LUNG CLEARANCE INDEX IN ADULT CF PATIENTS : THE ROLE OF CONVECTION-DEPENDENT LUNG UNITS.

Online Supplement

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1. nitrogen washout curve simulation

The nitrogen washout curves depicted across the various panels of Figure 4, using the compartment volumes in Table OS1, can be obtained by simple computation as follows. If we consider that tidal volume partitioning is determinant of flow partitioning into each lung compartment, nitrogen washout concentration in each subsequent exhalation i can be estimated as :

$C(i)=C_1(i) *VT_1/VT +C_2(i)*VT_2/VT$

where $C_1(i)$ and $C_2(i)$ are nitrogen concentration obtained by dilution in each compartment, as :

$C_1(i)= C_1(i-1)*FRC_1/(FRC_1+VT_1)$

$C_2(i)= C_2(i-1)*FRC_2/(FRC_2+VT_2)$

and for the first tidal breath (i=1), $C_1(i-1)$ and $C_2(i-1)$ equal the pre-test alveolar nitrogen concentration (normalized to 100%).

The predicted relationship between washout curvilinearity (Curv) and lung clearance index (LCI), on basis of all scenarios considered here, is shown in FigureOS1. The relationship between LCI and Curv was determined using a 2nd order polynomial, using scenario1b and scenario2 data sets of Table OS1 in the range up to Curv=0.7. It can be seen in FigureOS1 that depending on whether ventilation heterogeneities derive from scenario 1 or 2, the relationship between LCI and Curv is slightly different. This can also be understood from their slightly different respective dependencies on ventilation heterogeneity in FigureOS2, where all LCI and Curv values of TableOS1 are graphically represented. In FigureOS2, some additional cases of extremely low ventilation can also be appreciated. For instance in scenario1a, the case of low ventilation tends to the limit where 20% of the lung receives none and 80% receives all of the tidal volume, in which case LCI and Curv correspond to homogeneous ventilation but in a smaller lung (a 2400ml lung produces an LCI of 4.4 instead of 4.3 and Curv is still 0).

2. Comparison of 2-, 3- and 10-compartment models

We first used a model with 2 compartments to simulate a case of mid-range ventilation heterogeneity as a reference (generating a Curv of approximately 0.5). We then compared this to a model with 3 compartments (Figure OS3A) and 10 compartments (Figure OS3B,C). In order to obtain the 3 compartment ventilation distribution in FigOS3, 20% was severely underventilated (receiving 10% of nominal inspired volume), 30% was mildly underventilated (receiving 50% of nominal inspired volume), and balance of the inspired volume was attributed to the remaining half of the lungs. In this case, the most underventilated unit produces an additional tail in the washout curve, representing a delayed emptying of that unit. However, because this very slow unit is small in size (20% of total lung volume), it becomes only visible far below the threshold of 2.5% where LCI is determined. To obtain the case of 10 compartments, the ventilation of the least ventilated unit of the 2 compartment-model was first attributed to 5 of the 10 compartments. Then, a variability was introduced on these 5 least ventilated compartments to obtain a coefficient of variation of 35% while maintaining the same average ventilation. The same was done for the 5 best ventilated compartments. Note that the actual location or proximity of the best and least ventilated compartments is immaterial to the outcome in terms of the washout curve, i.e., the distributions in FigOS3 B and C are equivalent. The outcome shows that the main determinant of the washout curves is the global difference in ventilation between the best and worst ventilated units

FIGURE LEGENDS

Figure S1 : Scatterplots of predicted LCI and Curv values computed from the model with 2 compartments (and no dead space) and the best fit polynomial (dashed line). The best fit line is superimposed on the experimental relationship between LCI and Curv in Figure 3 (panel C).

Figure S2: Graphical representations of simulated Curv and LCI values corresponding to the various scenarios of Table OS1. Additional simulations in the low ventilation ranges - below 20% in scenario 1(a) and 1(b) - are included to illustrate the transition to homogeneous limit cases.

Figure S3: Washout simulations (panel D) obtained by using 3 versus 2 compartments (panel A), or using 10 versus 2 compartments (panel B); arranged in a different order, the distribution of tidal volumes in panel C leads to exactly the same washout curve as that in panel B.

Table S1 : Compartment volumes, and Curv, FRC and LCI corresponding to washout concentration curves in scenarios (1) and (2)

			Lung volume at FRC comp1 (FRC_1)	comp2 (FRC_2)	Inspired/tidal volume comp1 (VT_1)	comp2 (VT_2)	Curv	LCI	FRC
Scenario1a :	(1)	homog (100%)	600	2400	200	800	0.00	4.27	3000
20% of lung volume gets	(2)	50%	600	2400	100	900	0.12	4.53	2966
variable inspired volume	(3)	40%	600	2400	80	920	0.17	4.67	2940
(10-50%; 100%)	(4)	30%	600	2400	60	940	0.23	4.84	2891
	(5)	20%	600	2400	40	960	0.28	4.99	2805
	(6)	10%	600	2400	20	980	0.24	4.86	2645
Scenario1b :	(7)	homog (100%)	1500	1500	500	500	0.00	4.27	3000
50% of lung volume gets	(8)	50%	1500	1500	250	750	0.32	5.22	2931
variable inspired volume	(9)	40%	1500	1500	200	800	0.44	5.80	2891
(10-50%; 100%)	(10)	30%	1500	1500	150	850	0.57	6.67	2824
	(11)	20%	1500	1500	100	900	0.70	7.96	2693
	(12)	10%	1500	1500	50	950	0.85	9.11	2304
scenario2 :									
variable part of lung volume	(13)	0%	0	3000	0	1000	0.00	4.27	3000
(0%; 10-50%) gets 20% of	(14)	10%	300	2700	20	980	0.12	4.55	2898
nominal inspired volume	(15)	20%	600	2400	40	960	0.28	4.99	2805
	(16)	30%	900	2100	60	940	0.49	5.68	2731
	(17)	40%	1200	1800	80	920	0.65	6.78	2692
	(18)	50%	1500	1500	100	900	0.70	7.96	2693

Total lung volume at FRC is 3000ml and tidal volume is 1000ml.
Note that case (5) and (15) are identical ; case (11) and (18) are identical.