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Estimation of the Site of Wheezes in Pulmonary Emphysema: Airflow Simulation Study by the Use of A 4D Lung Model

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Abstract— **Adventitious lung sounds in pulmonary emphysema, wheezes, are continuous musical sounds during expiration with 400 Hz or more. The textbook tells that expiratory airflow limitation in emphysema occurs at the peripheral airways and that wheezes are generated there. We have recently proposed a novel hypothesis based on image analysis and theoretical consideration that expiratory airflow limitation in emphysema occurs at the intra-mediastinal airway (trachea, main bronchi, and right lobar bronchi) due to compression by overinflated lungs. We performed expiratory airflow simulation by the use of a 4D finite element lung model, and found periodical vortex release with 300-900Hz at the end of protrusion of the the tracheal posterior wall. Relationship between the peak frequency of pressure fluctuation and airflow velocity was in agreement with Strahal's law either in normal or emphysematous condition. Contrarily, airflow simulation in a small bronchus (1.5 mm in diameter) indicated no apparent periodic vortex release.**

I. Introduction

Wheezes, the most common adventitious lung sounds in pulmonary emphysema and bronchial asthmatic attack, are continuous musical sounds during expiration with the duration of more than 250 ms and a dominant frequency of 400 Hz or more [1]. Even in normal subjects, wheezes are sometimes audible during forced expiration. The origin of wheezes is thought to be interaction of turbulent airflow (vortex) and the airway wall oscillation. It has been generally believed that expiratory airflow limitation in emphysema occurs in the small airways and that expiratory wheezes are generated there. However, wheezes are often audible directly around patients. In contrast, fine crackles, generated in the lung parenchyma, are never audible without stethoscope. Are wheezes in emphysema really generated in lung periphery?

Gavriely et al. indicated experimentally and theoretically that airflow limitation was a necessary condition for the generation of forced expiratory wheezes [2]. They also indicated that sufficient levels of effort and negative transmural pressure must exist before generation of wheezes in order to induce flattening of intra-thoracic airways downstream from the choke point [3,4]. In other words, wheezes are never generated without airflow limitation. Does the airflow limitation in emphysema really occur in the small airways ?

In 1963, Reiner et al. observed severe tracheal collapse during maximum forced expiration in emphysema patients with cine bronchography [5]. Since the posterior wall of the intra-mediastinal airway (intra-thoracic trachea, bilateral main bronchi, and right lobar bronchi) consists of smooth muscles without cartilages, it is called "membranous part" and is deformable according to its muscular contraction and the transmural pressure. Indeed, the experiments by Gavirly et al indicated that airflow limitation and wheezes occurred at the trachea in normal subjects [4].

Although Reiner et al. reported that the airflow limitation in emphysema occurred there, the small airway obstruction hypothesis proposed by Millic-Emmilli's group [6] has been accepted in the American Thoracic Society for several decades. Recently, Wright stated that expiratory collapse of the trachea and main bronchi is a form of tracheobronchial malacia, which often, but not always, is associated with chronic obstructive pulmonary diseases (COPD) [7].

We think that tracheobronchial malacia associated with COPD should be regarded not primary but as secondary change caused by frequently repeated expiratory collapses due to pulmonary emphysema. We have stated for these years based on theoretical reconsideration of single-breath nitrogen washout curve that the small airway obstruction hypothesis are wrong [8]. Furthermore, we have stated based on volumetric investigation using inspiratory and expiratory 3D CT images that the airflow limitation in emphysema are intra-mediastinal airway [9].

Fig. 1 shows a sequential 2D electron beam CT image set during tidal breath of a 61-year-old male emphysema patient (Courtesy of Prof. Hajime Kurosawa, Tohoku University, Japan). (A) Just before the beginning of expiration, the tracheal space is nearly round. (B) Just after the beginning of expiration, the membranous part is shifted into the tracheal space (C) During expiration, the membranous part keeps concave. The tracheal cross section area during expiration is about 70 % of that during inspiration. Although the degree of deformation is much smaller than that during maximum forced expiration as reported by Reiner et al.[5] and Wright et al.[7], the difference in the tracheal cross sectional area between inspiratory and expiratory phases shown in Fig. 1 is consistent with the difference in respiratory resistance between inspiratory and expiratory phases at rest.

