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Numerical Study on the Effect of Nerve Control on Upper Airway Collapse in Obstructive Sleep Apnea

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Abstract: Obstructive sleep apnea syndrome (OSAS) is a respiratory disease characterized by the upper airway collapses and reopens repeatedly during sleep. Though the nerve control plays a key role in the upper airway collapse, it has been considered in previous studies only with lumped parameter models. Based on a finite element model including airway and surrounding structures, the effect of nerve control on the upper airway collapse was studied with fluid-structure interaction method. Spring elements were used to simulate the function of the muscle group. The simulation results show that the nerve control reduces the deformation of airway successfully and avoids the risk of OSAS.

Keywords: Upper airway collapse, fluid-structure interaction, nerve control, finite element analysis, biomechanics.

1 Introduction

Obstructive sleep apnea syndrome (OSAS) is a respiratory disease characterized by the upper airway collapses and reopens repeatedly during sleep. The collapsed airway restricts or even blocks the airflow totally until the obstructive site disappears (Fig.1).

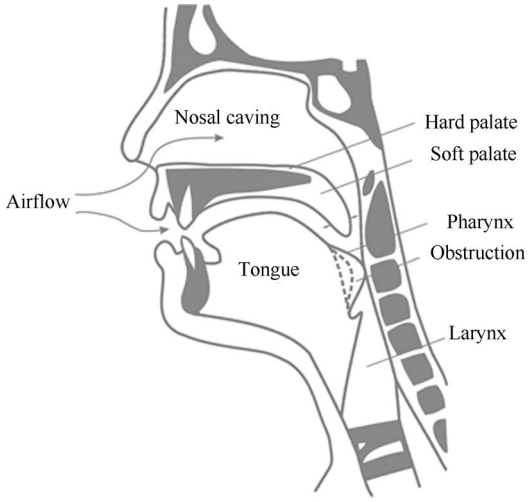

Fig. 1 Obstructive sleep apnea syndrome

Severity of OSAS is measured by the apnea-hypopnea index (AHI, defined as cessation of airflow for at least 10 s). The hypopnea was defined by one of three features: substantial reduction in airflow ($> 50\%$), moderate reduction in airflow ($< 50\%$) with desaturation ($> 3\%$), or moderate reduction in airflow ($< 50\%$) with electroencephalographic evidence of arousal.

The most representative symptoms of OSAS are snoring and excessive daytime somnolence. Not only the terrible snoring caused by rapid obstruction and reopening of the airway annoys the surrounding people and disturbs their sleep, but also the arousal resulted from hypopnea and apnea makes the duration of the sleep segmented, which lead to sleepiness in the daytime. Moreover, other correlative symptoms might occur in some patients, such as abnormal actions during sleep (somnambulation, etc.), confusion of the sleeping period, and arrhythmia.

The cessation and limitation of the flow in the airway directly decrease the oxygen and increase carbon dioxide in blood, which then lead to hypercapnia, hyoxemia, and lower pH value in blood. Lack of oxygen in the blood and repetitive arousal will stimulate the sympathetic nerve, and then make the capillary blood vessel contract, finally leading to hypertension, myocardial infarction, stroke, and congestive heart failure. In addition, some patients even die during sleep because of severe arrhythmia or myocardial infarction. Furthermore, fragmentation of the sleep will result in the excessive daytime somnolence, which will decrease quality of life, and increase risk of motor vehicle and occupational-related accidents. Therefore, OSAS is a latent lethiferous disease indeed.

Results from studies in Wisconsin, Pennsylvania, and Spain show that roughly 1 of every 5 adults has at least mild OSAS and 1 of every 15 persons has at least moderate OSAS. The prevalence varies with gender, age, and race and ethnicity of people. Men seem to be more susceptible to the disease than women according to the statistics from

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most studies, a 2-fold to 3-fold greater risk for men compared with women. A steady raise of prevalence occurs to the population in midlife, and some studies have estimated that the prevalence in the population older than 65 years is approximately 3-fold higher than those in middle ages[1].

The pathogeny of the OSAS is complicated. The pathophysiological process is a combination of passive mechanical properties and active neural mechanisms, and the exact cause of the disease is still unclear.

