Conducting airways <2mm in diameter, with little or no contribution of their own to ventilatory function in the normal lung, however these same airways become the major site of obstruction in COPD. Furthermore, using an acquisition of clinical multi-detector computed tomography (MDCT) and micro-CT it has been shown that narrowing and loss of terminal bronchiolitis contributes to peripheral resistance in COPD. Due to the age-related prevalence of COPD, here we use a structure-based mathematical model to study how FEV1 changes in response to loss of terminal bronchiolitis in combination with age-related decline in lung tissue elastic recoil.

**Methods**

- 6 normal healthy subjects (M, F). Table 1 shows a subject summary.
- Structure-based lung and array models from FVC (1) (See Figure 1).
- Finite deformation elasticity for tissue displacement and elastic recoil (2).
- Artery tree embedded in model lung tissue.
- Wave-speed model (3) to predict maximum flow at all lung volumes.
- Viscous pressure drop using relationship developed by Collins et al. (4).
- Artery compliance determined using Lambert’s model (5).
- Model included total lung capacity (TLC) from which a forced vital capacity (FVC) is calculated (1).
- Ageing of lung simulated by: 1. decreasing lung elastic recoil, 2. removing terminal bronchiolitis.
- Baseline model generated for one healthy 63 year old male. Subject extrapolated to other ages that were studied here.

**Forced expiration in the baseline model**

- Figure 2 shows baseline model results for subject M1 along with measurements from pulmonary function tests.
- Parameterisation of the baseline model by fitting peak muscle (driving) pressure and rate of decrease of airway diameter with decreasing order.
- Variation between measurements and computational results for all six subjects are: PEF, 2.4 ± 1.2 %; PEF25, 4.3 ± 1.8%; PEF75, 2.0 ± 0.3 %.

**Loss of elastic recoil & terminal bronchiolitis**

- Figure 3 compares two causes of PEF, decline.
- Removing 50% of the terminal airways without a change in elastic recoil from the 25 years value (green) decreases PEF, by 15%. Decreasing elastic recoil to the 75 years value without removing terminal airways decreases the FEV1, more in females than males (blue). Results show more subject variability.
- Removing 50% of terminal airways from the model with 75 years elastic recoil decreased PEF, by 15-20%, with larger decrease in males.

**Loss of tissue elastic recoil**

- Figure 3 shows model predictions in healthy, male (a) and female (b) age as a % of FEV1, calculated at 25 years for each subject (males green, females blue).
- Lung tissue compliance by decade for all subjects; tissue pressure and airway dimensions parameterised to baseline young data.
- Loss of tissue elastic recoil in the model results in decreased FEV1, and increased inter-subject variability.
- The models are in accordance with the literature, including an – on average – more rapid decline in FEV1, with age in females.

**Modelling Older Subjects**

- Figure 5 shows baseline results for a 63 year old healthy, male subject.
- Parameterisation of baseline model using peak muscle driving rate, rate of decrease of airway diameter, maximum expiratory pressure (from PFTs) to measured values at age 63.
- Change in lung tissue compliance specified to be the same as that defined earlier at age 65 for younger subjects.
- % decrease in muscle pressure equivalent to that from previous study.
- No removal of terminal airways.
- Model prediction errors: FEV1, 12.5%; PEF25, 56.6%.
- Large discrepancy between calculated and actual PFTs. Airway closure not incorporated into model, model therefore over-predicting results.

**Summary & Conclusions**

- The model suggests that significant variation in decline of FEV1 across subjects with age can be attributed to loss of elastic recoil interacting with the subject’s specific airway geometry.
- Removing terminal bronchiolitis causes decline of FEV1, and increased the age-dependent inter-subject variability, however without an accompanying decline in elastic recoil; very large numbers of terminal airways must be lost before FEV1 decreases below the threshold of 80% predicted.
- Removal of terminal bronchiolites had a more consistent effect across subjects (Figure 5) compared with loss of elastic recoil. Women were on average – more sensitive to loss of recoil than men.
- Large decreases in tissue elasticity and numbers of terminal airways are possible before threshold for disease is reached (FEV1 < 80% predicted).
- The results support the hypothesis that large numbers of terminal airways can be lost with age, without detection on forced spirometry.

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