

Sacin responds to total compliance heterogeneity, and is less sensitive to regionalisation than scnd.

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Rationale

The Multiple-breath washout (MBW) is experiencing increased uptake as a pulmonary function test. However, due to the test's complexity, there is still uncertainty around the precise nature of test index responses to various types of lung disease. In this study, we perform hundreds of simulations of respiratory zone tissue stiffening, to highlight different sensitivities of MBW indices.

Methods

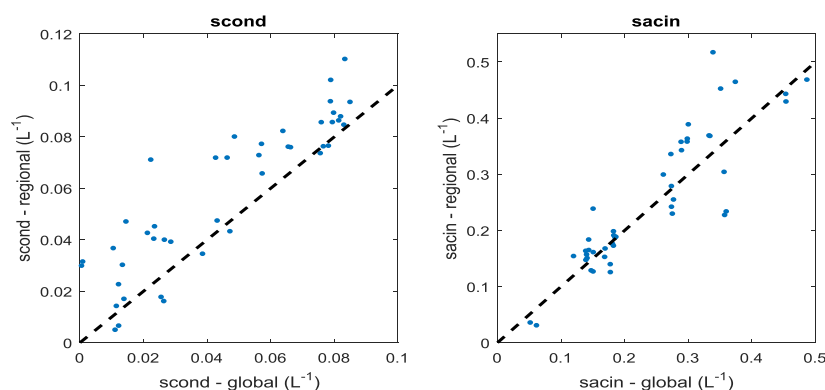
Simulations were performed on a series of patient-specific virtual models of the conducting airways (1), consisting of on average 80,000 branches. Each terminal bronchiole was connected to an independently expanding acinar region, with compliance scaled evenly from a total lung value. Ventilation was simulated using a pressure-driven flow model, and used to drive a gas transport model (2). The pleural pressure was modified using a gravitational gradient, to mimic an upright test position. For each virtual patient two MBWs were simulated; the first with a randomly chosen 20% of acinar regions having local compliance reduced by 50% (global compliance heterogeneity), and the second with all acinar regions in the left-lower lobe having compliance reduced by 50% (regional compliance heterogeneity). For each simulation two MBW indices were derived; scnd and sacin.

Results

The comparison of MBW indices under global and local compliance heterogeneity can be seen in Fig 1a and 1b. As seen, the response from sacin is quite stable, with no consistent change when tissue stiffening is regionalised. However, the scnd response is consistently higher under local compliance heterogeneity. This was further illustrated by performing a t-test on the difference in response between the two groups. Sacin showed no significant difference ($p > 0.05$), while the change in scnd was strongly significant ($p = 0.00001$).

Conclusions

The results from this study have illustrated that scnd is much more sensitive to regionalisation of compliance changes than sacin. Localised tissue stiffening (as can occur in a variety of lung diseases) will cause a much larger response in scnd than sacin, despite sacin being the more common respiratory zone index. This is an important factor that should be accounted for during interpretation of MBW outputs in clinical settings.



BFoy is funded by the Rhodes Trust.

References

- (1) Bordas, R, Lefevre, C, Veeckmans, B, Pitt-Francis, J, Fetita, C, Brightling, CE., Kay, D, Siddiqui, S, & Burrowes, KS (2015). Development and analysis of patient-based complete conducting airways models. *PLoS one*, 10(12), e0144105.
- (2) Foy, BH, & Kay, D (2017). A computational comparison of the multiple-breath washout and forced oscillation technique as markers of bronchoconstriction. *Respiratory Physiology & Neurobiology*, 240, 61-69.