Contents

Useful Links

COSMED Homepage

http://www.cosmed.com

Innocor® LCI

Multiple Breath Washout

Multiple breath washout testing in adults with pulmonary disease and healthy controls - can fewer measurements eventually be more?

Trinkmann F, Götzmann J, Saur D, Schroeter M, Roth K, Stach K, Borggrefe M, Saur J, Akin I, Michels J. BMC Pulm Med. 2017 Dec 11;17(1):185.

BACKGROUND: Multiple breath washout (MBW) became a valuable research tool assessing ventilation heterogeneity. However, routine clinical application still faces several challenges. Deriving MBW parameters from three technically acceptable measurements according to current recommendations prolongs test times. We therefore aimed to evaluate reporting only duplicate measurements in healthy adults and pulmonary disease.

METHODS: One hundred and fifty-three subjects prospectively underwent conventional lung function testing and closed-circuit SF_6-MBW. Three technically acceptable MBW-measurements were obtained in 103 subjects.

RESULTS: Lung clearance index (LCI) differed significantly among 19 controls (7.4 ± 0.8), 19 patients with sarcoidosis (8.1 ± 1.2), 32 with bronchial asthma (9.2 ± 1.9) and 33 with COPD (10.8 ± 2.2, $p < 0.001$). Within-test repeatability was high (coefficient of variation between 2.5% in controls and 3.6% in COPD) and remained unchanged when only including the first two measurements. Likewise, LCI remained stable with mean absolute changes ranging from 0.9 ± 0.8% in controls to 1.5 ± 0.9% in COPD ($p = 0.1$). Mean test time reduction differed significantly between groups reaching 200 s in COPD ($p = 0.01$).

CONCLUSIONS: Duplicate SF_6-MBW-measurements are sufficient in adult patients with pulmonary disease and healthy controls. LCI values and intra-test repeatability are not affected reducing total test time statistically significant. Our findings have the potential to further facilitate application of MBW in research and clinical routine.

New time-saving predictor algorithm for multiple breath washout in adolescents.

Grønbæk J, Hallas HW, Arianto L, Pedersen K, Thomsen A, Chawes BL, Bisgaard H. Pediatr Res. 2016 Jul;80(1):49-53.

BACKGROUND:Multiple breath washout (MBW) is an informative but time-consuming test. This study evaluates the uncertainty of a time-saving predictor algorithm in adolescents.

METHODS: Adolescents were recruited from the Copenhagen Prospective Study on Asthma in Childhood (COPSAC2000) birth cohort. MBW trials were performed at 13 y of age with Innocor model Inn00400 using sulfur hexafluoride (SF6) as tracer gas. Measurements were analyzed using a mixed model focusing on two prediction points doubling (t5%) and quadrupling (t10%) the standard end point (t2.5%).

RESULTS: One hundred and seventy-two MBW trials conducted in 78 adolescents with and without asthma from COPSAC2000 were included. At t10%, the washout time (WoT) was reduced by 41%, and an uncertainty of 0.159 lung clearance index (LCI) units was introduced (±2 SD), ±1.27). At t5%, the WoT was reduced by 25%, with an uncertainty of 0.083 LCI units (±0.558). The optimal prediction point, which led to most saved time and least uncertainty was t5%.

CONCLUSION: The predictor algorithm is capable of shortening the MBW test time but introduces an increasing uncertainty with earlier prediction points. This first-of-a-kind prediction algorithm holds promise in shortening the MBW test in children but should be used with caution in subjects with normal LCI values.

COSMED
The Metabolic Company

SF_6

Feasibility and clinical applications of multiple breath wash-out (MBW) testing using sulphur hexafluoride in adults with bronchial asthma

Trinkmann F, Lenz SA, Schäfer J, Gawlitza J, Schroeter M, Gradinger T, Akin I, Borggrefe M, Ganslandt T, Saur J. Sci Rep. 2020 Jan 30;10(1):1527.

ABSTRACT: Ventilation heterogeneity is frequent in bronchial asthma and can be assessed using multiple breath wash-out testing (MBW). Most data is available in paediatric patients and using nitrogen as a tracer gas. We aimed to evaluate sulphur hexafluoride (SF_6) MBW in adult asthmatics. Spirometry, whole-body plethysmography, impulse oscillometry and SF_6-MBW were prospectively performed. MBW parameters reflecting global (lung clearance index, LCI), acinar (S_{acin}) and conductive (S_{cond}) ventilation heterogeneity were derived from three consecutive wash-outs. LCI was calculated for the traditional 2.5% and an earlier 5% stopping point that has the potential to reduce wash-out times. 91 asthmatics (66%) and 47 non-asthmatic controls (34%) were included in final analysis. $LCI_{2.5}$ and LCI_5 were higher in asthmatics ($p < 0.001$). Likewise, Sacin and Scond were elevated ($p < 0.001$ and $p < 0.01$). Coefficient of variation was 3.4% for LCI2.5 and 3.5% for LCI5 in asthmatics. Forty-one asthmatic patients had normal spirometry. ROC analysis revealed an AUC of 0.906 for the differentiation from non-asthmatic controls exceeding diagnostic performance of individual and conventional parameters ($AUC = 0.819$, $p < 0.05$). SF_6-MBW is feasible and reproducible in adult asthmatics. Ventilation heterogeneity is increased as compared to non-asthmatic controls persisting in asthmatic patients with normal spirometry. Diagnostic performance is not affected using an earlier LCI stopping point while reducing wash-out duration considerably.

