

4D Model Generator of the Human Lung, “Lung4Cer”

Hiroko Kitaoka, Salim Koc, Satoshi Tetsumoto, Satoshi Koumo,
Haruhiko Hirata, and Takashi Kijima

Abstract— We have developed a free software applications which generates 4D (= 3D + time) lung models for the purpose of studying lung anatomy, physiology, and pathophysiology. The coinage of 4C is originated from Japanese words, Catachi (= shape, structure) and Calaccli (= machine, function). *Lung4Cer* makes 4D finite element models from the trachea to alveoli, which allow airflow simulation by means of computational fluid dynamics. Visualization of the generated models is expected to use a popular free software application, *ParaView*. There are several versions of *Lung4Cer* from basic lung morphology to advanced airflow computations simulating various clinical pulmonary function tests (*PFT4Cer*). All versions are designed so as to be operated on a common PC. Users can select model types and the element number according to their purposes and available computer resources.

I. INTRODUCTION

While respiratory muscles periodically change the thoracic shape, the atmospheric air goes into the lung, and comes back from the lung. Within the lung, inhaled air is distributed according to periodic change of spatial arrangement of the lung parenchyma. Conventional respiratory physiology uses an analogy of tube-balloon combination, in which the lung parenchyma, consisting of several hundred millions of alveoli, is replaced by one or two empty air bags. However, this analogy is too simple to explain intrapulmonary phenomenon. In order to study respiratory physiology and pathology, knowledge regarding 4D (= 3D + time) structure of the lung is necessary. We have developed free application software which generate 4D lung models based on four algorithms previously published [1-4]. Several algorithms are added which convert geometric models into 4D finite element (FE) models for airflow simulation by the use of computational fluid dynamics (CFD). Thus, generated model has one continues surface of the air pathway from the trachea to alveoli.

The application software is named “*Lung CataChiCalaCli-er*”, alias “*Lung4Cer*”, which consists of two Japanese words, Catachi (= shape, structure) and Calaccli (= machine, function). Furthermore, Catachi consists of Cata and Chi, and Calaccli consists of Cala and Cli. These four words, Cata, Chi, Cala, and Cli mean space, energy, action, and periodic time,

H. Kitaoka is a science advisor of JSOL Corporation, Nagoya, Japan (corresponding author to provide phone: +81-52-253-8181; fax: +81-52-253-8172; e-mail: hirokokitaoka000@hotmail.com).

S. Koc is with Division of Engineering Technology, JSOL Corporation, Nagoya, Japan (e-mail: koc.salim@jsol.co.jp).

S. Tetsumoto, S. Kohmo, H. Hirata, and T. Kijima are with Department of Respiratory Medicine, Osaka University Graduate School, Suita Japan (e-mail: satotetsu1210@yahoo.co.jp, skomotosi@gmail.com, charhirata@imed3.med.osaka-u.ac.jp, tkijima@imed3.med.osaka-u.ac.jp).

respectively. Indeed, they are the most basic concepts of physics. Therefore, CataChiCalaCli (alias, 4C) is thought to be an adequate word indicating 4D behaviors of the living structure.

We have released several versions of *Lung4Cer* since 2011. The original version is only for visualization so as to be operated by a Windows 32-bit PC with memory below 2GB. *Lung4Cer* generates a text file which is visualized by a free software application, *ParaView*. It is one of the most popular visualization software developed in the US, and easily obtained via internet. All pictures presented here are generated by *ParaView*. Pathologic *Lung4Cer* (*PL4Cer*) is a pathologic version for simulating histologic sections of micro structures in the lung diseases. Those versions are useful for basic education for lung anatomy and pathology.

CFD4Cer is designed so as to output a file set for simulating airflow during breathing by the use of computational fluid dynamics (CFD). Since CFD requires much more shape information than only visualization, it requires a 64-bit PC with memory more than 2GB. *PFT4Cer* is an advanced version of *CFD4Cer* for simulating clinical pulmonary function tests (PFT). All versions can be downloaded through the first author’s personal homepage (<http://www.7b.biglobe.ne.jp/~lung4cer>).

Although *Lung4Cer* provides mathematically constructed virtual models at present, it is possible to incorporate individual information obtained from clinical image data in the near future. In this paper, we will introduce the original version of *Lung4Cer* and *PFT4Cer*.

