CFD MODELS OF THE BRONCHIAL AIRWAYS WITH DYNAMIC
BOUNDARIES

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By
Gihad Ibrahim
Department of Engineering
University of Leicester

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To my father

Who encouraged and supported me throughout my life
CFD models of the bronchial airways with dynamic boundaries

Gihad Ibrahim

ABSTRACT

Obtaining reliable CFD predictions of the bronchial flow that reflects the actual flow within a living lung requires the development of a deforming airways model, and the imposition of physiological subject-specific boundary conditions. This thesis addresses these two issues by the development of dynamic CFD models of the bronchial airways using a dynamic CT data set covering the breathing cycle of a laboratory animal. A deformation algorithm is proposed that matches the CFD mesh of the subsequent airway geometries generated from the dynamic CT data set. In addition, a novel nonlinear dynamic airway model generated from a pair of CT images is introduced. The proposed non-linear deforming model is capable of successfully capturing the non-linear motion characteristics of the bronchial airways based on the clinical measurements of the lung volume change. Furthermore, a technique to drive physiological subject-specific boundary conditions for the terminal surfaces of the CFD models of the bronchial airways is introduced. The proposed technique depends on approximating the lung volume associated to each terminal surface over several time points over the breathing cycle based on the mechanical coupling between the bronchial airways and the vascular tree. The computed dynamic subject-specific boundary conditions were imposed on the terminal surfaces of the deforming airway model and the effect of wall motion on the flow features during tidal breathing is investigated for the first time.

The outcome of this thesis is expected to improve the fidelity of the CFD predictions of the bronchial flow compared to the actual flow within a living lung. In addition, the availability of a new non-linear dynamic model of the bronchial airways that requires one pair of CT images as input, which complies with the radiation dosage restrictions for humans will facilitate the development of well-resolved CFD models of the human bronchial airways.
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I would also like to thank Dr Richard Jacob and his research team from the Biological Sciences division at the Pacific Northwest national laboratory, Washington, USA, for supplying the animal data used in this research. Not to forget his continuous support and valuable suggestions. In addition, I would like to thank Professor Chris Brightling and his team from the Institute of Lung Health at Glenfield Hospital (Leicester, UK) for supplying the human CT-scans used in this study. My appreciation also goes to Dr Jasper Kidger, the ANSYS UK global training curriculum manager, for his inputs and valuable guidance in developing user-defined functions to control deforming meshes. I must also acknowledge my colleagues at the Mechanics of Materials and Thermofluids research groups and all the members of staff at the University of Leicester for providing such a friendly and healthy research environment.

I tip my hat off to my wonderful family for their unlimited moral and financial support through the course of this research, particularly my father, Professor Abdul-Aziz Ibrahim and my dearest brothers Dr Saud Ghani and Dr Faysal Ibrahim. Without their exceptional support, this research could never be accomplished. Finally, a special thanks to my beautiful and beloved wife, Mrs Sulafa Ibrahim, who was always there for me. Her love has always been a source of inspiration, encouragement, and strength.
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1 INTRODUCTION & BACKGROUND

1.1 Motivation
Respiratory conditions impose an enormous burden on society. According to the World Health Organisation (WHO) statistics report in 2011 (World Health Organization, 2011), respiratory diseases account for 16.7% of all death worldwide. The global strategy for the prevention and control of non-communicable diseases, developed in a direct response to the global threat posed by non-communicable diseases and endorsed by the Fifty-Third World Health Assembly, cites respiratory diseases as one of the four priority disease groups to be addressed.

Chronic respiratory diseases, which are the second cause of death after lung cancer, affect an estimated 300 million people worldwide and the burden is likely to rise substantially in the next few decades. Additionally, chronic respiratory diseases result in a large burden of disability. For instance, patients with inadequately controlled severe persistent asthma are at a particularly high risk of exacerbations, hospitalisation and death, and often have severely impaired quality of life. Although this group represents a relatively small proportion of the asthma population (5-10%), they consume two-thirds of the health care costs attributed to asthma. This disproportionate use of health care resources means there are considerable unmet needs of other patients and financial pressure on health care providers.

There is a paucity of biomarkers to identify patients that will have recurrent exacerbations or develop persistent airflow obstructions. Therefore, there is a need to understand the complexity of the multidimensional phenotypes of airway diseases. The airflow pattern and distribution through the lung determine how the inhaled toxic materials as well as the drug aerosols access the human body. Therefore, analysing the airflow pattern and distribution through the lung can be a key reference to target therapy and predict disease progression. However, due to the inaccessible nature of the bronchial airways, obtaining such information by in vivo experiments is challenging.
Computational fluid dynamics (CFD) has been extensively used for the past two decades as a research tool to predict the airflow pattern and particle deposition through models of the bronchial airways. However, an accurate computational representation of the bronchial airways is not yet achievable (Kleinstreuer and Zhang, 2010). This is due to the multi-scale complexity of the airway structure as well as the biological and the physiological aspects that involve in the process of breathing. Most of the CFD computational models of the bronchial airways to date have imposed a steady flow on a rigid subject-specific model of the bronchial airways with the atmospheric pressure applied at the terminal branches. However, the bronchial airways are compliant in nature and the airway tissue expansion imposes the physiological boundary conditions that govern the distribution of ventilation through the semi-closed structure of the bronchial airways. Thus, further development is required to obtain higher fidelity simulations of the bronchial flow.