Simultaneous sulfur hexafluoride and nitrogen multiple-breath washout (MBW) to examine inherent differences in MBW outcomes.

Bayfield KJ, Horsley A, Alton E, Irving S, Bush A, Davies JC. ERJ Open Res. 2019 Nov 4;5(4).

Multiple-breath washout (MBW) can be performed with different gases (sulfur hexafluoride (SF6-) and nitrogen (N2)) and different devices, all of which give discrepant results. This study aimed to confirm previously reported differences and explore factors influencing discrepant results; equipment factors or the physical properties of gases used.

METHODS: Healthy controls (HCs) and participants with cystic fibrosis (CF) completed MBW trials on two commercially available devices (Exhalyzer D (N2) and Innocor (SF6)). Simultaneous washout of both gases at the same time on the commercial equipment and simultaneous washouts using a respiratory mass spectrometer (RMS) were completed in subsets. Primary outcomes were lung clearance index (LCI), breath number and time required to washout.

RESULTS: Breath number was higher with N2 washout than SF6 in both HCs and patients with CF, whether washouts were completed individually or simultaneously. The difference was greater in more advanced disease, largely caused by differences in the final part of the washout. Results from commercial devices were similar to those obtained with the RMS.

CONCLUSIONS: N2 MBW results were higher than SF6 MBW, with some of the largest differences reported to date being observed. The biggest impact was at the end of the washout and this was even the case when gases were washed out simultaneously. N2 and SF6 MBW results are inherently different and should be considered as independent measurements.

Closed Circuit

Lung clearance index in healthy volunteers, measured using a novel portable system with a closed circuit wash-in

Horsley AR, Alrumuh A, Bianco B, Bayfield K, Tomlinson J, Jones A, Maitra A, Cunningham S, Smith J, Fullwood C, Pandyan A, Gilchrist FJ. PLoS ONE. 2020 Feb 25; 15(2). e0229300.

INTRODUCTION: Lung clearance index (LCI) is a sensitive measure of early lung disease, but adoption into clinical practice has been slow. Challenges include the time taken to perform each test. We recently described a closed-circuit inert gas wash-in method that reduces overall testing time by decreasing the time to equilibration. The aim of this study was to define a normative range of LCI in healthy adults and children derived using this method. We were also interested in the feasibility of using this system to measure LCI in a community setting.

METHODS: LCI was assessed in healthy volunteers at three hospital sites and in two local primary schools. Volunteers completed three washout repeats at a single visit using the closed circuit wash-in method (0.2% SF_6 wash-in tracer gas to equilibrium, room air washout).

RESULTS: 160 adult and paediatric subjects successfully completed LCI assessment (95%) (100 in hospital, 60 in primary schools). Median coefficient of variation was 3.4% for LCI repeats and 4.3% for FRC. Mean (SD) LCI for the analysis cohort (n = 53, age 5–39 years) was 6.10 (0.42), making the upper limit of normal LCI 6.8. There was no relationship between LCI and multiple demographic variables. Median (interquartile range) total test time was 18.7 (16.0–22.5) minutes.

CONCLUSION: The closed circuit method of LCI measurement can be successfully and reproducibly measured in healthy volunteers, including in out-of-hospital settings. Normal range appears stable up to 39 years. With few subjects older than 40 years, further work is required to define the normal limits above this age.

Closed circuit rebreathing to achieve inert gas wash-in for multiple breath wash-out.

Horsley AR, O'Neill K, Downey DG, Elborn JS, Bell NJ, Smith J, Owers-Bradley J. ERJ Open Res. 2016 Jan 22;2(1). pii: 00042-2015.

ABSTRACT: Multiple breath wash-out (MBW) testing requires prior wash-in of inert tracer gas. Wash-in efficiency can be enhanced by a rebreathing tracer in a closed circuit. Previous attempts to deploy this did not account for the impact of CO2 accumulation on patients and were unsuccessful. We hypothesised that an effective rebreathe wash-in could be delivered and it would not alter wash-out parameters. Computer modelling was used to assess the impact of the rebreathe method on wash-in efficiency. Clinical testing of open and closed circuit wash-in-wash-out was performed in healthy controls and adult patients with cystic fibrosis (CF) using a circuit with an effective CO2 scrubber and a refined wash-in protocol. Wash-in efficiency was enhanced by rebreathing. There was no difference in mean lung clearance index between the two wash-in methods for controls (6.5 versus 6.4; p=0.2, n=12) or patients with CF (10.9 versus 10.8; p=0.2, n=19). Test time was reduced by rebreathe wash-in (156 versus 230 s for CF patients, p<0.001) and both methods were well tolerated. End wash-in CO2 was maintained below 2% in most cases. Rebreathe-wash-in is a promising development that, when correctly deployed, reduces wash-in time and facilitates portable MBW testing. For mild CF, wash-out outcomes are equivalent to an open circuit.