II. ORIGINAL VERSION OF *Lung4Cer*

A. Basic constitutions

Lung4Cer can potentially make a whole airway tree model with several hundred million alveoli. However, it requires extremely huge amount of computer resource. Instead, it is feasible to select a model type according to user’s interest and available computer resource. Fig.1 shows a parameter box in *Lung4Cer*.

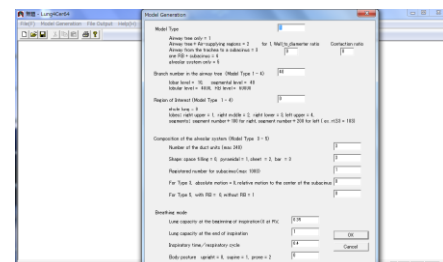


Figure 1. Main window and a parameter panel in *Lung4Cer*.

Model types are: (1) airway tree only, (2) airway tree with air-supplying parenchymal regions, (3) air pathway from the trachea to a subacinus with alveolar structure, and (4) alveolar system only. “Branch number in the airway tree” assigns the anatomical hierarchical level of terminal branches in the airway tree. Segmental bronchi are generated when the number is 40. Lobular bronchi are generated when it is around 4000. “Region of Interest” assigns a target region for modeling, from the whole lung down to lung segments. There are four parameters to assign breathing mode, lung capacities at the beginning and the end of inspiration, time ratio of inspiratory phase to the respiratory cycle, and the body posture. When the time ratio is assigned at 1, the respiratory motion is set for only inspiration. If the lung capacity at the beginning is smaller than that at the end and the time ratio is 1, the respiratory motion is set for only expiration.

After assignment of necessary parameters for model generation, a sequential set of files for finite elements (triangles for surface) are generated.

B. Model examples

B-1. Airway tree model with five lung lobes

The left part in Fig.2 depicts a lobar bronchial tree model with five lobes at total lung capacity (TLC). Ends of lobar bronchi are continuously connected with their corresponding lobes. Lobes are expressed as sets of cubes whose side lengths are equal to diameters of their corresponding bronchi. In this model, inside of five lobes are empty in order that inner structures may be observed simultaneously as shown in the right part in Fig.2. This airway tree model consists of 2,921 bronchi. Each bronchus is colored according to its belonging lung segment. This model is useful for learning lung segmental anatomy in relation to radiologic diagnosis of lung diseases.

B-2. Air pathway model from the trachea to alveoli

The lung consists of about three hundred millions of alveoli, tiny air bags with the size of about 0.3 mm [5]. The pulmonary acinus is defined as the respiratory unit supplied air by a terminal bronchiole, whose diameter is about 0.5 mm and whose total number is about 30,000[5]. The pulmonary acinus contains about eight last respiratory bronchioli, which supply air to the respective subacini. One subacinus contains about a thousand alveoli in average.

Fig.3 indicates an air pathway model from the trachea to alveoli in a subacinus in the basal posterior segment of the right lower lobe (rS10). The upper and lower rows indicate at functional residual capacity (FRC) and TLC, respectively. The last respiratory bronchiole is the 19th generation with 0.37 mm in diameter at TLC. The left column shows the whole pathway at foot-to-head direction. The central column shows horizontally thin-sliced images of the subacinus with 0.25 mm in thickness. The whole shape of the subacini is translucently superimposed. Net-like patterns of the alveolar wall at FRC and TLC are apparently different because of the alveolar structural change, although the present clinical CT can detect only the change of CT value, which is proportional to the tissue density of the lung parenchyma.

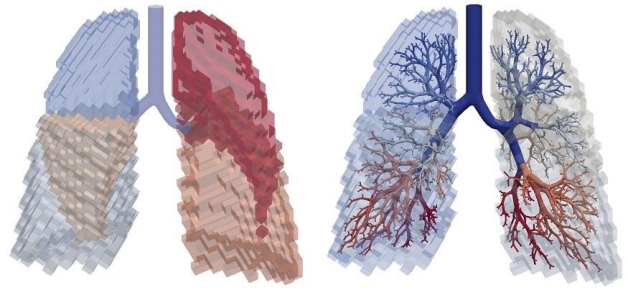


Figure.2. Airway tree model with five lobar lobes.