The configurations of the upper airway of human beings are similar. Being the pathway of both air and food, the upper airway displays a compromised character—a collapsible tube.

Abnormal anatomical structure is one of the important factors that can cause OSAS. Some inherent configuration of upper airway, such as palatopharyngeal stenosis, will remarkably increase the airflow resistance which gives rise to a sharply declining pressure gradient, therefore the airway collapses under the large negative internal pressure. Nevertheless, although the upper airway structures of some OSAS patients are similar, the degree of severity differs greatly from each other. Moreover, the breath apnea occurs only at night instead of daytime. Based on these two phenomena, a hypothesis can be made that besides abnormal anatomical structure, weak or absent nerve control on respiration is another important factor that can bring about OSAS.

Required by the needs of speech, swallowing, respiration and other physiological function of the upper airway, more than 20 significant muscles take part in the complex motor control system[1]. The muscles which constrict and dilate the airway lumen can be classified into four groups: muscles regulating the position of the soft palate (alai nasi, tensor palatini, levator palatini), tongue (genioglossus, geniohyoid, hyoglossus, styloglossus), hyoid apparatus (hyoglossus, genioglossus, digastric, geniohyoid, sternohyoid) and the posterolateral pharyngeal walls (palatoglossus, pharyngeal constrictors)[2]. These groups of muscles interact in a complex fashion to determine the patency of the airway. Then, genioglossus which attracts most investigators′ attention might be the key factor of the upper airway patency[2−4].

There are evidences from research results that can confirm the important role of muscle excitability on respiration[5−13]. With the help of polysomnography, it can be found that neuromuscular myoelectricity around upper airway is higher for OSAS patients than normal persons in the daytime while it drops sharply during sleep especially rapid eye movement sleep. This phenomenon is most obvious among hypoglossal and genioglossus muscle. Moreover, there exist several types of neurotransmitters distributed around the airway wall which can apperceive the change of physical or chemical environment, such as pressure variation inside the airway or the fluctuation of oxygen saturation in blood. This information is transmitted by neurotransmitter to the respiratory central nervous system which is in control of the hypoglossal motor neurons that innervate the muscles associated with upper airway. In other words, the control strength of muscles on upper airway varies with some physical and chemical parameters which reflect the breath state under normal circumstances.

Usually, the pressure inside the upper airway is in negative state during the normal inspiration. However, the initial stiffness and correlative muscles group can keep the airway from collapse, and the airflow can pass through without restriction. Contraction or relaxation of muscles group is under respiratory nerve centre′s control according to the actual breath condition. As for OSAS patients, the muscle′s activity involved in respiration is more exciting than normal people in the daytime in order to make up for some inherent structural defect, yet this compensatory mechanism falls off or even disappears at night. So some part of the upper airway becomes prone to collapse during sleep even under a slight negative pressure and the apnea continually occurs as a consequence. From the mechanical point of view, the breathing process is in fact a mechanical problem with fluid and structure interaction.

The motion state of upper airway in breath apnea can be studied with mechanical methods. The biomechanical models of OSAS can be classified into two main types: namely lumped parameter models and distributed parameter models. Lumped parameter models take advantage of quickly and conveniently studying how the sleep apnea develops as each control parameter changes. But it can give only qualitative descriptions. It is necessary to develop a mechanical model which not only possesses high geometrical similarity and material similarity but also reflects real physiological respiratory conditions. In recent years, finite element method was more and more applied to study the mechanism of OSAS. Some studies focused on the air flow patterns, while others focused on numerical methods of fluid-solid interaction. Unfortunately, there are few numerical studies of OSAS considering nerve control by now. The purpose of this paper was to study the effect of nerve control on OSAS based on a three-dimensional finite element model of the upper airway developed previously[14−16].

2 Finite element modeling

The computed tomography images from a 26-year-old male person were used for finite element modeling. The segmentation of different structures and tissues were conducted in the medical images processing software Mimics 10.0. The geometrical data were then imported to the software Geomagic studio 10 for building non-uniform rational B-spline surfaces. The whole model was assembled in Ansys 11.0. Due to the complexity, all parts of the model were meshed in tetrahedral element. The mesh data were transferred to Adina 8.5.0 to accomplish the fluid-structure coupled simulation.

