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SOME ASPECTS REGARDING RECENT ADVANCES IN LUNG MECHANICS MODELLING

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Abstract: The paper presents a review of most recent progresses in lung and respiratory mechanics modelling. Models are practical in understanding the physiological function or process and can lead to advance of new treatments or strategies. A model can also be used to simulate and predict a body’s reaction to certain stimuli without really testing on patient, to develop and evaluate new methods of artificial ventilation or new measurement methods and instruments for investigation. Modern models developed on classical mechano-pneumatic elements proved to be better for teaching and training of medical personal while mathematical-computer models developed on the basis of image acquisition and software are extremely accurate.

1. INTRODUCTION

Interdisciplinary research is a most of modern times and under this view, biomechanics can be defined as the application of the principles of mechanics to biology and physiology, the main intend of biomechanics being to explain the mechanics of life and living, Fung, [1], Suki and Bates, [2].

Models are practical in understanding the physiological function or process and can lead to advance of new treatments or strategies. A model can also be used to simulate and predict a body’s reaction to certain stimuli without really testing on patient, Chase et al., [3].

Classical biomechanics has given attention to describing the macroscopic structural and mechanical properties of tissues and organs by founding the constitutive equations relating the stress variation to strain changes, as result of size and shape of the body variation. The constitutive equations are often nonlinear and can describe stress-strain relations for the static case. More realistic equations include time dependency of stress-strain relations and the tissue models are viscoelastic. All living tissues show viscoelastic behaviour, [1], as the constitutive elements of the tissues require time to adjust their local configuration when a strain is applied. Relaxation and creep are the main viscoelastic features and these can be modelled following dynamic tests concerning mechanical characteristics of the tissues. The mechanical properties of the tissues depend both on the constitutive macromolecules and their connections. The advance of novel techniques such as imaging techniques and quantitative computational modelling have allowed the study of micromechanics of tissues and improved the understanding of relationships between tissue composition, microstructure and macrophysiology, [2].

Models can be used to develop and evaluate new methods of artificial ventilation applied for different lung disease treatment, to develop new measurement methods and instruments for investigations, to create standards for medical instruments and measurements procedures, for testing of ventilation and spirometric instruments, for education of students and training of medical staff by demonstrating an influence of lung pathology on lung functions or different respiratory strategies applied in diseases treatment, Kozarski et al., [4]. [5].

2. ELEMENTS OF LUNG ANATOMY AND MECHANICS

The different tissue components (collagen, elastic fibres, proteoglycans, interstitial cells) interact resulting a composite viscoelastic structure with significant load-bearing capacity over a wide range of external forces to which the lung is exposed, [2]. In Fig.1, the diagram of force transmission from the lung, according to Suki and Bates, [2], is shown. The phenomenological quasi-static stress–strain curve of lung tissue, [1] can be modelled by various models but the relationship between the molecular organisation of collagen and elastin fibres and the *in vivo* pressure-volume curve is not yet fully understood.

