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A lung model considering age, sex and height: an *in-silico* study – lung mechanics

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Abstract: We present an in-silico study by simulating the respiratory system of a healthy virtual cohort as a use case for testing highly automated functions in mechanical ventilators in a model-based way. As a first part of the in-silico study, this article focuses on the lung mechanics while the individual gas exchange is published in a separate article. For this purpose, a linear single-compartment model of the lung is adapted based on literature results, so that it can represent the changes in a patient's lung mechanics resulting from the specific personal characteristics age, sex and height. The results confirm the ability of the adapted model to show the main predicted individual changes of the lung volume as they are in agreement with literature data.

I. Introduction

Mechanical ventilation is becoming increasingly complex with the aim of providing a lung-protective ventilation therapy. Thus, automated functions could be useful as they can respond to the patient's behaviour during ventilation and may enable the clinical staff to focus on the patient-individualised care more accurately. To ensure patient safety and reveal potential risk cases, automated functions must be extensively tested and examined for a broad variety of differently combined parameters [1]. For testing these functions, an in-silico cohort that functionally represents the respiratory system could be used. Hence, in this article we propose a first approach of simulating the lung mechanics of a healthy virtual cohort considering the influence of age, sex and height. This is achieved by adjusting model parameters of an existing lung model to the different physiological properties based on literature. In addition to the lung mechanics, the gas exchange, which is discussed in [2], should be considered to get an entire overview of the respiration. *Fig.1* shows the structure of the respiratory model with the adapted model parameters.

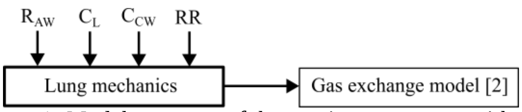

Figure 1: Model structure of the respiratory system with the model-parameters: airway resistance R_{AW}, lung compliance C_{L}, chestwall compliance C_{CW} and breathing frequency RR.

II. Material and methods

In this article, a one-compartment-RC model is used to simulate the lung mechanics of various subjects. The model can be described by the modified equation of motion [3]

$$P_{\mathrm{mus}} = \frac{1}{C_{\mathrm{RS}}} \cdot V + R_{\mathrm{AW}} \cdot \dot{V}, \quad (1)$$

where P_{mus} defines the pressure exerted by the respiratory muscles. By solving (1) the time courses of the lung volume V and the flow $\dot{V}$ can be determined. P_{mus} can be idealised by an upper sinusoidal wave defined by a heuristic choice with an amplitude $A_{\mathrm{mus}} = 9.8$ mbar. The lung mechanics is characterised by the airway resistance R_{AW} and the respiratory compliance C_{RS}, which in turn can be separated into lung compliance C_{L} and chest wall compliance C_{CW}. To evaluate the respiratory behaviour of a simulated cohort, the tidal volume V_{T} is taken into account and calculated by subtracting the respective minima from the corresponding maxima of the time course $V(t)$. The simulated V_{T} is compared with literature data under spontaneous breathing and thereby evaluated on the matter of physiological correctness [7,11,12]. During aging the average V_{T} changes while the average minute volume remains the same [12].

In order to simulate the lung mechanics of healthy, resting, recumbent subjects as a function of age, sex and height, the following adjustments of the model parameters have been made. Pelosi et al. [4] proposed a relationship between the body-mass-index (BMI) and R_{AW}, so that sex and age dependencies, represented by a varying BMI, are considered [5]. A quadratic function was used to describe the changes of the BMI accompanying aging for both sexes to render the approximation more precisely (*Table.1, l.2*).

Age-related differences in C_{L} and C_{CW} occur throughout the aging process [6, 9]. Mittman et al. [6] measured the C_{L} of seated males with different ages. A linearisation of the data results in an age-dependent C_{L} for males with a standard deviation (*Table.1, l.3*). Based on the assumption of simulating a supine cohort, C_{L} needs to be adjusted. According to [8], an adjustment factor of 0.76 which considers the change in body positioning is used (*Table.1, l.3*). To determine the C_{L} for females, the factor 0.84 is added to the equation since the lung volume of females is on average about 16 % smaller than that of males [7]. Estenne et al. [9] examined the age-related changes of the C_{CW} based on a clinical study with individuals in supine position. A linearisation of the measurements results in sex-