The final finite element model includes skull, neck, hyoid, airway and the surrounding soft tissues, as shown in Fig. 2. The material parameters for different tissues are listed in Table 1. In this study, a viscous incompressible laminar transient flow model is chosen. The density of airflow is 1.297×10^{-6} g/mm^3 and the viscosity coefficient is

1.81×10^{-5} Pa.

Table 1 Summary of experimental results for close-up retrieval

	Young's modulus (Pa)	Poisson ratio
Bone	1.37×10^{10}	0.3
Soft tissue	1.0×10^{4}	0.45
Nasopharynx	1.37×10^{10}	0.3
Cartilage	2.02×10^{6}	0.3

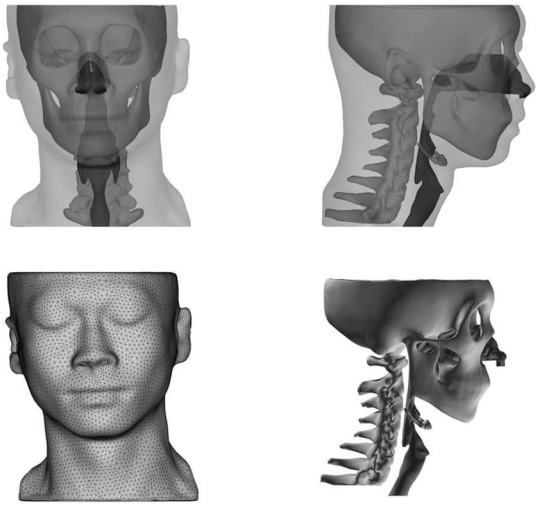

Fig. 2 Finite element model of the upper airway and the surrounding structures

A type of linear spring element was chosen to simulate the effect of nerve control. The spring elements were created directly by nodes. The stiffness matrix of element has only one component. The action force of the spring element depends on the relative displacement of the nodes. The directions of the muscles applied on the upper airway depend on the spatial distribution and attachments of the muscles. Whichever, the force direction is, the final effect turns out to inhibit excessive contraction of the airway and retain regular conformation of the airway. Thus, the spatial distribution of the action forces was not taken into consideration in this study, and all spring elements are along the sagittal direction. The muscle group distributes just in front of the neck, so only the anterior wall of the airway will be exposed to muscle forces. The spring elements were applied on nodes of the airway from oropharynx to the anterior of the hyoid. The spring elements were shown in Fig. 3.

By now, there are no quantitative studies on muscle stiffness under nerve control during sleep. In this study, the relationship of muscle force and displacement was assumed to be

$$F = F(D) \times D \tag{1}$$

where D is the displacement of the upper airway wall and $F(D)$ is the parameter depending on the neuromuscular response. Therefore, the muscle force depends nonlinearly on the displacement. The concrete force-displacement curve of the muscles was shown in Fig. 4.

The loading conditions and boundary conditions are the same as in [14]. As boundary condition, the area in contact with the bed was assumed to be fixed, as shown in Fig. 5. All degrees of freedom of the skull and the neck were fixed due to their tiny displacements. The hyoid can move freely because it is imbedded in muscle and connects to neither the skull nor the neck.