The reason why emphysema causes the expiratory tracheal deformation is schematized in Fig. 2 [9]. In normal condition, the lungs and the thoracic space expand at the same ratio during inspiration. Therefore, the intra-mediastinal airway (IMA) expands enough wide at end-inspiration. On the other hand, in emphysema, the thoracic wall cannot expand like the emphysematous lung, because the distensibility of the

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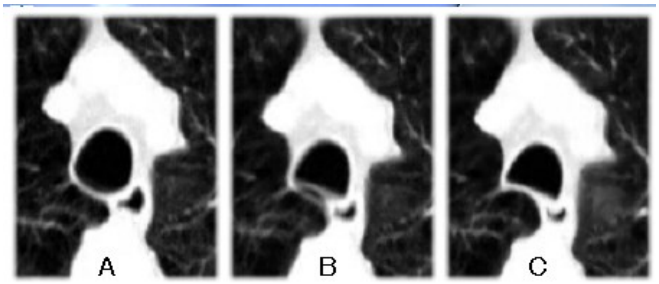

Figure 1. 2D dynamic CT images of the trachea during resting expiration of a pulmonary emphysema.patient. Just before (A) and after (B) the beginning of expiration, and during expiration (C).

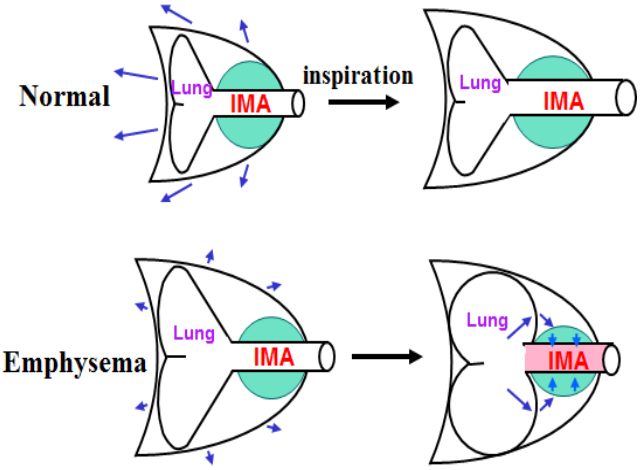

Figure 2. Volume changes in the thorax during breathing. IMA: intra-mediastinal airway.

thoracic wall is close to the limit even at functional residual capacity. Hence, the mediastinal space including the airway space is relatively narrowed at end-inspiration. The reason why tracheal deformation during maximum forced expiration is much severer than that at rest is thought due to the difference in airflow velocity. The higher velocity generates more negative pressure inside of the trachea according to Bernoulli's theorem. We therefore hypothesize that airflow limitation and wheeze generation occur at the deformed trachea in emphysema patients.

Although Gavriely et al. pointed out the importance of fluid force [5], their simulation works were not based on computational fluid dynamics (CFD). Since material properties and boundary conditions of the tracheal wall and surrounding organs are unknown, it is impossible to numerically solve this fluid-structural interaction. However, airflow through the airway can be analyzed under a moving boundary condition [10], if its shape and motion are given adequately based on clinical image information. In this paper, we estimated the sound source of wheezes by airflow analysis with CFD.

II. Methods

A. 4D finite element lung model

A 3D finite element (FE) lung model was constructed geometrically as shown in Fig.3. Displacements of all nodes for all time steps were assigned in order that all solid elements could keep their Jacobians positive in spite of deformation. Therefore we call such a FE model 4D-FE model. A cylindrical trachea opened to the atmosphere at the position of the subglottic cavity. The diameter of the trachea was assigned at 18 mm at TLC, and decreased proportionally as the lung volume decreased through expiration. The diameter after expiration of 2.5 L was 14.2 mm. The lung part was a set of cubes whose side lengths were equal to the tracheal diameter. The lung part was not empty but had branched air pathway with the same width as the tracheal diameter [11].

The tracheal part consists of very fine meshes (3,132,608 tetrahedrons with 592,385 nodes) and lung parts consist of coarse meshes (59,944 tetrahedrons with 17,539 nodes). The circumference of the tracheal cylinder was equally divided into 64 segments and the radius was unequally divided into 24 segments. The cubic unit of the lung part is divided into 24 congruent tetrahedrons.

Three conditions corresponding to normal expiration without tracheal deformation (Case1), normal forced expiration with slight deformation (Case2), and emphysematous expirations with severe deformation (Case3) were assigned as shown in Fig.3. Case 2 is corresponding to resting expiration in an emphysema patient as shown in Fig. 1. In Cases 2 and 3, membranous parts are protruded at 20 % and 80 % of the inner diameter, respectively, with a range of 35 mm in length. In Case 3, slight bilateral tracheal deformations were added corresponding to oppression by overinflated lungs.