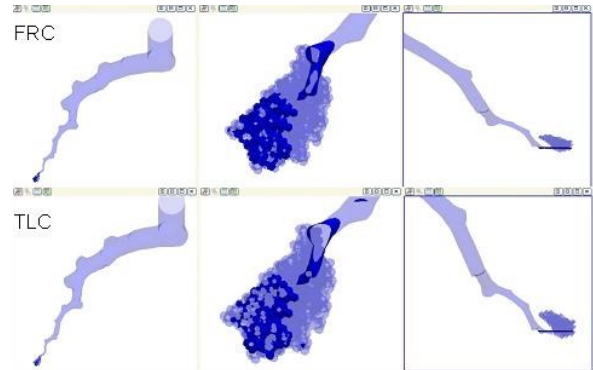


Figure.3. Air pathway model from the trachea to alveoli

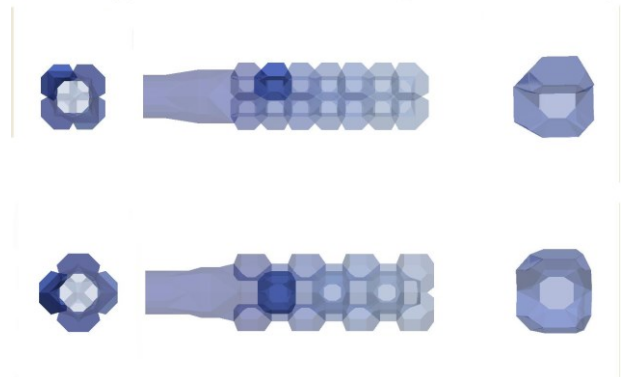


Figure.4. Straight alveolar duct model at FRC

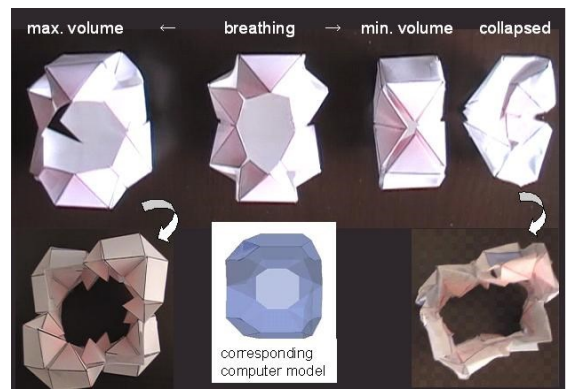


Figure 5. Origami models for single alveolus and alveolar duct unit.

3-3. Alveolar duct model

The alveolus is a tiny air bag whose mouth is open to the alveolar duct. The alveolar duct is an air pathway connecting to the bronchiole and its wall is completely replaced by the alveolar wall. Fig. 4 shows a straight alveolar duct model at FRC. The view angles are different at 45 degrees between the upper and lower rows.

Lung4Cer contains Origami models for the alveolar duct nearly equivalent to the computer model, as indicated in Fig.5. It is known that the elastin fibers are mainly distributed at the alveolar mouth [6] and that the alveolar mouth is narrowed as the lung volume decreases [7]. As shown in Fig.5, when the alveolar mouth is folded up, inner diameter of the alveolar duct becomes small, because dihedral angles between walls become small. When the alveolar mouth is completely folded, the mouth is closed and the alveolar duct volume reaches the minimum. Since the Origami patterns are included in the manual for *Lung4Cer*, users can make an alveolar duct model by themselves and handle the model in reality. They can feel the airflow on their palms while contracting the model with both their hands.

III. PULMONARY FUNCTION TEST VERSION, *PFT4Cer*

Ventilation is air shift generated by displacements of intra-pulmonary structures associated with the thoracic wall motion. Therefore, a 4D finite element (FE) model enables us to simulate airflow in the lung during breathing by solving incompressive Navier-Stokes equation under moving boundary conditions [8]. The CFD version of *Lung4Cer* (*CFD4Cer*) generates a mesh file set for a CFD solver. Although the file format in the present version is for a certain commercial CFD solver (*AcuSolve*, Altair Engineering Co., USA), the file conversion into another CFD solver is possible because all files *CFD4Cer* generates are text files. *PFT4Cer* is the advanced version for simulating clinical pulmonary function tests. The total computing time for modeling, CFD, and visualization is less than one hour with a 4-core PC.

