Closed circuit rebreathing to achieve inert gas washin for multiple breath washout

ONLINE SUPPLEMENT OF ADDITIONAL METHODS AND RESULTS

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1. Details of the lung model

The 2-compartment computer lung model was prepared in Matlab (Mathworks Inc, MA, USA). The model, illustrated in Figure S1, consists of three frictionless pistons, one representing the bag and two in parallel representing the lung compartments (Volumes V1 and V2). Tidal (breath) volume and the fixed volumes of all three compartments, as well as the resistance to flow (impedance) to the two lung compartments can be altered. As the bag fills and empties, the tidal volume is distributed to the two lung compartments according to the ratio of impedance between them. There are deadspaces in the two lung compartments as well as a common deadspace in the connecting airway that can also be altered. Gas is assumed to mix instantly and completely beyond the deadspace. The model thus allows control of lung, bag and breath volumes, as well as the two major factors that influence washout progression: ventilation heterogeneity and deadspace. Washin can also be performed from an open circuit, and can incorporate a deep inspiration protocol, allowing comparison of different open and closed circuit washin protocols. For these experiments, the following parameters were set to approximate those seen in a healthy adult male and were not varied: FRC was set at 3L, tidal volume at 1L, common deadspace (DS) was 0.1L, with DS1 and DS2 both set to 0.1L, giving a total DS of 0.3L. For deep inspiration washin, the first 6 breaths were set to 2.4L. The following scenarios were then explored for all three washin protocols:

1. Increasing specific ventilation heterogeneity to two equal volume lung compartments: impedance (Z1) was varied from 0.15 to 0.5, with V1=V2.
2. Increasingly unequal volume of the two lung compartments: V1 was increased in 0.1L steps from 0.1 to 0.9L. Z1 was fixed at 0.3 to introduce a modest degree of ventilation heterogeneity.

Washin was run for 30 breaths. As in clinical testing, apparent completeness was defined as the percent difference between inspired and expired [SF_6%]. The model however also allows measurement of the true completeness of washin – here defined as the difference in [SF_6%] between the two lung compartments, expressed as a percentage of the mixed expired [SF_6].

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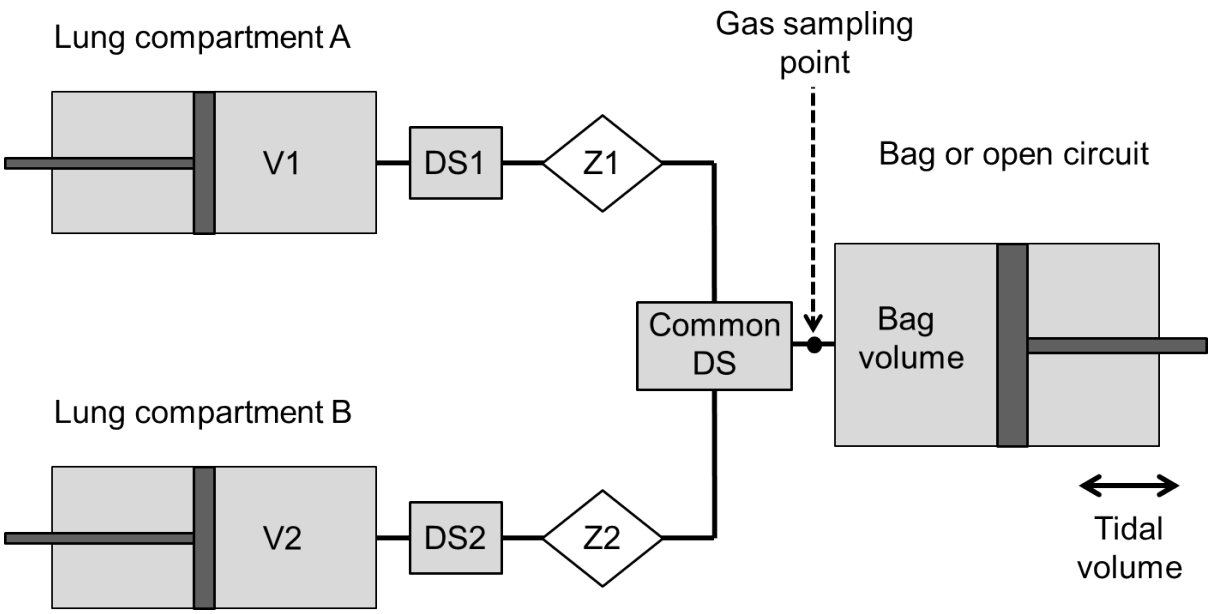