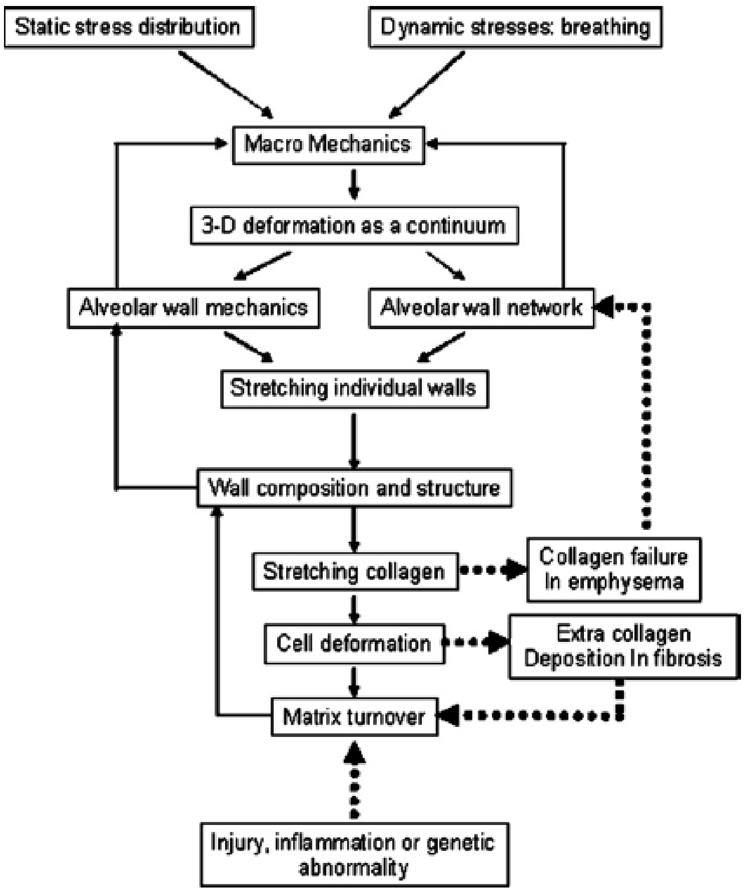

Fig.1. Scheme of force transmission from the whole lung level to single cell with feedback mechanisms, Suki and Bates, [2]

3. RECENT MODELS

There were developed different models, mechanical, mathematical, pneumatic, electronic or combinations of interdisciplinary models. In our time, many models use computer programs and software to simulate the mechanics of respiration, [3]. These models become like a black box losing clarity in illustrating the inner working dynamics that represent the physiology, and under this consideration the model developed by Chase et al., [3] is of interest. The model, from Fig.2 , is completely mechanical, it simulates the physiological lung completely and identifies and verifies the fundamental mechanics of any ventilated lung. The lung is represented by six bellows connected to a ventilator and a platform is placed on top of rubber bellow to support weights, used to vary the driving pressure of the bellow. A volume limiter sets the maximum height of the platform, thus limits the height which the bellow is allowed to expand vertically, each bellow is connected to the larger common tube through an adjustable valve.

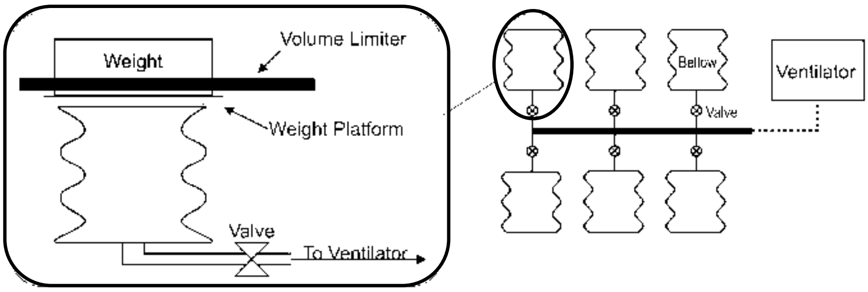

Fig.2. Mechanical model of the lung, Chase et al., [3]

The model can also be connected to a ventilator and it can be used for teaching and training lung mechanics, as its completely mechanical nature and simple mechanism illustrate the behaviour of different lung volumes and their interaction with the ventilator settings.

It was shown above that physical models of lung reproducing their mechanical properties are still a helpful tool in many applications. Almost all physical lung models developed till now consist of more or less complex connections of mechanical discrete elements such as springs, pistons, bellows and pneumatic resistors representing lung abilities to accumulate potential energy and to dissipate energy, [4], [5]. But this method presents limitations as far as complexity of the model structure is concerned and it also is very difficult to reproduce nonlinear properties of lung. Kozarski et al, [4] proposed and designed a hybrid model, following the steps shown in Fig.3; the aim of the model is to describe the impedance of the lung that is the ratio of air pressure and corresponding flow in any point of lung tree.

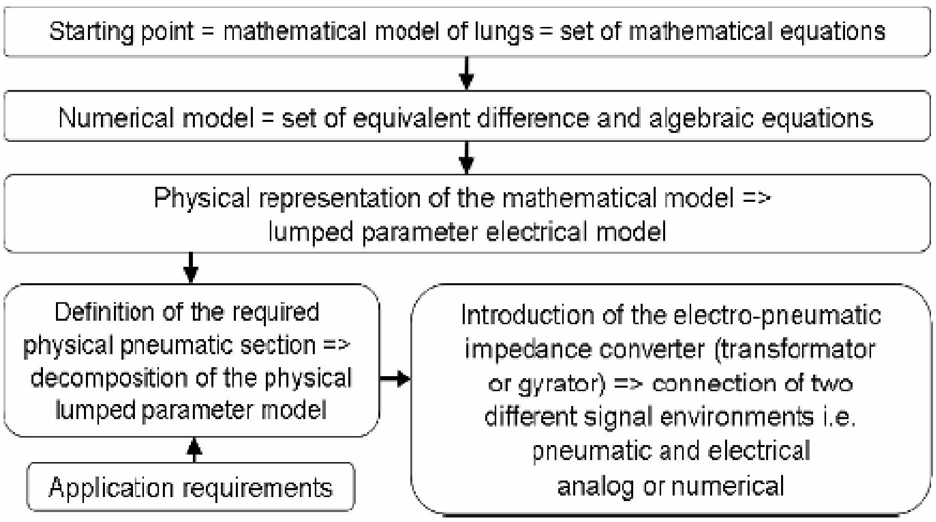

Fig.3. General procedure of Kozarsk et al., [4]