A. Flow-volume curve

Flow-volume curve is the most commonly used for diagnosis of airflow limitation. The lung volume during maximum forced expiration is expressed by an exponential function of time where the time constant is given by the product of the airflow resistance and the lung compliance if they are constant. At that time, the slope of the flow volume curve is linear, but the slope becomes concave if the airflow resistance largely increases during expiration. Therefore, the deformation of the lung model was assigned by the value of lung compliance (= constant) and the value of airflow resistance (= variable). Since the most effective site for changing the airflow resistance is the trachea, and the airflow resistance is given by the ratio of the mean alveolar pressure to the airflow rate, the most suitable tracheal deformation was inversely obtained by computing the pressure distribution during expiration. As shown in Figure 6, a flow volume curve typical of pulmonary emphysema is obtained by the combination of high lung compliance and the tracheal

dynamic deformation where the tracheal diameter is reduced down to 50 % between 0.1 and 0.3 sec after the beginning of expiration. When the trachea is unchanged (left part in Fig.6), the descendent limb of flow volume curve is linear.

B. Respiratory impedance by forced oscillation technique

Respiratory impedance measured by the forced oscillation technique is now in clinical use because the measurement can be performed without efforts [9]. However, interpretations of measured values have been unclear. We have constructed a 4D lung model in which the lung displacement due to forced oscillation is superimposed on the breathing motion. We simulated airflow during forced oscillation with CFD, and calculated the respiratory impedance caused by airflow with Fourier transformation function in Excel (MicroSoft Inc., USA). Figure 7 shows a simulation example of 5 Hz forced oscillation during resting expiration where the airflow rate and mean alveolar pressure are computed. The airflow impedance at the peak flow in this case is calculated at $1.68 - 0.5i$ (cmH₂O/L/s). In order to compare it with the real value of respiratory impedance, the airflow resistance in the upper airway and the respiratory tissue resistance should be added to the real part, and the reactance caused by the respiratory compliance should be subtracted from the imaginary part.

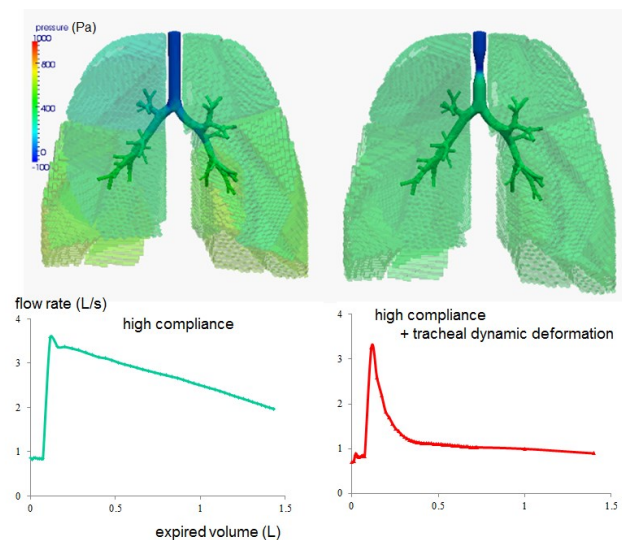


Figure 6. Flow-volume curve simulation

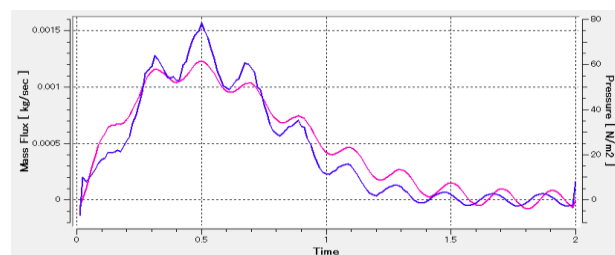


Figure 7. Airflow rate and pressure during expiration with 5 Hz forced oscillation.

C. Single-breath nitrogen washout test

The single-breath washout test has been regarded as a sensitive test for detecting small airway obstruction for decades [10], although there have been no experimental evidences [4]. Our 4D alveolar model has proved that closing volume is due to not small airway closure but the contraction limit of the lung parenchyma at which the alveolar mouth is closed in normal subjects [3, 4]. Figure 8 indicates how the nitrogen concentration distribution changes while the test is performed in normal condition.