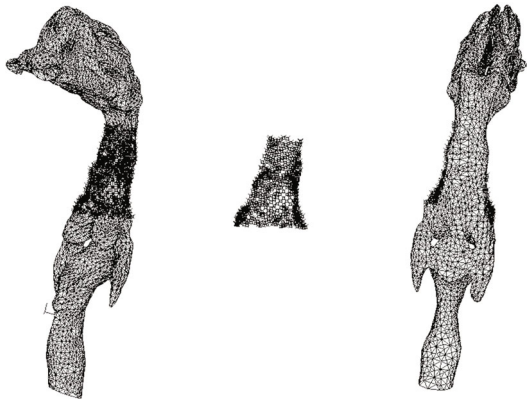

Fig. 3 Position of spring elements

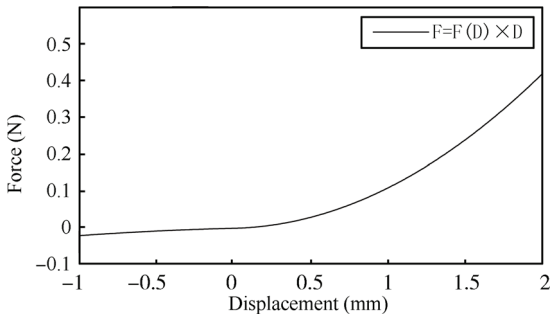

Fig. 4 Force-displacement curve of spring elements

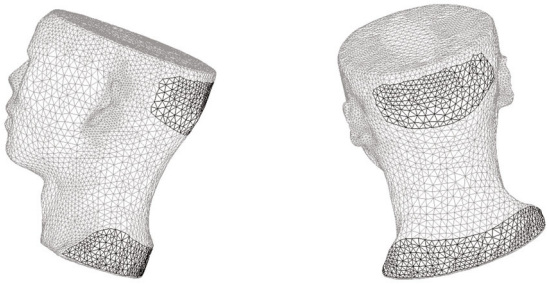

Fig. 5 Back side of the head was fixed due to supine position during sleep

The dynamic pressure in laryngeal part was applied as the load condition. A typical set of pressure data, lasting about 12 s during the apnea episode was applied as the distributed pressure on the outlet surface of the lumen, as shown in Figs. 6 and 7. At the nostril, namely the airflow inlet, a zero pressure was applied instead of the atmospheric pressure since the pressure value used in the outlet has been already subtracted from the atmospheric pressure according to the titration principle used in the measurement.

The fluid-structure coupled simulation of respiratory process was carried out using finite element (FE) software Adina (auto dynamic incremental nonlinear analysis, 8.5.0), which has a structural analysis capability as well as a fluid analysis capability. It offers a one-system program that specializes in fluid structure interaction. For fluid-structure interaction problems, the fluid model must be based on an arbitrary-Lagrangian-Eulerian coordinate system since the fluid-structure interface is deformable. The fundamental conditions applied to the fluid-structure interfaces are kinematic condition or displacement compatibility

$$\boldsymbol{d}_f = \boldsymbol{d}_s \tag{2}$$

and the dynamic condition or traction equilibrium

$$\boldsymbol{n} \cdot \boldsymbol{\tau}_f = \boldsymbol{n} \cdot \boldsymbol{\tau}_s \tag{3}$$

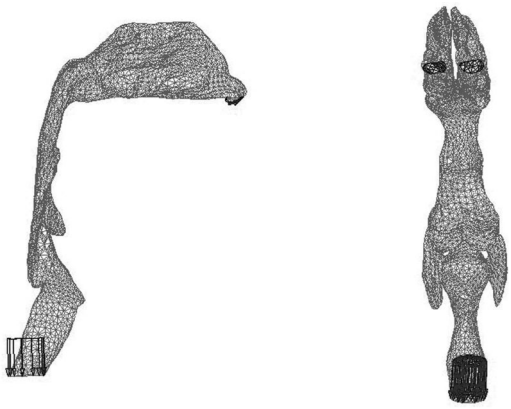

Fig. 6 Measured pressure data was applied to the outlet surface of the lumen, while a zero pressure was applied to the inlet.

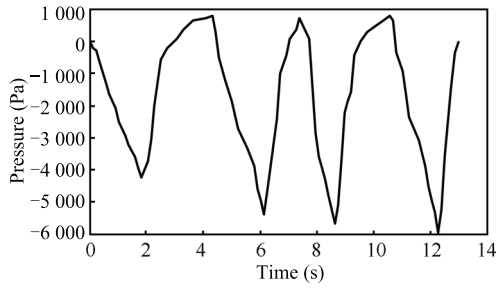

Fig. 7 Pressure data during the apnea episode

where $\boldsymbol{d}_f$ and $\boldsymbol{d}_s$ are the fluid and solid displacement respectively, and $\boldsymbol{\tau}_f$ and $\boldsymbol{\tau}_s$ are stresses in fluid and solid respectively[17]. The fluid and solid parts are coupled as follows: The fluid nodal positions on the fluid-structure interfaces are determined by the kinematic conditions. The displacements of the other fluid nodes are determined automatically by the program to preserve the initial mesh quality. The governing equations of fluid flow in their arbitrary Lagrangian-Eulerian formulations are then solved. In steady-state analyses, the mesh velocities are always set to zero even the fluid nodal displacements are updated. Accordingly, the fluid velocities on the fluid-structure interfaces are zero. According to the dynamic conditions, on the other hand, the fluid traction is integrated into fluid force along fluid-structure interfaces and exerted onto the structure node

$$\boldsymbol{F}(t) = \int h^d \boldsymbol{\tau}_f \cdot \mathrm{d}\boldsymbol{s} \tag{4}$$

where h^d is the virtual quantity of the solid displacement.