The element enabling transformation of electrical impedance to a pneumatic one is an electropneumatic proportional converter, analog or hybrid-numerical-pneumatic, Fig. 4.

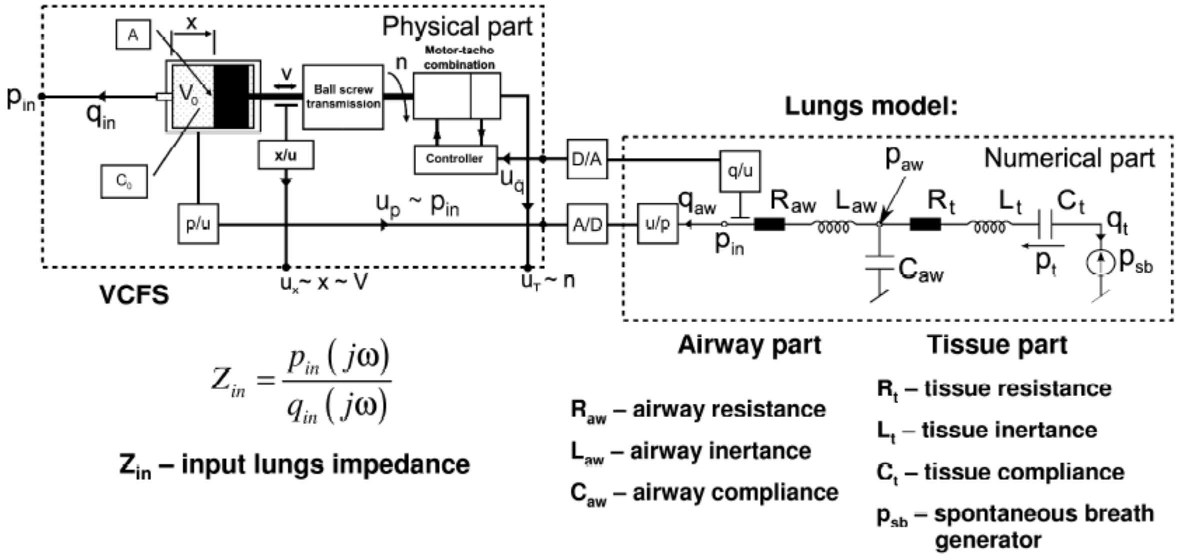

Fig.4. The hybrid lung model of Kozarski et al. [ ]

The flow courses traced with the model confirmed the good dynamic properties of the model and the good volume traces are attributed to direct volume measurements with a piston-displacement transducer. The hybrid model proved to be accurate and thus allowing to eliminate numerous *in vivo* experiments with lab animals. The hybrid model proved the advantage of flexibility, accuracy and modelling complex mechanical lung structure and function.

Athanasiades et al., [6] developed a model which gives analytical expressions that predict the work of breathing associated with natural breathing manoeuvres in non-ventilated subjects. They proposed a nonlinear model of respiratory mechanics, Fig. 5 and Fig. 6 and on its basis found the relations that explicitly identify the work of breathing. It features separate resistive coefficients for the upper, middle and small airways, a compliant characterisation of partially supported airways, a modified Kelvin body describing the compliance of lung tissue and a static compliance for the chest wall.