Figure S1: Diagram of lung model, showing two lung and one bag compartment represented as pistons. DS1 and DS2 are deadspace components for lung compartments A and B respectively, and there is an additional common deadspace (Common DS). V1 and V2 are the volumes of lung compartments A and B respectively, and Z1 and Z2 are their respective impedances to gas flow for lung, the ratio of which determine ventilation heterogeneity.

2. Lung model results

The lung model outputs are summarised in the additional Figures S2 and S3. These show the impact of increasing ventilation heterogeneity (Figure S2) or increase lung compartment heterogeneity (Figure S3) on washin progression for the three different washin protocols.

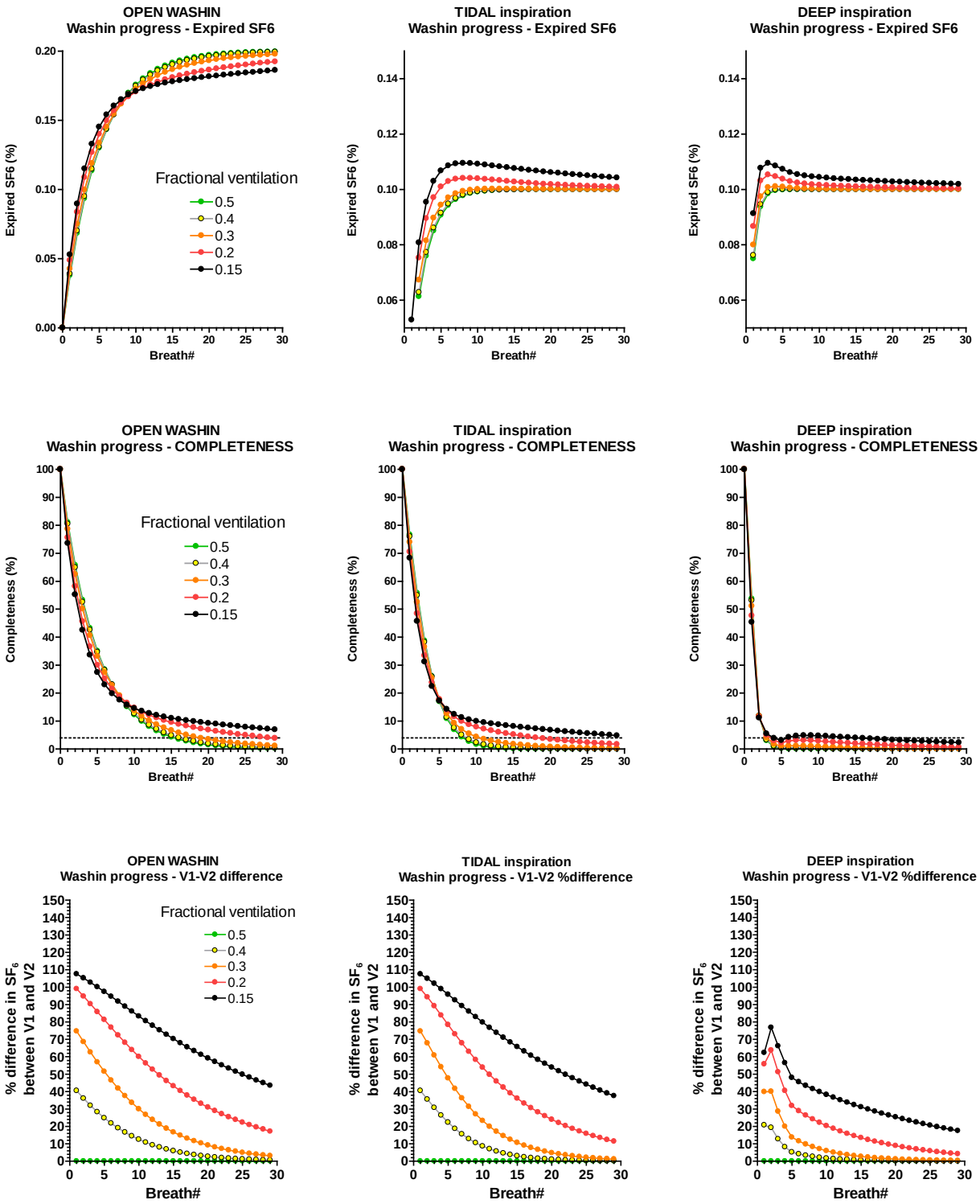

Figure S2: Effect of increasing specific ventilation heterogeneity (impedance) on washin progression in a 2 compartment lung model. Graphs are shown for open circuit washin (left), closed circuit with a tidal breathing protocol (middle) and closed circuit with 6 deep breaths at start of washin (right). In all cases, washin breath number is on the x -axis. Mixed expired SF_6 is shown in the top line, apparent completeness of washin (% difference between inspired and expired SF_6) in the middle row, and true completeness of washin (%difference between SF_6 concentration in the two compartments) in the bottom row.

