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Title: Increased within-test variability may bias estimates of the LCI

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Body: Background: The Multiple Breath Washout (MBW) test has been shown to be an important research tool and has the potential for wider use in clinical practice. Feasibility for pediatric clinical settings may be improved if the testing time can be shortened. We investigated whether it is possible to minimize the number of trials performed, without affecting the precision of the test. Method: 42 healthy and 37 children with CF performed nitrogen MBW (Exhalyzer D, Eco Medics AG, Switzerland). The mean LCI and coefficient of variation (CV) were calculated from all technically acceptable trials (i.e. no obvious leaks, end of test criteria met, etc., with some adaptations for children). In addition, the first acceptable trial, and the best trial (defined as the first acceptable trial with a breathing pattern most reflective of quiet tidal breathing) were selected. The mean LCI was compared to the LCI of the first, as well as the best trial. Results: As the CV increased, the magnitude of the difference between the mean LCI and first LCI also increased. Compared to the best LCI, the mean LCI was higher in 70% of subjects. The difference between the best LCI and mean LCI also increased as the CV increased. Using the best LCI as a benchmark, 70% of subjects had a reproducible LCI within 5% and 97% within 10%. Conclusions: These findings suggest that the average LCI from several MBW trials can over-estimate LCI, especially if the variability between trials is high. Reporting the LCI from the best trial, which reflects an ideal quiet tidal breathing pattern, may minimize testing time and improve the accuracy of the test without affecting precision. In addition the CV may be a useful quality control measure.