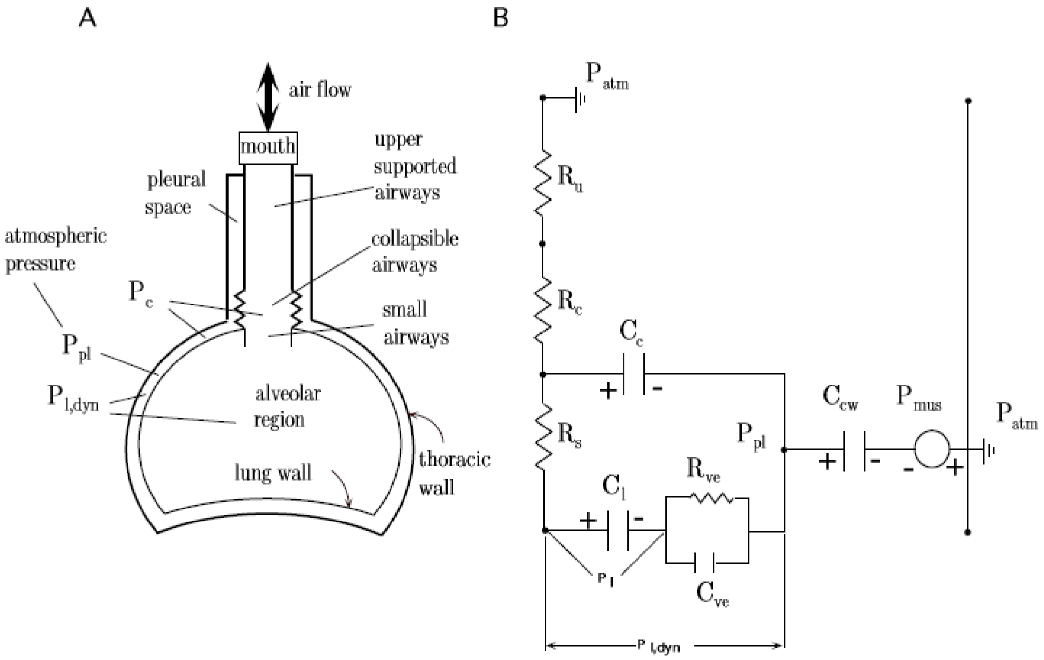

Fig.5. Physical model of respiratory system (A) and pneumatic analog model (B) proposed by Athanasiades at al, [6]

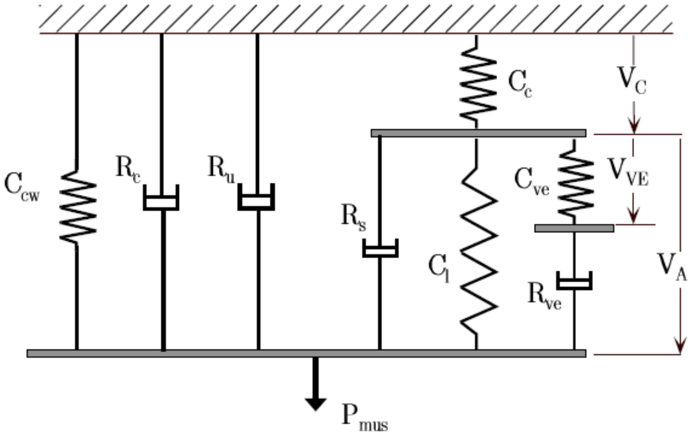

Fig.6. Mechanical equivalent of respiratory mechanics model, Athanasiades et al, [6]

The advantage of the model, afforded by the completeness of the proposed model and its nonlinear nature, lies in the fact that it can estimate the work of breathing for three different manoeuvres more fully and precisely than was allowed by conventional models of respiratory mechanics.

Ionescu et al.,[7] used a four and five parameter constant phase model related to the lung tissue damping and elastance. The measurement of air pressure P and air flow Q and using the electrical analogiey where P correspond to voltage and Q corresponds to current, the respiratori impedance Z can be defined as their frequency domain ratio relationship, $Z_r(j\omega) = S_{PU}(j\omega)/S_{QU}(j\omega)$. The model used for impedance is defined by a Newtonian resistance R, a frequency dependent inertance L and a tissue part described by a constant-phase impedance:

$$Z_4(j\omega) = R + L(j\omega) + \frac{1}{C(j\omega)^{\beta}}; \qquad Z_5(j\omega) = R + L(j\omega)^{\alpha} + \frac{1}{C(j\omega)^{\beta}} \tag{1}$$

From experimental tests, they identified the parameters of the model for healthy and diseased subjects and the five parameters model was validated by the data.

For infant lung models, there are fewer researches and models developed. Kent et al., [8] proposed a mechanical viscoelastic model, Fig.7a, that accurately describe the measured ramp-hold and erratic applied volume waveforms and, compared to an existing model, Fig. 7b generated realistic tracheal pressure responses.

