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Realistic glottal motion and airflow rate during human breathing

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ABSTRACT

The glottal geometry is a key factor in the aerosol delivery efficiency for treatment of lung diseases. However, while glottal vibrations were extensively studied during human phonation, the realistic glottal motion during breathing is poorly understood. Therefore, most current studies assume an idealized steady glottis in the context of respiratory dynamics, and thus neglect the flow unsteadiness related to this motion. This is particularly important to assess the aerosol transport mechanisms in upper airways.

This article presents a clinical study conducted on 20 volunteers, to examine the realistic glottal motion during several breathing tasks. Nasofibroscopy was used to investigate the glottal geometrical variations simultaneously with accurate airflow rate measurements. In total, 144 breathing sequences of 30s were recorded.

Regarding the whole database, two cases of glottal time-variations were found: “static” or “dynamic” ones. Typically, the peak value of glottal area during slow breathing narrowed from 217 ± 54 mm^2 (mean ± STD) during inspiration, to 178 ± 35 mm^2 during expiration. Considering flow unsteadiness, it is shown that the harmonic approximation of the airflow rate underevaluates the inertial effects as compared to realistic patterns, especially at the onset of the breathing cycle. These measurements provide input data to conduct realistic numerical simulations of laryngeal airflow and particle deposition.

1. INTRODUCTION

Inhaled therapies play a major role in the treatment of lung diseases like asthma or chronic obstructive pulmonary diseases. Basic advantage of aerosol therapy lies in the direct delivery of high local concentrations of the drug to the site of action [1]. However, characteristics of inhaled particles, airways morphology, carrier gas and flow properties can largely influence the transport mechanisms and treatment efficiency [2–5]. Particularly, the upper airways (UA) anatomic arrangement can act as an unwanted filter, which limits the amount of drug delivered to the lungs. Recent clinical experiments have been conducted to quantify the distribution of radiolabeled aerosols in the human airways using combined single photon emission computed tomography (SPECT) and X-ray computer tomography (CT) [6,7]. It was shown that particle deposition in extra-thoracic region can reach as much as 40% of the inhaled mass in the worst cases.

More specifically, within the larynx, the glottis (the space between vocal folds) narrows the airways to a minimal transition cross-section. Therefore its geometrical variations can affect breathing flow resistance [8–11]. This anatomical singularity yields to a complex jet-like glottal airflow, important recirculation zones and a locally turbulent behavior [12–19], which can be determinant on particle deposition by inertial impaction [3,20,21]. Regarding the glottal geometry’s impact on the tracheal flow during breathing, a devoted description has been given by Brouns et al. [18,19]. This numerical study demonstrates the effect of the glottal size and shape on the overall fluid dynamics behavior, using a 3D idealized model of upper airways comprising a static glottis of parametrical aperture. This typical flow alteration can yield to the rise of the tracheal deposition of nano- and micrometer particles by factors ranging from 2 to 10 [20]. However, as pointed out in Brouns et al. [18], there is a current need for rendering the design of future upper airway models even more realistic, including glottal shape, area and kinematics in correlation with a given inlet inhalation flow rate. Thus, the knowledge of realistic

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Table 1
Physical characteristics of the subjects. (* subject finished only *slow breathing* tasks; † subject finished only Eup$_{f}$ task).

Females			Males		
Subject	Age [year]	BMI [kg.m^{-2}]	Subject	Age [year]	BMI [kg.m^{-2}]
F01	27	21.0	M01	25	21.2
F02	24	20.0	M02	26	24.3
F03	24	17.3	M03	24	22.5
F04	22	21.1	M04	28	20.3
F05	25	21.5	M05	25	23.1
F06	23	22.5	M06	27	23.0
F07	25	19.9	M07†	26	20.5
F08	23	23.4	M08	26	21.0
F09*	23	17.6	M09	26	20.1
F10	26	21.3	M10	27	21.8
Mean	**24.2**	**20.6**	**Mean**	**26**	**21.8**
SD	1.5	1.9	SD	1.2	1.4

glottal motion during human breathing will enable to further assess the filtration efficiency of the upper airways.

In this context, the purpose of the present study is to determine the glottal motion during several oral breathing tasks, and to investigate the correlation between this motion and the measured breathing flow rates. The first *in vivo* observation of the glottal motion dates back to the 19th century, with Garcia's laryngeal mirror [22]. Since the 1980s, advances in the medical equipment have allowed a refined exploration of the vocal-fold dynamics using laryngoscopy [9,10], high-speed cinematography [23,24], videokymography [25], electroglottography [26] or photoglottography [27]. These experimental techniques were extensively used to characterize the vocal-fold vibrations during human phonation (e.g. see a review by Ziethe et al. [28]). By contrast, however, the glottal variations during different human breathing regimes have been barely investigated so far. Despite a few reference studies [9,10,29], the relationship between the glottal area and the inhaled airflow rate is still poorly understood. In the present work, a clinical database comprising 8 breathing tasks recorded on 20 healthy subjects is presented. The physiological mechanisms of the respiratory cycles were observed using video-recording of laryngofiberscopic examinations, and synchronized oral airflow measurements. A quantitative characterization of glottal motion was derived from the processing of the recorded laryngeal images. The impact of the glottal motion on flow parameters is discussed as a function of breathing task and subject gender.

