discovery studies to hypothesis-driven targeted analysis, an essential step for clinical application. *Staphylococcus aureus* is a common bacteria found in children with CF. We aimed to test the feasibility of targeted exhaled breath analysis in children with CF in a proof-of-concept study for the detection of *S. aureus* using previously identified VOCs and whether this could discriminate between *S. aureus*-positive and -negative cultures.

Methods: Children with CF aged 1 to 6 were included. Exhaled breath samples were stored in thermal desorption tubes and analyzed using gas chromatography–mass spectrometry (GC-MS). Microbiological cultures were collected on the same day. After a literature review to identify *S. aureus*-related VOCs, targeted peak detection using AMDIS (v.2.68) was performed on the GC-MS dataset, and the resulting peak intensities were used for multivariate modeling using sparse partial least squares discriminant analysis (sPLS-DA), after which the predicted outcomes (*S. aureus* positive or negative) were compared with the actual microbiological outcomes. Statistical analyses were performed in R-Studio (v.1.3).

Results: Exhaled breath collection was attempted in 24 children with CF, and was successful in 83% ($n = 20$, median age 4, interquartile range 2–6). Of nine patients who had a positive culture for *S. aureus*, six were taken by a nasopharyngeal swab, two from sputum, and one from bronchoalveolar lavage fluid. Two patients had a positive culture for *Haemophilus influenzae* and one for *Moraxella catarrhalis*. Eight patients had a negative culture. We identified five VOCs associated with *S. aureus* from the literature review (≥ 2 consistent notations), which were used to predict culture positivity for *S. aureus*, resulting in accuracy of 70%, specificity of 89%, and sensitivity of 55%. The positive predictive value of the test was 86%, and the negative predictive value was 62%.

Conclusions: Targeted analysis of MS-driven exhaled VOC profiles appears to enable detection of pathogens in exhaled breath. We showed that noninvasive breath collection for targeted exhaled breath analysis is feasible in young children and that VOCs associated with *S. aureus* were detectable. One of the limitations of this study is the small sample size and that most microbiology cultures were taken using a nasopharyngeal swab, which may explain the low sensitivity of the model. More research should be done to evaluate this promising methodology in larger cohorts, preferably using more-sensitive microbiological sampling methods.

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179

Inflammation-based scoring systems and ratios to identify people with cystic fibrosis at risk for intravenous antibiotic therapy

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Background: Pulmonary disease in cystic fibrosis (CF) is characterized by chronic bacterial infection with recurrent pulmonary exacerbations (PEX), which are associated with high systemic inflammatory marker levels. Because PEX are associated with higher morbidity and mortality, prevention is an important therapeutic goal in the treatment of people with CF (PwCF). Identifying patients at risk for future PEX can be challenging in clinical practice. The objective of this study was to compare established and novel markers of chronic inflammation and their ability to predict the need for intravenous antibiotic therapy (nIVT) as a surrogate marker for PEX or decline in pulmonary status in PwCF.

Methods: Individuals aged 18 and older treated between 2014 and 2018 in the adult CF center of the university hospital Munich, Germany, who had at least two pulmonary function tests per year for a 3-year period were included in this retrospective, longitudinal study. Baseline was defined as the first year after the first measurement. The follow-up period was time between baseline and end of follow-up. Neutrophil/lymphocyte ratio, lymphocyte/monocyte ratio, C-reactive protein (CRP)/albumin ratio, Glasgow prognostic score, and CF-Able score of patients with and without nIVT during follow-up were compared. In the univariate analysis, we used chi-square and Fisher exact tests to compare categorical scores and t-tests to compare numerical scores. In the multivariate analysis, we used