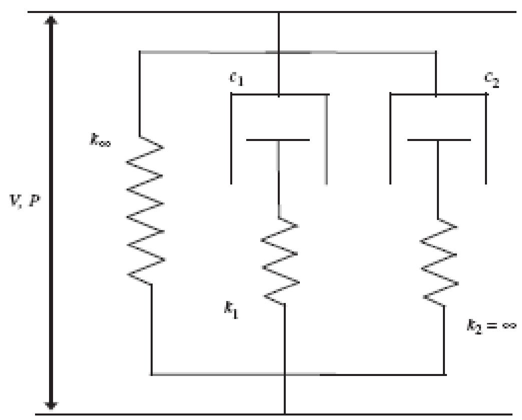

Fig.7a. Mechanical viscoelastic model, [8]

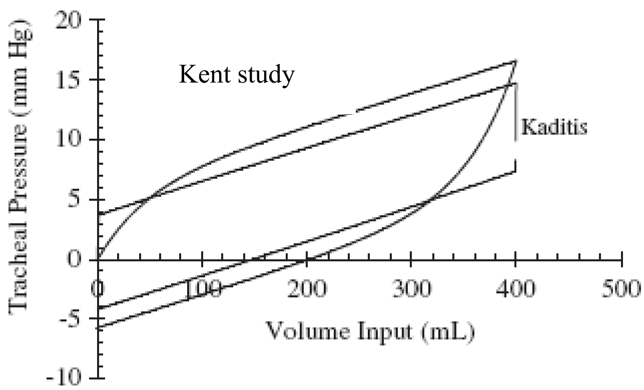

Fig.7b. Kaditis-Kent model comparison, [8]

Kent et al., [8] adopted the model of Fung, [1]:

$$P(t) = t \int_{-\infty}^{t} G(t-\tau) \frac{\partial P_e(v)}{\partial V} \frac{\partial V(\tau)}{d\tau} d\tau \qquad (2)$$

where *P(t)* is the transient change in pressure and *V(t)* is the volume of air and $P_e(V)$ is the pressure response to a step volume; both linear and nonlinear equations were considered for $P_e(V)$. the pulmonary impedance of healthy infants can be adequately described over a wide volume and frequency range using a relatively simple 5-parameter model that is linear both spatially and temporally.

Concerning newborns, Haase et al., [9], used a four parameter model for the lung, developing a new technique to estimate parameters (airway resistance, inertance, tissue damping, elastance, RIGH) of a viscoelastic lung. The nonlinear RIGH model was linearized by reparametrization and the parameters were calculated by one dimensional line search of least square estimations. The forced oscillation technique is a non invasive method for determining the frequency response of the respiratory system adequate for infants. Model linearization proved to be reliable and accurate lung mechanics parameter estimation by forced oscillation technique using a nonlinear viscoelastic model.

A theoretical model developed by Bates and Irvin, [10] concerns the role of lung periphery in determining overall lung function. The model developed, [10], is based on the hypothesis that the recruitment and derecruitment of air spaces during inspiration and expiration, one of the mechanisms that determines lung volume change, is governed by critical opening and closure pressures. The dynamic aspect to lung mechanics manifested in stress adaptation after sudden change in volume and the dependence of lung resistance and compliance on the flow frequency are considered. The mathematical/computer model of the lung produces realistic time-dependent mechanical behaviour on the basis of recruitment and derecruitment, for instance it can mimic the pressure-volume loops with an appropriate choice of parameters, Fig.8. The model can be used both in the inverse sense for extracting physiological insight from experimental data and in the forward sense as virtual laboratories for testing of specific hypothesis about mechanism.

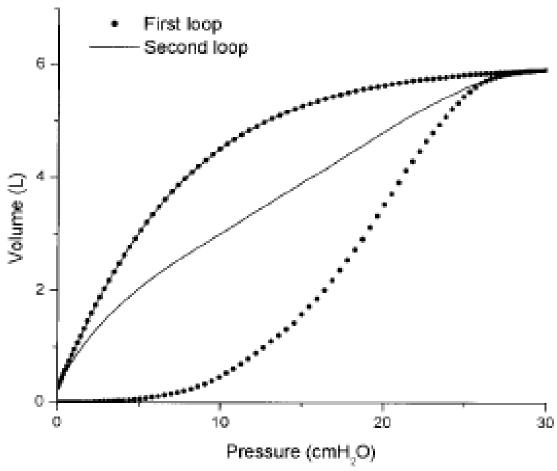

Fig.8. First and second P-V loops, model of Bates and Irvin, [10]

To model the overall function of the whole organ, knowing the mechanical properties of lung periphery is very important. From experimental methodologies the data can be interpreted in terms of inverse mathematical model, including constant phase model, [11]. Anatomically accurate forward models of the lung based on data from imaging modalities such as computer tomography and magnetic resonance imaging were recently developed.

