Appendix

The most significant influence of pleural effusion on ventilation and blood oxygenation is related to the impact of the hydrostatic pressure exerted by pleural fluid on the lungs, bronchi and pulmonary vessels: if this pressure significantly increases local P_{pl} in dependent regions, it may cause collapse of both the alveoli, bronchi and pulmonary vessels. Therefore, the equations that describe the compliant properties of these elements are crucial.

The particular layer is described by the following equation[20]:

$$Ptps(V) = \frac{\tan\left(\frac{\pi}{2} \cdot \frac{V_A - V_{A0}}{Size}\right)}{(\rho / \rho_0) \cdot Compl}$$

where:

V_A - the layer volume;

Ptps - the static transpulmonary pressure (the recoil pressure) equal to the difference between P_A and P_{pl} (if the layer tissue does not move);

Size - a parameter related to the layer size;

V_{A0} **-** the lung volume when the recoil pressure is equal to zero (i.e., the atmospheric pressure);

Compl - a parameter characterizing compliant properties of the lung parenchyma; it can be interpreted as the specific compliance at ***$V_A=V_{A0}$***;

ρ_0 - the normal, physiological surface concentration of the surfactant;

ρ - the current surfactant surface concentration (if for any reason ***$\rho>\rho_0$***, then the value of ρ/ρ_0 is assumed to be equal to 1).

Note that if for a layer $P_A<P_{pl}$ (i.e., Ptps<0), then V_A has the minimal possible volume; thus, the layer is collapsed.

Bronchi of the middle order in a layer are simulated as one collapsible tube and described with the following equation derived elsewhere[19]:

$$Q = \frac{Pb - P_X - b \cdot \arctan\left(b \cdot \frac{Pb - P_X}{b^2 + (Pb - Pp) \cdot (P_X - Pp)}\right)}{k}$$

where:

Q - the airflow through this tube to/from the layer,

Pb - the pressure inside the tube at the proximal end, i.e., in the left or right main bronchus (depending on which lung is considered);

P_x - the pressure at the distal end;

Pp - the local P_{pl};

k - the parameter that characterizes the resistive properties of the bronchi and corresponds to the airway resistance for a very large lung volume;

b - a parameter characterizing the elastic properties of the bronchi.

It can be shown that if Pp>Px, then $Q = (-Ptp(V) + b \times \arctan((Ptp(V)/b)/k$, and thus, the airflow depends only on the lung volume, which is the foundation of the forced spirometry[19]. Certainly, if V=0 due to lung collapse, there is no flow.

The smallest bronchi and ducts of a layer are also simulated by one tube. Like alveoli, they are components of the parenchyma; therefore, their current lumens, and thus also their resistance, depend on the current lung volume, in general. If a layer is collapsed, the mean resistance of the tube is almost infinite (the resistance is high but not infinite at the proximal end connected with the tube simulating bronchi of the middle order). If the local P_{pl} around the collapsed layer falls below the atmospheric pressure, some airflows exist at the proximal part, which increases the lumen of the other tube parts and thus decreases the resistance, enabling the flow of air into the collapsed alveoli. The value of this airflow determines the rate of layer recruitment.

The relationship between the ribcage and the mediastinum is described by the following equations[20]:

Pp_L-Pp_R =Pm; $Pm=(V_L-V_R)/Cm$; $Pw=(Pp_L+Pp_R)/2$

where P_{PL} and P_{PR} are the mean P_{pl} in the left and right hemithoraxes, respectively; thus, *Pm* is the pressure acting on the mediastinum of the compliance characterized by *Cm* if *Pm* is not equal to zero due to the difference between the volumes of the left and right hemithoraxes. As has been shown by several authors (*e.g.,*[27]), the chest wall expands symmetrically, even when these volumes are significantly unequal. Therefore, we assumed that the pressure *Pw* acting on the ribcage is the mean of P_{PL} and P_{PR}.

Three kinds of equations describe pulmonary vessels depending on their size (for details and derivations, see the Supplement for[6]). The greatest vessels are described with the following equation:

$$P_{tm} = \frac{E_0}{a} \cdot (e^{a(V-V_0)} - 1)$$

where: P_{tm} – the transmural pressure, V – the vessel volume, V_0 – V for P_{tm}=0, E_0– the elastance of the unstressed vessel, *a* – a coefficient.

Smaller vessels are described with the following equation:

$$P_{tm} = \frac{V - V_0/\alpha}{c_1/\alpha} = \frac{V \cdot \alpha - V_0}{c_1}$$

where α and C_1 characterize the ability to cause hypoxic vasoconstriction and the vessel compliance, respectively.

The above vessels are compliant, but their resistance is not very significant; therefore, we have assumed that there is no significant drop in the transmural pressure along the vessel, determining its volume. This enabled us to directly connect the vessel volume and its resistance according to the Hagen–Poiseuille law. Capillaries are both significantly compliant and significantly resistive; thus, a partial differential equation had to be used for their mathematical description[6]. A form of a differential equation, which enabled to solve this equation manually, was chosen; and the following solution is used in the virtual patient:

$$R_{cap} = \frac{P_{pro} - P_{dis}}{Q_{blood}} = \left(\frac{1}{g_{cap} \cdot (P_{pro}^2 + P_{pro} \cdot P_{dis} + P_{dis}^2)} \right)$$

where R_{cap} is the Ohm resistance, i.e., the ratio of the difference between the pressures at the proximal and distal ends (P_{pro} and P_{dis}, respectively), and the blood flow Q_{blood} (see the Supplement for[6] for g_{cap} meaning).

Intercostal muscle activity during breathing is simulated by means of a pressure source, whereas hemidiaphragm activity is simulated by changes in the volume between the unstressed hemidiaphragm and the horizontal plane through the diaphragm origin[5].