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Title: Short and long term repeatability of N2 multiple breath washout indices in children with cystic fibrosis

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**Body:** Rationale: Multiple breath washout (MBW) is increasingly used as a highly sensitive endpoint in cystic fibrosis (CF) studies. However, repeatability of output variables such as Lung Clearance Index (LCI) and the clinical indices  $S_{cond}$  and  $S_{acin}$  in children with CF (Respiration 2009; 78: 339) are sparsely reported despite being essential prerequisites to implementation in studies of lung disease. We assessed within and between occasion repeatability in CF children during one year. Methods:  $N_2$  MBW (Exhalyzer D, EcoMedics AG) in triplets was prospectively performed every month during one year in eight children excluding occasions with clinical pulmonary exacerbations and less than two acceptable trials. Within occasion (Wo) and between occasion (Bo) repeatability of LCI,  $S_{cond}$  and  $S_{acin}$  were expressed as SD and CV%. Results: Ninety-eight test occasions were performed and 90% fulfilled inclusion criteria. Mean (SD) LCI,  $S_{cond}$  and  $S_{acin}$  of all tests: 9.01 (1.73), 0.071 (0.031) and 0.090 (0.025), respectively. Estimates (SD) of Bo repeatability of LCI,  $S_{cond}$  and  $S_{acin}$  suggest that changes > 1.55, 0.027 and 0.064 units (mean + 1.96 SD), respectively, could be regarded significant. Conclusion: We reported estimates of short- and long-term repeatability of N2 MBW indices in children with CF. These estimates are essential prerequisites to future studies of CF lung disease using N2 MBW variables as primary outcome parameters.

Age, yrs	11.9 (2.9)
FEV1 at 1. visit, % pred.	94.9 (13.8)
LCI at 1. visit	9.4 (1.8)
LCI Wo SD / CV%	0.34 (0.20) / 3.6 (1.3)
LCI Bo SD / CV%	0.77 (0.40) / 8.1 (2.4)
Scond Bo SD / CV%	0.015 (0.006) / 22.1 (5.5)
Sacin Bo SD / CV%	0.033 (0.016) / 36.0 (10.5)