The simplest and still most widely invoked anatomically based model of pulmonary mechanics is that consisting of a single homogeneously ventilated alveolar compartment served by a single conduit, Fig.9, [11]. The transpulmonary pressure P_{tp} across the system depends on the elastic constant E of the alveolar compartment, the flow-resistive constant R to the conduit, P_0 is the pressure across the lung at functional residual capacity and V is the volume.

$$P_{tp}(t) = R\dot{V}(t) + eV(t) + P_0 \tag{3}$$

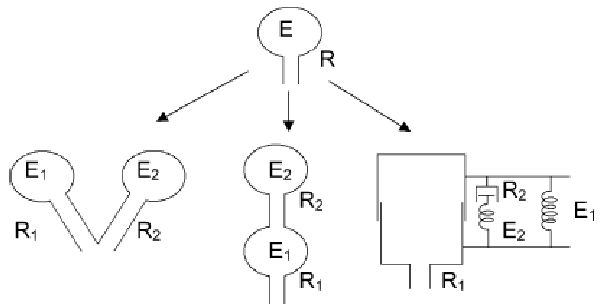

Fig.9. The single-compartment linear model and its three two compartment extensions: parallel model (left), series model (middle) and viscoelastic model (right), Bates and Lutchnen, [11]

The viscoelastic model, named Mount model, predicts the stress adaptation to a sudden change in strain will follow an exponential time course. On its basis, a constant-phase model was developed, with impedance:

$$Z_L(f) = R_N + i2\pi fI + \frac{G - iH}{(2\pi f)^{\alpha}}; \qquad \alpha = \frac{2}{\pi}\tan^{-1}(H/G) \tag{4}$$

where R_N is a Newtonian flow resistance, *I* an inertance due to mass of gas in central airways , *G* term reflecting viscous energy dissipation within tissue and *H* reflects energy storage in tissue, [11]. Using the inverse modelling approach, it is mot possible to discover a structure with wherever near the complexity of a real lung. Therefore, a major effort has focused on the use of forward modelling. The anatomy of airway tree, named Horsfield anatomy,[11], is incorporated into a computational model to predict the input impedance of the lung up to several thousand Hz. The airway tree can be encapsulated in a very efficient recursive algorithm. The forward modelling was extended to 3D, according to Bates, [11], obtaining the volume from a CT or MRI image of the thorax and then assigning mechanical properties to this model and developing an algorithm to calculate dynamic lung properties versus frequency. This model can be synthesized with ventilation imaging and oscillatory mechanics data. By extending the approach one can adjust the airway dimensions heterogeneously throughout the entire 3D model in order to best match the image based ventilation distribution; in Fig.10, an example of model predicted airway diameter distribution after constriction using ventilation images from Positron Emission Tomography. This image-functional modelling may allow for the personalized diagnosis of lung disease.

This image-functional modelling may allow for the personalized diagnosis of lung disease.
The major advantage of these models based on high resolution three dimensional imaging consists in an advance in better understanding the link between structure and function in the lung periphery.

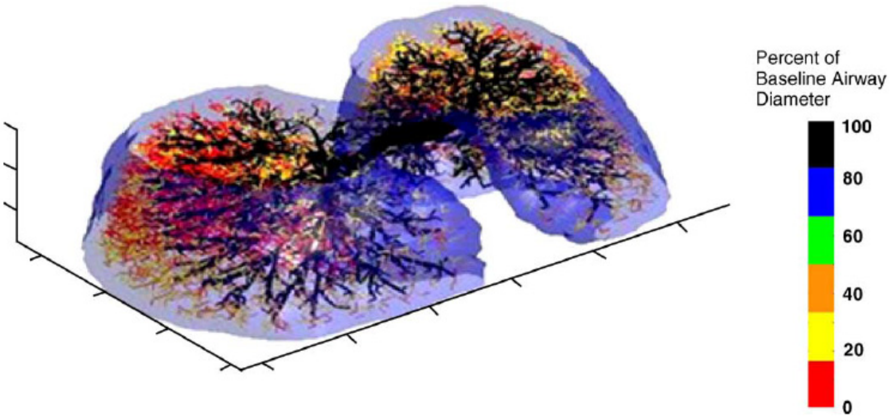

Fig.10. Color coded constriction pattern in airway tree of a computational model of the human lung, Bates and Lutchnen, [11]