2. Materials and methods

The recording sessions took place at the Otolaryngology Department of the La Timone Adults Hospital (APHM, Marseille, France). In the following, the "realistic glottal motion" is defined by the 2D time-variations of the space area separating both free edges of the vocal folds, as observed *in vivo* on their superior transversal plane.

2.1. In vivo recordings

2.1.1. Subjects

From 20 healthy volunteers (10 females Fi, and 10 males Mi, i ∈ [01, 02, … , 10]) were obtained informed consents for the study. All subjects were non-smokers, without any professional sportive activity, any previous laryngeal or respiratory disorders, aging between 22 and 28 years. Table 1 lists the subject's age and body mass index (BMI).

2.1.2. Breathing tasks and database

Each subject was asked to produce eight 30s-tasks of slow or rapid breathing, described as follows:

Slow breathing tasks—below 20 cycles.min^{-1}:

(i) **Eup**$_{\mathbf{f}}$: task of free *eupnea* (quiet breathing)
(ii) Repetition of **Eup**$_{\mathbf{f}}$
(iii) **Eup**$_{\mathbf{15}}$: task of *eupnea* with a controlled breathing frequency at 15 cycles.min^{-1}.
(iv) **Hyper**$_{\mathbf{f}}$: task of free *hyperpnea* (deep breathing with maximal respiratory volume)

Rapid breathing tasks: above 20 cycles.min^{-1}:

(v) **Tachyp**$_{\mathbf{30}}$: task of *tachypnea* with a controlled breathing frequency at 30 cycles.min^{-1}.
(vi) **Tachyp**$_{\mathbf{60}}$: task of *tachypnea* with a controlled breathing frequency at 60 cycles.min^{-1}.
(vii) **Tachyp**$_{\mathbf{90}}$: task of *tachypnea* with a controlled breathing frequency at 90 cycles.min^{-1}.

Specific inhalation task:

(viii) **Aerosol**: task mimicking the breathing gesture typically performed when using a dry powder inhaler to deliver medication (quick and deep inspiration followed by slow expiration).

For all tasks, the subject's nose was closed to ensure that the subject breathed only through his mouth. Note that both tasks of *free eupnea* (**Eup**$_{\mathbf{f}}$) were intentionally presented to the subject as a phase of acquisition trials. This aimed to prepare him before the recording of the controlled tasks, which were described as the target of the study. Thereby, by reducing the effect of a motor control focused on the respiration, tasks (i) and (ii) were acquired in condition of spontaneous breathing. By contrast, the other tasks corresponded to cases of controlled breathing, for which the subjects were asked to synchronize their breathing frequency with a metronome projected on an instruction computer. These tasks intended to explore the extent of glottal motion and breathing capacity in specific respiratory contexts. In the end, 18 volunteers only (9 females and 9 males) successfully performed the entire protocol, thus yielding to a database comprising 144 sequences of 30s.

2.1.3. Measurements

All measurements were done in the seated posture. The glottis was observed using a flexible nasofiberscope equipped with a PAL camera (Storz endovision XL 202800) and a continuous cold light source. Laryngeal images were captured at a frequency of 25 Hz (768 × 576 pixels). The airflow rate was simultaneously registered by means of a pneumotachograph placed at the mouth, the EVA2^{TM} system (S.Q.Lab, www.sqlab.fr) [30]. It consists of a two-grid flowmeter characterized by a small dead volume, specific linearized response for the inhaled and exhaled flow, and an accuracy of 1 cm^{3}s^{-1}. The sampling frequency of the flow rate signal was 6250 Hz. A trigger generated by an acquisition tool developed in NI LabWindows^{TM}/CVI was used to synchronize the recordings of laryngeal images and flow rate signal. Note that for several subjects, a local anesthetic (Lidocaine Aguettant 5%) was sprayed in the naris before the fiberscope introduction, so as to provide a better comfort during the invasive examination. Ambient temperature T_a [K] was also measured.

2.2. Data processing

All data was processed using Matlab®. Any point in the upper airways was located by the (x, y, z) coordinates as introduced in Fig. 1.

2.2.1. Airflow rate

Within each recorded 30s-sequence, every respiratory cycle was detected on the airflow signal, Q, using a zero-tracking method. Conventionally, positive and negative flow rate values correspond to inspiration and expiration, respectively. A BTPS correction (Body Temperature Pressure Saturated) was applied to convert the flow measured at ambient conditions to the thermodynamic conditions