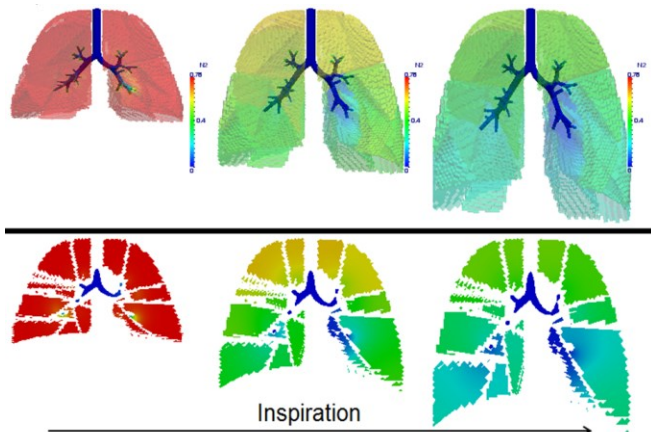


Figure 8a. Nitrogen concentration distribution during inspiration in single-breath washout test

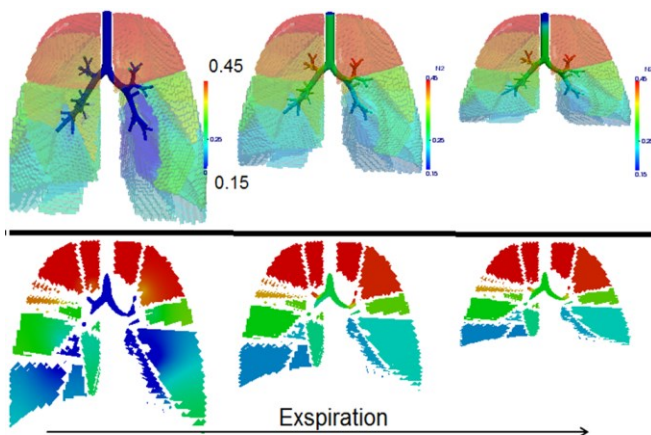


Figure 8b. Nitrogen concentration during expiration. Note color scale is smaller than that in Fig. 8a.

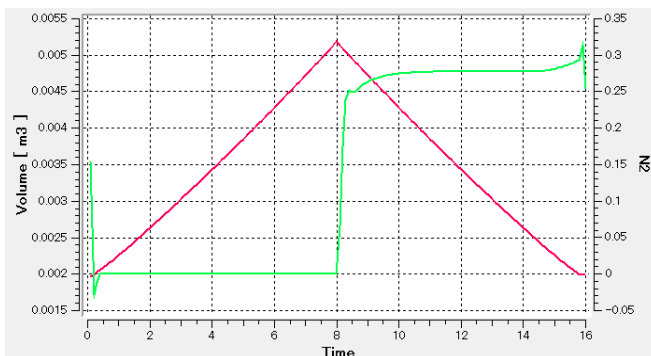


Figure 8c. Expired airflow rate and the nitrogen concentration

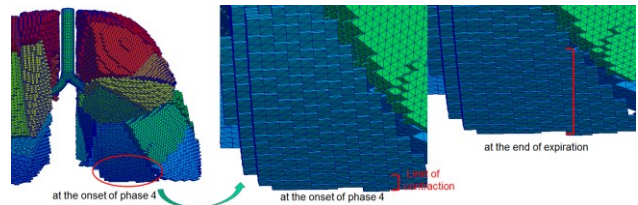


Figure 9. Deformation of the lung parenchyma in the most dependent zone at upright posture

Fig. 9 shows how the lung parenchyma in the most dependent zone is deformed during the phase four, regardless of small airway closure.

IV. DISCUSSION AND CONCLUSION

Conventional textbook tells little regarding alveolar motion during respiratory cycle. *Lung4Cer* has brought a new concept of “breathing alveoli” which play essential roles both for ventilation and gas exchange. Furthermore, *PFT4Cer* has revealed that clinical pulmonary function tests should be reconsidered in terms of fluid dynamics apart from conventional electric circuit analogy. Although the present model is purely geometric, a patient-specific model based on clinical image data will be obtained in the future, and more precise simulation will be performed. The 4D respirolgy is now beginning.

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