INTRODUCTION
The great development and diffusion of Liquid Assisted Ventilation (LAV) techniques (perfluorocarbon (PFC) lavage, Tidal Liquid Ventilation (TLV), and Partial Liquid Ventilation (PLV)) [1] is mainly due to the benefits they provide to patients with respect to other methods of ventilatory support. Such benefits derive from eliminating the liquid-gas interface in the alveoli. In fact, the instillation of liquid PFCs into the lungs increases pulmonary compliance and improves alveolar recruitment; in addition, it provides lavage of the debris that may be present in the airways, and may support surfactant secretion. TLV and PLV were demonstrated to be extremely useful in the case of very premature lambs, whose saccules (the precursors of alveoli) have a tendency to remain collapsed due to scarce or absent surfactant production secondary to lung immaturity.

Up to now, the ranges for TLV ventilatory settings (breathing frequency \(f\), tidal volume \(TV\), inspiratory to expiratory time ratio \(I:E\)) that yield adequate CO\(_2\) removal have been suggested by means of animal studies. However, the effects of the variations of such settings on blood arterialization and lung mechanics have not been studied quantitatively.

This work is about the development of a lumped-parameter mathematical model of airway mechanics during a volume-controlled neonatal TLV treatment. The mechanics model has been coupled with a model of O\(_2\) and CO\(_2\) transport in PFC, from the trachea to pulmonary capillary blood and vice versa.

The overall model allows the treatment effectiveness to be simulated at any variation of the ventilatory settings, so as to shed light upon possible ventilation strategies that allow for an optimal management of blood arterialization and lung mechanical load.

METHODS
The overall model consists of two sub-models (Figure 1):

**Airway mechanics sub-model (M1)**
On the basis of the input ventilatory settings, M1 outputs the pressure and shear stress acting on the airway epithelium; in addition, it supplies module M2a with the PFC flows calculated for each airway branch. M1 is an evolution of our previous rigid-airway model [2], where non-linear elastic characteristics for airway walls have been included. Airways belonging to the same branching generation were modeled by a double dipole, accounting for: 1) PFC inertia; 2) non-linear hydraulic airway resistance, according to Pedley [3] and Collins [4] for inspiration and expiration, respectively; 3) airway compliance, according to different pressure-volume relationships [5,6].
Gas transfer sub-model (M2)

The gas exchange sub-model (M2) is organized in two modules:

- Module M2a, which, on the basis of the ventilatory settings and of PFC flows from sub-model M1, calculates the diffusive and convective gas transfer through the PFC-filled airways [7]. It supplies the partial pressure of the respiratory gases (pO₂ and pCO₂) in the airways and in the saccules, the latter being passed to module M2b.

- Module M2b is aimed at predicting the gas transfer rate between sacicular PFC and pulmonary capillaries, with description of the transport and kinetics of respiratory gases in the pulmonary blood. It was obtained [7] by properly adapting and scaling a three-component model by Hill, et al. [8]. Module M2b uses sacicular pO₂ and pCO₂ from module M2a to compute gas transfer rates V̇O₂ and V̇CO₂, which are returned to M2a in a closed loop until convergence is reached.

Sub-model M1 and module M2a are based upon a regular dichotomous scheme of the bronchial tree, whose morphometric relationships were assumed according to Weibel [9].

The input of the overall model are the ventilatory settings (breathing frequency f, tidal volume TV, inspiratory to expiratory time ratio I:E, PFC flow waveform Q(t), and the oxygen/carbon dioxide partial pressure in the PFC entering the trachea during inspiration pO₂ₐₕ, pCO₂ₐₕ). The model outputs are the pressure and shear stress acting on the airway walls and gas transfer rates V̇O₂ and V̇CO₂, that is, the cycle-averaged amounts of O₂ and CO₂ exchanged between sacculae and pulmonary capillaries per unit time.

RESULTS

Simulations showed that the most influential ventilatory settings are frequency f and tidal volume TV. Increases in f or TV both improve gas transfer and increase the mechanical stresses acting on the airways, i.e. the maximum positive pressure acting along the lung at different airway generations, the maximum shear stress applied at the airway walls, and collapse risk.

Fig. 2 exemplifies how to compare the effects of f and TV on the maximum inspiration pressure acting on the airways, taking the resulting gas transfer into account. For example, to keep the maximum pressure of the median (10th generation) airways constant, gas exchange may be improved by increasing f and decreasing TV (as exemplified by arrow AB), because the slope of the iso-(maximum pressure) in median airways is lower than the slope of iso-(gas transfer) curves. Similar diagrams may be drawn for minimum pressure, shear stress or airway collapse danger.

At highest values for f or TV, tracheal collapse phenomena were predicted during expiration.

DISCUSSION

By means of the iso-output curves, strategies may be defined to increase gas transfer taking the mechanical stresses into account, or to reduce the mechanical stress without affecting gas transfer. Fig. 2 refers to the most appropriate strategy when the main danger considered is the damage of the airways and saccules due to an over-inflation: this is the case of very compliant or fragile airways.

With respect to the previous, rigid-airway approach, with the current model airway collapse events may be predicted. Collapse usually takes place in the trachea. In reality, the tracheal collapsibility not only depends on its own mechanical characteristics, but also on the stiffening effect exerted by surrounding tissues and on the protective effect of the endotracheal tube, acting as a constraint against collapse. The first effect is not reproduced by the model, wherein the mechanical features of the tracheal tissues were implemented on the basis of measurements performed on excised tracheae.

REFERENCES


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