In view of the enormous degrees of freedom and the fluid-structural coupled algorithm, the equations for structural dynamics were solved with the sparse solver and the nonlinear finite volume equations for airflow were solved iteratively with Newton-Raphson method. The time step length is set quite small at the beginning, for the purpose of obtaining a reasonable initial condition for the iteration in the transient analyses. However, the time step length depends on the pressure gradient variation, especially around the peak value as well as the moment when expiratory phase transits to inspiratory phase or vice versa. Therefore, the time step length was artificially set only at the initial moment, and then was automatically regulated by the algorithm. The computation was accomplished with a PC (CPU3.00 GHz, 8.00 GB RAM) in 12 and 26 hours, for the normal episode and apnea episode, respectively.

3 Results and discussion

A sagittal section and a cross section located on the oropharynx part were selected to describe the deformation and stress of the upper airway, as shown in Figs. 8 and 9. The airway model with spring elements contracted lesser under the same negative pressure, and expanded less under the same positive pressure than that without spring elements. Therefore, the spring elements resist the excessive deformation of the airway. The posterior wall of the airway has no spring elements, consequently, there is no difference in the posterior walls of the airway between models with and without spring elements.

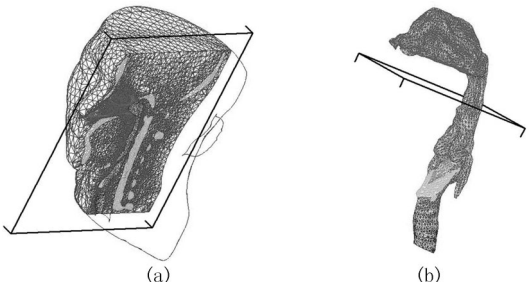

Fig. 8 A sagittal section and a cross section of the upper airway

It should be noted that although the deformation of the airway in sagittal direction decreased due to regulation of the spring elements, inward contraction of the sidewalls of the airway increased, especially under larger negative pressure during inspiration. Without regulation of the spring elements, serious inward collapse of the anterior wall of the airway led to increase of the curvature of the sidewalls of the airway, which in turn enhanced anti-bend stiffness of

the sidewalls so that its inward collapse was not obvious. In the model with spring elements, reaction forces of the spring elements and bone tissue support the anterior and posterior walls of the airway respectively, yet the sidewalls lack support so as to have got obvious collapse.

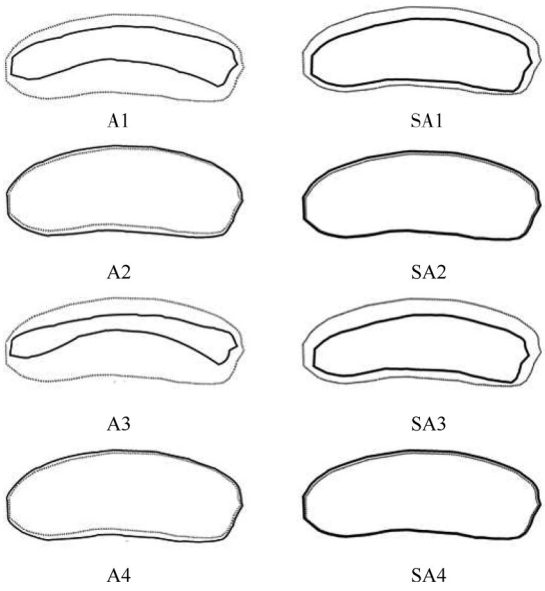

Fig. 9 Deformation of the airway section under sleep apnea pressure condition. Solid line: airway section before deformation; dotted line: airway section after deformation. A1-A4: results of the model without spring elements; SA1-SA4: results of the model with spring elements. Time and pressure of the sections: A1, SA1: $T = 1.7\,\mathrm{s}$, $P = -3\,900\,\mathrm{Pa}$; A2, SA2: $T = 4.2\,\mathrm{s}$ $P = 760\,\mathrm{Pa}$; A3, SA3: $T = 8.6\,\mathrm{s}$, $P = -5\,500\,\mathrm{Pa}$; A4, SA4: $T = 10.5\,\mathrm{s}$ $P = 780\,\mathrm{Pa}$.