Latest mathematical models based on 3D imaging tend to make a clear distinction between the central and peripheral compartments of the lung by encapsulating functional differences between the conducing airways, the terminal airways and the parenchyma, Bates and Suki, [12]. Such a distinction becomes problematic in disease because of the inevitable onset of regional variations in mechanical behaviour throughout the lung. Pathologies like asthma, acute lung injury and emphysema can alter the mechanical properties of the lung periphery through direct alteration of intrinsic tissue mechanics, development of regional heterogeneities and complete derecruitment of airspace. The combined use of direct physiological measurement, imaging and inverse modeling are now allowing understanding the contributions of the various factors to pathological alterations in lung mechanics.

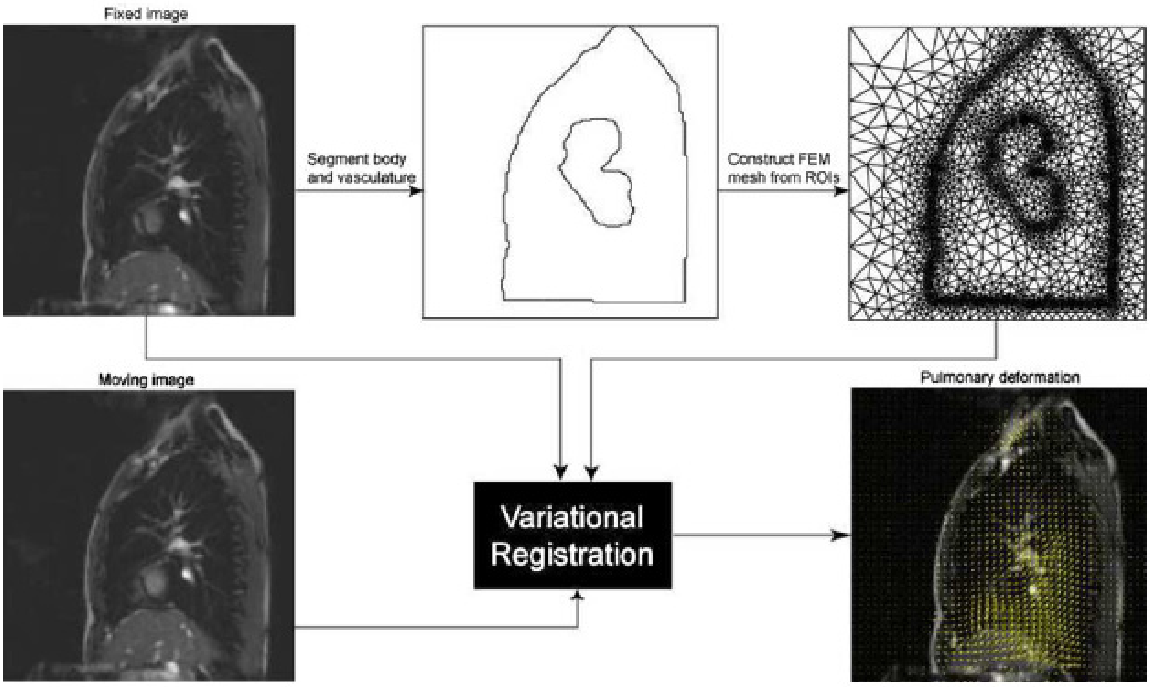

Fig.11. Use of anatomic specific meshes for registration based estimation of pulmonary deformation, Sundaram and Gee, [13]

An approach toward the quantification of pulmonary deformation via non-rigid registration of serial MR images of the lung using the variational framework implemented in the Insight toolkit was made by Sundaram and Gee,]13]. Segmentation of the body and vasculature on fixed image produces contours that are input to a freeware quality constrained mesh generator, Fig.11. The resulting finite element mesh is then the input to the variational registration along whit the fixed and moving images and use to solve the registration at anatomic sample points over the domain, [13].

The model and method provide an introduction towards biomechanical modeling of pulmonary deformation. The program is able to quantify differences in lung motion between health and disease state. These differences indirectly represent changes in the material character of the tissue which cannot directly be estimated using structural imaging modalities.