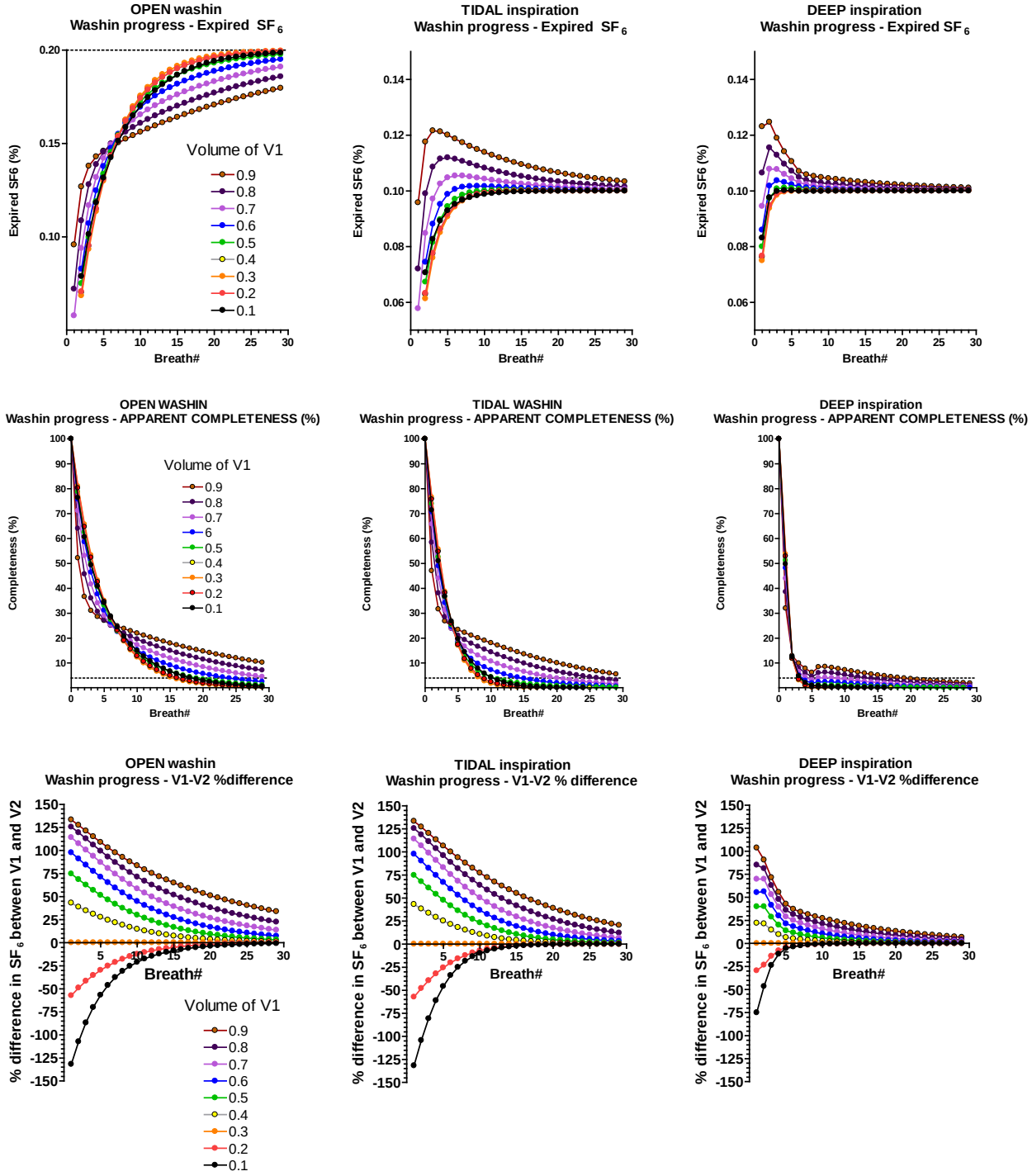

Figure S3: Effect of increasing heterogeneity of lung compartment volumes on washin progression in a 2 compartment lung model. V1 is the slow ventilated compartment, receiving 0.3 of the total volume. Graphs are shown for open circuit washin (left), closed circuit with a tidal breathing protocol (middle) and closed circuit with 6 deep breaths at start of washin (right). In all cases, washin breath number is on the x -axis. Mixed expired SF_6 is shown in the top row, apparent completeness of washin (% difference between inspired and expired SF_6) in the middle row, and true completeness of washin (%difference between SF_6 concentration in the two compartments, V1 and V2) in the bottom row

3. Effect of CO2 on washin / washout

Six CF patients completed an additional study to explore the effects of washin CO_2 on washout parameters. This involved performing open circuit washin, and open circuit washin modified to contain added CO_2 to the washin gas mix. Gas supply was from a Douglas bag filled with 0.2% SF_6 in air, along with additional 100% CO_2 to give a final CO_2 concentration of 1-3%. Subjects inspired from the Douglas bag and expired to room air through a two-way valve (Hans Rudolph, Kansas, USA).