It can be seen from Figs. 10 and 11 that, in both inspiratory and expiratory phases, strain concentrations in the oropharynx and basement of the tongue disappeared after spring elements were added in the model. At the maximum magnitude of the negative pressure, the boundary of the airway did not present obvious variations. There is no obvious difference in the strain distributions of the posterior wall of the airway between models with and without spring elements, which shows that spring elements only affect the anterior wall of the airway. In addition, the maximum strain in the model with spring element has changed, and the contractions in typical moments are shown in Table 2. It can be seen that in both positive (from the anterior wall to the posterior wall) and negative (from the posterior wall to the anterior wall) phases, the maximum strains have been decreased by various levels under regulation of the spring elements. It should be noted that in the expiration phase, the less the pressure in the airway, the more decrease of the strain, while in the inspiration phase, the more the pressure in the airway, the more decrease of the strain.

Fig. 12 shows the pressure during breathing. The negative pressure in the upper airway occurred mainly in the inspiratory phase. The velocity of the air flow reached its maximum also in the inspiratory phase. The air flow was influenced obviously by the anatomical structure of the upper airway, as shown in Fig. 13. So it cannot keep in the state of laminar flow during the whole breathing process. It is necessary to consider the effect of turbulence in the future studies.

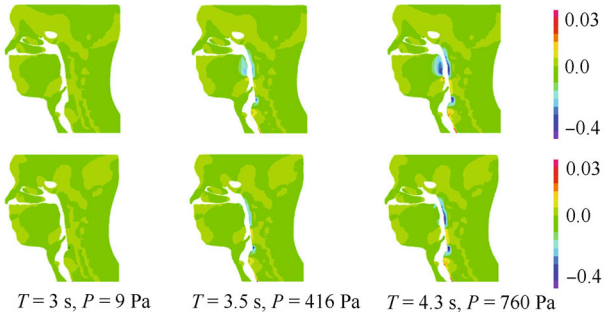

Fig. 10 Expiration: strain distribution of solid model with (bottom) and without (top) spring elements during expiration in sagittal direction under sleep apnea pressure condition

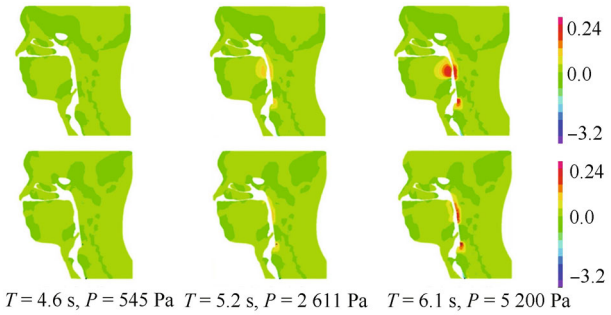

Fig. 11 Inspiration: strain distribution of solid model with (bottom) and without (top) spring elements during inspiration in sagittal direction under sleep apnea pressure condition

The airflows in the airway will be obstructed by deformed airway wall which produces flow resistance. The more serious the airway collapse, the larger resistance it generates to the airflow. Besides, the airflow gathers above the obstructive location after collapse of the airway, which in turn increases the pressure in the upper airway. As a result, resistance in the airway is relevant to both the oropharynx deformation and condition of the airflow, and it is also a reflection of breathing fluency. In this study, resistance of the airway is obtained by summing up resistance of every node on the oropharynx areas of the airway. The oropharynx is the most liable position to collapse, and resistance here indicates the general deformation and airflow status of the oropharynx. It can be seen from Fig. 14 that for the expiratory phase under positive pressure, the curves of resistance of the airway with and without spring elements are consistent. The reason lies in that during the expiratory phase, positive pressure expands the airway, and flow field grows, which decrease resistance of the airway wall to the airflow. The action force of the airflow passing the oropharynx to the airway wall is mainly tangential force. Consequently,

there is little difference of the airway expansion between models with and without spring elements, and the results of both models are the same during expiration. When it comes to inspiration phase, the airway without control of