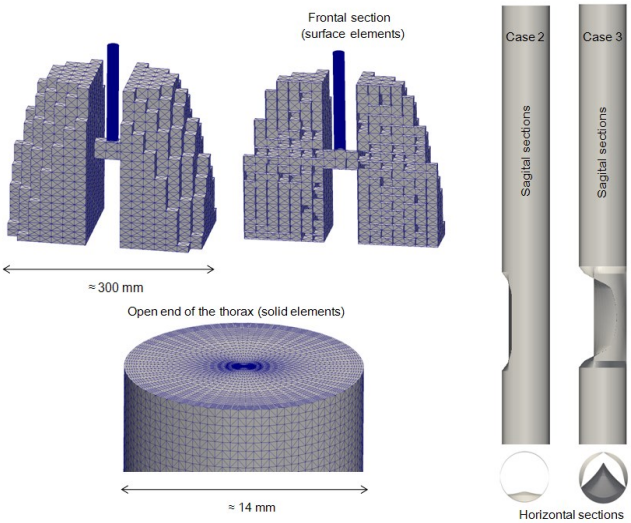

Figure 3. 4D finite element model of the whole lung with the intra-thoracic trachea

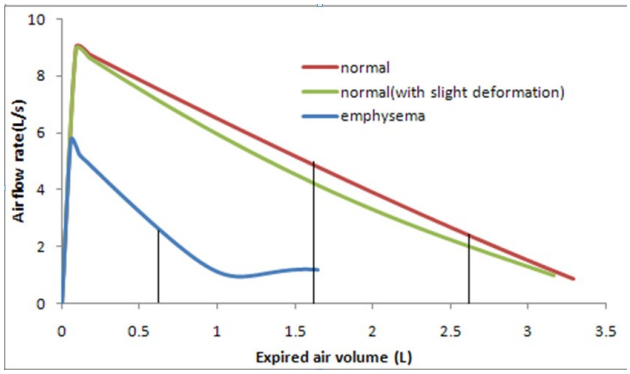

Figure 4. Maximum forced expiratory flow volume curves for three cases

It is known that the upper limit of expiratory airflow at any lung volume is not dependent of effort but determined by elastic recoil of the lung. We simulated flow-volume curve during forced expiration in the normal condition (Case 1) under the assumption of constant lung compliance and airway resistance. In this case, the pressure was described by an exponential function with time constant of the product of the compliance and the airway resistance. For other cases, the airway resistance changed during expiration corresponding to tracheal deformation. Fig.3 indicates forced expiratory flow-volume curves for three cases during one second. Airflow simulations for estimating sound sources were performed on three black lines, 0.6 L, 1.6 L and of 2.6 L in expired air volumes. The airflow rate was assigned less than the upper limits which were given by the maximum forced expiratory flow volume curve shown in Fig.4.

B. Airflow analysis by the use of CFD

Airflow analyses for three cases were performed by the use of finite element CFD software (AcuSolve, Altair Engineering Inc., USA). Time step was assigned at 0.0001 sec. for all cases in the period of 0.02 or 0.04 sec. The airflow velocity distribution was obtained by solving incompressible Navier-Stokes equation under moving boundary conditions using arbitrary Lagrangean-Eulerean method and the least square Galerkin method [10]. All nodes in the model were displaced homothetically at every time step so as to exhale air at the tracheal open end with a constant flow rate. The boundary condition of the open surface of the trachea was assigned at zero pressure.

Dynamic LES (large eddy simulation) model was applied to turbulent flow [12].

III. Results and Discussion

Fig. 4 indicates velocity (left) and pressure (right) fields in the tracheal central sagittal section for all cases at the flow rate of 1.5 L/s at the 150th time step (=0.015 sec after the beginning computation). The maximum displacement distances of the posterior wall were 2. 8 mm in Case 2 and 11.2 mm in Case 3. The maximum velocity in Cases 1 and 2 were about 20 m/s, and that in Case 3 was about 58 m/s.

In Cases 2 and 3, there are periodic pressure fluctuations in the downstream of the protruded portion in Fig. 5, which suggest vortex release at the end of the protruded portion. Fig. 3 indicates pressure fluctuation and its Furrier transformation in Case 2 (measured at the point of white asterisk) with the range from the 72th to 199th time steps (from 0.0072 sec. to 0.0199 sec.). There is an apparent peak at 640 Hz of the pressure fluctuation.