Another model based on MRI technique was developed by Tsuzuki et al., [14], who obtained 4D lung reconstruction method from unsynchronized MR sequential images. The lung does not have its own muscles and is impossible to see its real movements. The visualization of the lung in motion is an actual topic of research. Computerized tomography can obtain spatio-temporal images from heart by synchronizing with electrocardiographic eaves. The lung's movement is not periodic and is variable. Compared to CT, MR images involve longer acquisition time and it is not possible to obtain instantaneous 3D images, but only one temporal 2D image for each slice. But MR images are preferable as they do not involve radiation and Tsuzuki et al., [14], created an animated lung model based on unsynchronized images. With the algorithm developed, it is possible to reconstruct a 3D lung starting from any frame, Fig.12. Therefore, simulation, 4D modelling and visualisation of the lung was performed making possible to recognize several characteristics of the lung.

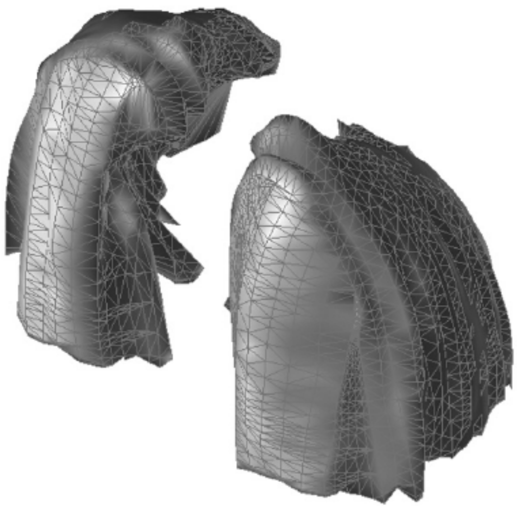

Fig.12a. Lateral view of the right and left lungs shaded and meshed, Tsuzuki et al., [14]

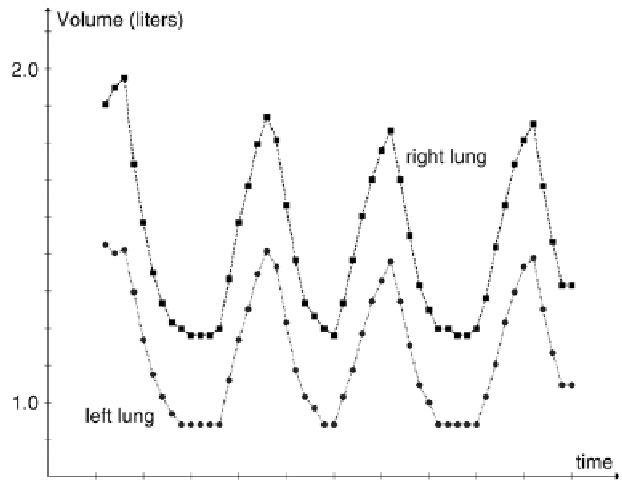

Fig.12b. Volume calculated for a sequence of MR images, Tsuzuki et al., [14]

4. CONCLUSIONS

Models are practical in understanding the physiological function or process and can lead to advance of new treatments or strategies. A model can also be used to simulate and predict a body's reaction to certain stimuli without really testing on patient. The phenomenological quasi-static stress–strain curve of lung tissue can be modelled by various models but the relationship between the molecular organisation of collagen and elastin fibres and the *in vivo* pressure-volume curve is not yet fully understood.

The mechanical model can be used for teaching and training lung mechanics, as its completely mechanical nature and simple mechanism illustrate the behaviour of different lung volumes and their interaction with the ventilator settings.

The hybrid model proved to be accurate and thus allowing to eliminate numerous *in vivo* experiments with lab animals. The hybrid model proved the advantage of flexibility, accuracy and modelling complex mechanical lung structure and function.

The advantage of nonlinear model lies in the fact that it can estimate the work of breathing for three different manoeuvres more fully and precisely than was allowed by conventional models of respiratory mechanics

The mathematical/computer model of the lung produces realistic time-dependent mechanical behaviour on the basis of recruitment and derecruitment and can be used both in the inverse sense for extracting physiological insight from experimental data and in the forward sense as virtual laboratories.

From experimental methodologies the data can be interpreted in terms of inverse mathematical model, including constant phase model. The forward modelling extended to 3D, obtains the volume from a CT or MRI image of the thorax and then assigns mechanical properties to this model and develops an algorithm to calculate dynamic lung properties versus frequency.

The combined use of direct physiological measurement, imaging and inverse modelling are now allowing understanding the contributions of the various factors to pathological alterations in lung mechanics.

The quantification of pulmonary deformation can be made via non-rigid registration of serial MR images of the lung using the variational framework. Also based on MRI technique, a model obtained extremely accurate 4D lung reconstruction from unsynchronized MR sequential images.

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