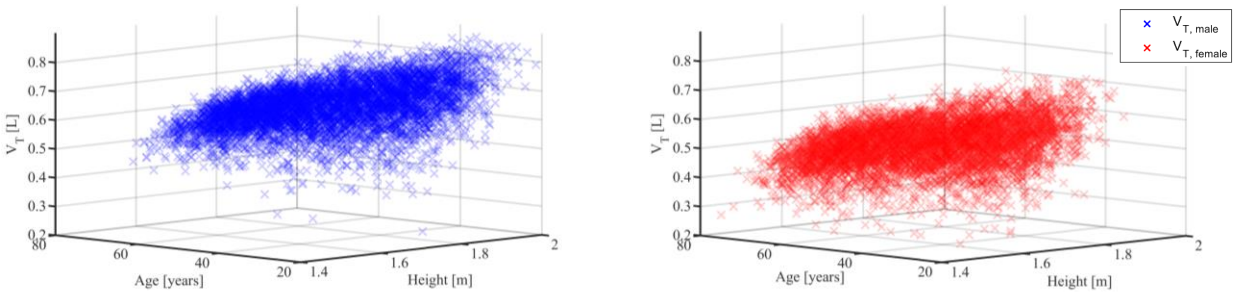

Figure 2: Changes of the specific tidal volume V_T in respect to age and height of a male (left) and a female (right) cohort. Each cohort is simulated with 6000 subjects, consisting of 100 different people of each age in the range of 20 to 80 years. For each subject a sex-specific Gaussian distributed height in the range of 1.4 m to 2 m, as well as a Gaussian distributed C_L and C_{CW} were chosen.

and age-specific equations with a standard deviation (*Table.1, l.4*). Additionally, the influence of height should be considered, as the average V_T depends on the person's height and increases with rising age. The average percentual change of the lung capacity TLC is accompanied on average by the same percentual change of V_T due to their fixed volume ratio [7]. This introduces another necessary multiplicator (proH) for the C_L and C_{CW} considering the height (*Table.1, l.6*).

The average breathing frequency RR is adapted to its age-related changes. Initially, based on literature data a RR of 14 breaths per minute (bpm) is assumed [10]. With increasing age, the RR constantly adjusts to the changes of V_T and the constant minute volume (*Table.1, l.7*) [12].

We simulated sex-dependent cohorts, each consisting of 6000 subjects evenly sampled in the range of 20 to 80 years with the Gaussian distributed parameters C_L and C_{CW} and their corresponding standard deviation. The height was chosen according to a Gaussian distribution with a mean for males and females of 1.78 m (σ: 0.073 m) and 1.66 m (σ: 0.067 m), respectively [5].

*Table 1: Literature-based model functions and the standard derivation σ of the lung parameters for males (m) and females (f) with A = age [y], H = height [m] and * = based on.*

Parameter		Function	
R_{AW} [mbar/L/s]		$2.55 \cdot \exp(0.03 \cdot \mathrm{BMI_i})$ for $i = m, f$	[4]
BMI [kg/m²]	m	$-0.002446 \cdot A^2 + 0.2956 \cdot A + 18.75$	[5]*
	f	$-0.001084 \cdot A^2 + 0.1776 \cdot A + 19.09$	[5]*
C_L [L/mbar]	m	$((0.2891 + 0.0011 \cdot A) \cdot 0.76) \cdot \mathrm{proH}$ $\sigma: 0.0411 + 0.001 \cdot A$	[6, 8]*
	f	$((0.2891 + 0.0011 \cdot A) \cdot 0.76 \cdot 0.84) \cdot \mathrm{proH}$ $\sigma: 0.0411 + 0.001 \cdot A$	[6,7, 8]*
C_{CW} [L/mbar]	m	$(0.2439 - 0.0016 \cdot A) \cdot \mathrm{proH}$ $\sigma: 0.0876 - 0.0009 \cdot A$	[7,9]*
	f	$(0.2133 - 0.0014 \cdot A) \cdot \mathrm{proH}$ $\sigma: 0.0408 - 0.0003 \cdot A$	[7,9]*
TLC [L]	m	$7.99 \cdot H - 7.08$	[7]
	f	$6.60 \cdot H - 5.43$	[7]
proH		$1.1429 \cdot H - 1.0467$	[7]*
RR [bpm]		$0.0008214 \cdot A^2 - 0.02607 \cdot A + 14.16$	[10]*

III. Results and discussion

The adjustments of the model parameters mentioned above enable first simulations of the lung mechanics of cohorts. For the exemplarily chosen virtual cohort, in *Fig.2* it can be seen that V_T decreases with increasing age and increases with rising height for both sexes. Furthermore, the results show that the V_T of females is lower compared to the V_T of males. These results are in agreement with the general literature and mostly in a physiologically plausible range [11]. Nevertheless, the simulations show some outliers that do not correspond to the expected physiological range, presumably due to the wide dispersion of C_{RS}.

IV. Conclusions

This article proposes an approach to simulate the lung mechanics of a cohort considering the influence of age, sex and height. First simulations may indicate that the model in general represent the essential changes of the lung mechanics in a cohort simulation. This work could thus be a first step for the testing of automated functions in highly mechanical ventilators. Our future work will focus on potential extensions of the in-silico study, such as considering pathological pulmonary diseases like the acute respiratory distress syndrome (ARDS).

Author's Statement

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