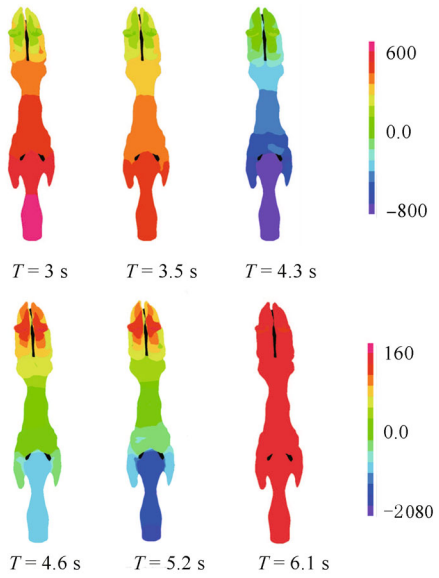

Fig. 12 The air flow pressure of the upper airway during breathing (Pa)

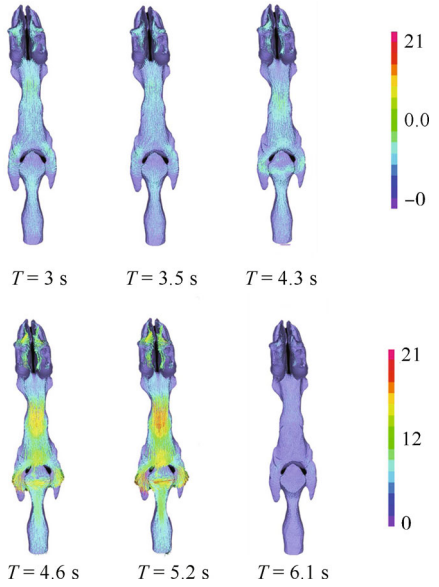

Fig. 13 The air flow velocity of the upper airway during breathing (m/s)

the spring elements shrinks inward, and airflow during inspiration applies on collapsed airway. Therefore, resistance of the airway increases as collapse gets larger under greater negative pressure. The spring elements significantly hinder collapse of the airway, which renders less airway resistance in the airway model with spring elements than that without, especially at the peak of the negative pressure.

Flux of the section can be obtained by integration of velocity in the section. It can be seen from Fig. 15 that, similar to that of the airway resistance, the curves of the positive flux during expiration of the two models with and without spring elements are basically accordant. However, negative flux during inspiration is obviously higher in the airway model with spring elements than that without spring elements. This is due to that decreased collapse in the airway with spring elements sustains relatively normal configuration of the airway under negative pressure, which guarantees fluent pass of the airflow. During expiration, positive pressure in the airway is lower than the negative pressure, which does not induce obvious expansion of the airway. In such a situation, the spring elements do not restrict airway expansion strongly, and the sectional areas don′t change obviously. Therefore, during expiration, there is little difference of the flux between the two models.

Since the occurance of OSAS increases steadily all over the world, it has attracted more and more attentions not only from doctors but also from engineers. There are many factors that can cause OSAS, such as the anatomical structures or the nervous feedback mechanism. It is a great challenge to find the real mechanism of OSAS. Many lumped parameter models and continuous medium models were developed in the last decades. The effect of different mechanical, anatomical, physiological and pathological factors were studied. The purpose of this investigation was to study the effect of nerve control on the prevention of collapse of upper airway.