Summary demographics and data are presented in Table S1 and Figure S4. Mean washin CO_2 was 1.6%. With the exception of a single subject, LCI from open washin was very similar to that from open circuit washin with added CO_2, and there was no significant difference between the two groups in LCI or FRC.

	Open	**Open with CO_2**
n	6	
Age	22.3 (3.2)	
M:F	4:2	
FEV_1%	76.8 (17.0)	
LCI	11.0 (3.4)	10.9 (4.0)
FRC (L)	2.86 (0.68)	2.93 (0.68)
Washin CO_2 (%)		1.6 (0.3)

Table S1: Summary demographic and washout data for 6 patients with cystic fibrosis who completed repeat washout measurements either with an open circuit washin, a modified open circuit with added CO_2 to the washin gas, or a bolus closed circuit washin.

*p<0.05 compared to open circuit washin

FEV_1: forced expiratory volume in 1 second, FVC: forced vital capacity, , LCI: lung clearance index.

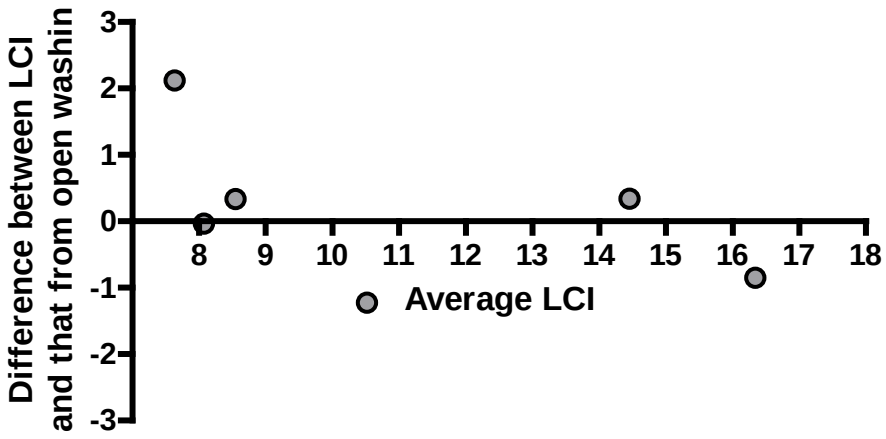

Figure S4: Bland-Altman comparison of lung clearance index (LCI) obtained from open circuit washin with that from an open circuit washin with added CO_2 in the inspired gas.