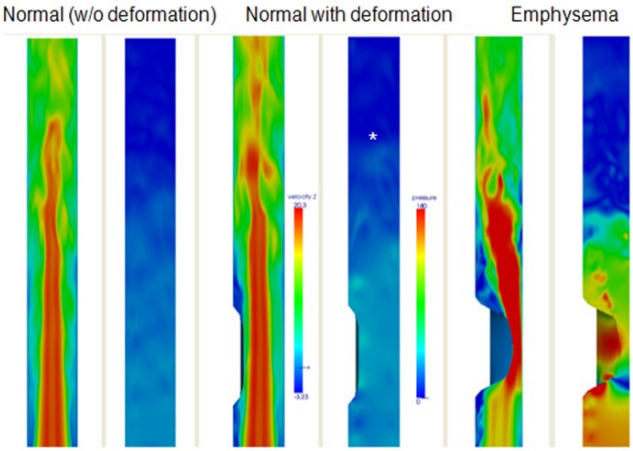

Figure 5. Velocities and pressures at the center of the trachea in three cases with the airflow rate of 1.5L/s

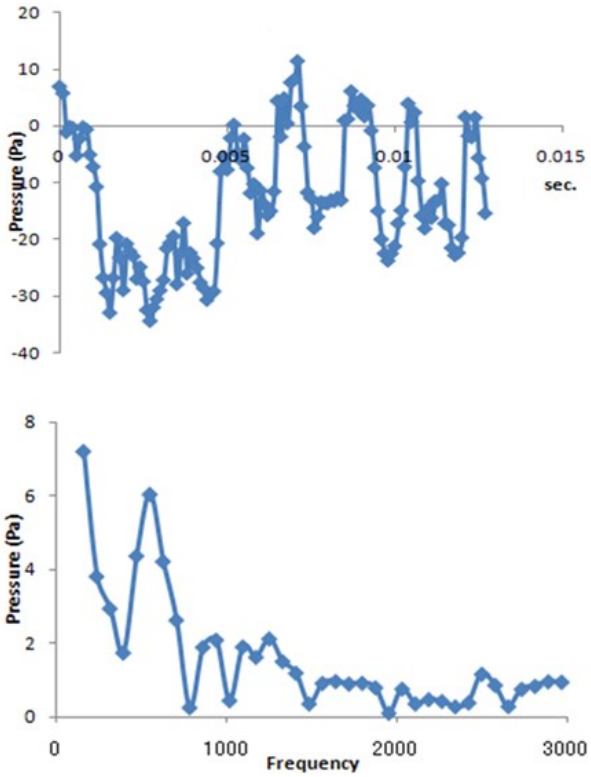

Figure 6. Pressure fluctuation in Case 2 with flow rate of 1.5L/s (upper) and its Fourier transformation (lower)

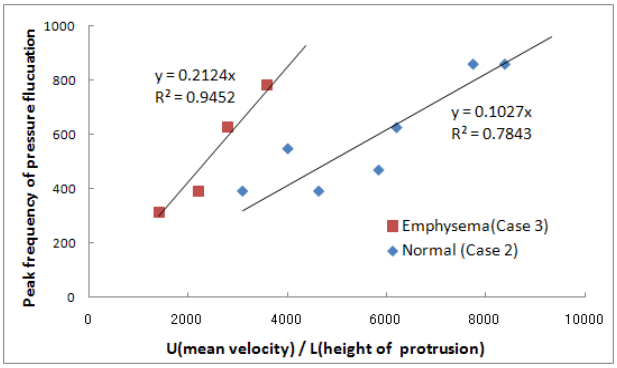

Figure 7. Relationship between peak frequency, mean velocity, and height of protruded part of the tracheal wall.

There is a classical relationship regarding generation of Kalman vortex between vortex frequency (f), flow velocity(U), and diameter of an obstacle in the flow (L)

$f = \mathrm{St} \cdot U/L$

, where St is Strahal number. We regarded the maximum displacement distance of the posterior wall as diameter of an obstacle and investigated relationships between peak frequency of pressure fluctuation and U/L for various airflow rate and lung volume. As shown in Fig. 5, there were agreements with the above equation in which St = 0.1 for slight deformation and 0.2 for emphysematous conditions. The value of 0.1 was interpreted that the slight protrusion was equivalent to a hemi-cylindrical obstacle. For Case 1, no frequency peak was found below 1,000 Hz.

Airflow simulation through the peripheral airway was performed using the same model with the scale of 1/10, corresponding to the lobular bronchus and its air-supplying lobule. No frequency peak was found beyond 200 Hz within the narrowed lobular bronchus.

IV. Conclusions

The present simulation study has strongly suggested that the origin of expiratory wheezes in emphysema is pressure fluctuation of the expiratory airflow generated by tracheal deformation and that this pressure fluctuation may cause fluttering of the tracheal wall, although complicated interactions between flow and tissues may modify the sound property. Not all, but some types of wheezes in asthma patients may occur by the same mechanism due to sudden overinflation of the lung caused by asthmatic attack.

The pulmonary emphysema has been regarded as one of phenotypes in COPD, in which the alveolar wall destruction is the secondary change due to air trapping caused by small airway obstruction. Our present work and past studies by Gavriely et al. [3-5] are inconsistent with the current concept. The concept of COPD should be reconsidered based on biomechanical grounds.

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