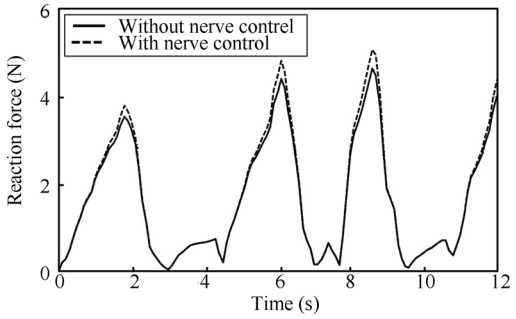

Fig. 14 Relationship of the resistance of the airway in oropharynx and the airway pressure

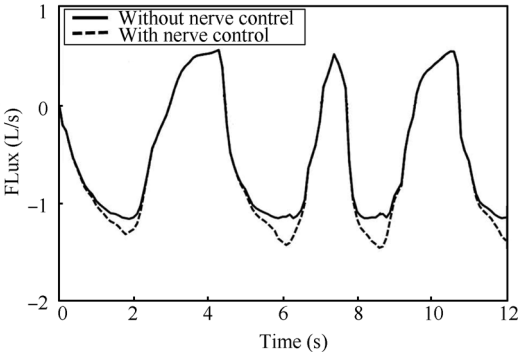

Fig. 15 Relationship of the flux of the horizontal cross-sectional area and the airway pressure under sleep apnea pressure condition

Table 2 Maximum strain in the solid zone in typical moments

	3 s	3.5 s	4.3 s	4.6 s	5.2 s	6.1 s
No nerve control (+)	0.001 56	0.052 5	0.077 6	0.047 5	0.177	0.347
Nerve control (+)	0.001 39	0.051 9	0.077 5	0.047 2	0.174	0.334
No nerve control (−)	0.001 02	0.038 2	0.056 4	0.064 6	0.263	0.567
Nerve control (−)	0.001 02	0.038 0	0.056 1	0.065 0	0.264	0.563

The nerve control plays an important role in OSAS. Some researchers study the nerve control mechanism using lumped parameter models. For example, Huang[18] simulated the pharyngeal airway by a compliant thin rubber tube which can collapse under a certain pressure. To highlight the nervous regulation, the oropharynx is represented by a plunger, which is attached to two springs. One spring represented the effect of muscle tissue around the channel wall, while the other represented the effect of nervous regulation. The dilator receives the signal from nerve receptor, and then after a small time delay, its stiffness will change to the sum of the original value and an increment which is the product of a dimensionless constant representing the nerve regulation intensity and the pressure value just after the delay time. Instead of using a sinusoidal variation for different pressure in the upper airway to simulate the breathing course, they use the displacement of the plunger as the controlling parameter. They found out that the upper airway must have enough stiffness. If the original stiffness cannot keep the stability of upper airway, nervous regulation mechanism becomes the key factor. Although their model considers the nerve regulation mechanism, there is no experiment data to verify the linear relation of nerve adjustment intensity and pressure distribution. Though the lumped parameter models can effectively study the intrinsic relations of different factors in OSAS, they cannot give quantitative results due to oversimplification.

Recently, Xu[19] developed a new computational model of upper airway in rats with consideration of regional material properties. The sensitivity of oropharynx collapse pressure to changes in the mechanical properties of various tissue regions could be used to test the effect of nerve-muscle stimulation on pharyngeal muscles. The main limitation of their study was using an oversimplified FE model.

The work in this study applied the fluid-solid interaction method to study the mechanism of OSAS. The advantage of FE simulation lies in the realistic geometric modelling, including all main parts of the upper airway and the surrounding tissues. It is the first try to study the effect of nerve control in FE method. Many problems need to be solved in future studies.

4 Conclusions

The respiratory nerve control has great physiological significance to the normal respiration. Weak or loss of nerve control is one of the major causes of OSAS. In this paper, the effects of nerve control on resisting collapse of the airway were investigated by spring elements. It has been shown that under sleep apnea pressure, after adding spring elements to the airway model, strain concentrations in the oropharynx and basement of the tongue disappeared; resistance of the airway diminished; and flux of the horizontal cross-sectional area increased at the peak of the negative pressure in the airway. This study reveals that nerve regulation effectively restrains the deformation of the airway, and in turn reduces the occurrence of OSAS. Although the spring elements cannot perfectly reflect the mechanism of the regulation of the respiration nerve, it is a meaningful attempt to simulate the dynamic process of respiration using the FE models of OSAS. In future studies, the quantitative relationship between neuromuscular response and muscle force under different clinical conditions should be clarified. The better understanding of neural mechanism of OSAS may offer new options for clinical treatments.

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