1.2 The anatomy and physiology of the lung

1.2.1 The structure of the respiratory system
The main components of the human respiratory system are illustrated in figure 1.1. The process of respiration or breathing is often classified into two parts: an external and an internal respiration. The external respiration is the process by which external air is drawn into the body in order to supply the lungs with oxygen and used air is expelled from the lungs to remove carbon dioxide from the body. The internal respiration, on the other hand, is the process of exchanging the oxygen and the carbon dioxide between the lungs and the blood (Costanzo, 2006). Mechanically, the bronchial airways are described as a complex system of branching tubes. They are categorised into three different compartments: the upper airway, which starts at the nose and the mouth down to the trachea, the central airways, which extend from the trachea down to the terminal bronchioles, and the lower airways, which continue from the terminal bronchioles down to the alveolar sacs. The upper and the central airways are responsible for conducting the air (external respiration) to and from the lower airways where gas exchange takes place (internal respiration). Thus, the upper airway and the central airways are known as the conducting airways, while the lower airways are known as the respiratory airways. The conducting airways are also responsible for cleaning, warming,
and humidifying the drawn air prior to the gas exchange process. The most common chronic respiratory diseases, such as asthma and bronchitis, affect the conducting airways. They are often described as an airway narrowing or obstruction of the airway tract that reduces the amount of air feeding the distal respiratory airways.

![Diagram of the human respiratory system](image)

Figure 1.1 The human respiratory system. Adapted from Mader (2004) and Boron (2009).

The upper airway is connected to the central and the lower airways by the trachea, which is the main conducting tube to the lungs. It branches into two primary bronchi, each bronchus leading into either lung. Each bronchus then divides to form the secondary or lobar bronchi, one for each lobe of a lung. In the human anatomy, there are three lobes at the right lung (upper, middle, and lower) and two lobes at the left lung (upper and lower). Each secondary bronchus then divides into two smaller airways. Usually, there is a cascade of 23 branchings in the human bronchial airways and each after a split group of airways is called a generation (G). As illustrated in figure 1.1, the conducting airways contain the first 17 generations of the human airways, while the respiratory airways include the last 7 generations (G17-G23). The airway diameter and length get successively smaller as the generation number increases. Although the branching pattern of the human bronchial airways is classified as dichotomous, the change in the diameter and length as well as the branching angle throughout the
generations is inhomogeneous. This inhomogeneity can significantly influence the distribution of the airflow within the lungs. The trachea and the main bronchi walls are lined by C-shape cartilages to prevent the airway collapse. Further down in the lobar bronchi, the airways are surrounded by plates of cartilage. At the bronchioles (G11), these cartilages are replaced by elastic tissues in the lung parenchyma in order to prevent these airways from collapsing. The wall of the lower airways is surrounded by millions of pouch-like structures called the alveoli. They are responsible for the gas exchange process between the lung and the blood through their thin walls.

The lung parenchyma is enclosed by a membrane known as the pleura. It consists of two connected layers: the visceral pleura, which covers the lung parenchyma, and the parietal pleura, which lines the inside of the thoracic cavity (Light, 2007). The space between the two layers is called the pleural space. The pleural space is very small and completely closed, filled with a pleural fluid that works as a lubricant to reduce the friction between the two layers during respiration. This fluid also prevents the lungs from collapsing even after full expiration by keeping the lungs attached to the chest wall due to the fluid surface tension.

1.2.2 Lungs anatomical differences in rats and humans

Rats have been frequently used to clinically assess the effect of drug aerosols during the development stages in order to expose some of the risk associated with human trials (Kola, 2008, Schroeter et al., 2012). This is due to the close physiologic and the genetic relationships between rats and humans that allow the researchers to develop rat models of the human respiratory diseases (Jacob and Kwitek, 2002, Irvin and Bates, 2003). However, there is a significant difference in the anatomical structure of the lungs in rats and humans. These anatomical differences are still under active research, table 1.1 summarises most of the published lung anatomical differences between the two.

Besides the significant difference in the lung size, the percentage of the airways lumen with respect to the total volume of the lung parenchyma is smaller in rats, which may result in a significant difference in the flow resistance. Specifically, this ratio is 82% in rats and 88% in humans (Irvin and Bates, 2003). Unlike humans, rats have four lobes at the right lung (cranial, middle, caudal, and accessory) and one lobe at the left lung as
shown in figure 1.2. The subdivision of the branches in the rat airways is classified as asymmetrical (monopodial) versus the symmetrical (dichotomous) branching pattern in humans as shown in figure 1.3. There are usually no respiratory bronchioles in rats. Thus, the number of generations is usually less in rats (13-17 generations) compared to humans (17-23 generations). Furthermore, there are no cartilages surrounding the secondary bronchi in rats.

Figure 1.2 Anatomy of the rat lungs. Adapted from Suarez et al. (2012).

<table>
<thead>
<tr>
<th></th>
<th>Rats</th>
<th>Humans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung lobes</td>
<td>4 right lobes</td>
<td>3 right lobes</td>
</tr>
<tr>
<td></td>
<td>1 left lobe</td>
<td>2 left lobes</td>
</tr>
<tr>
<td>Number of generations</td>
<td>13-17</td>
<td>17-23</td>
</tr>
<tr>
<td>Airway lumen volume/lung volume</td>
<td>82%</td>
<td>88%</td>
</tr>
<tr>
<td>Branching pattern</td>
<td>Monopodial</td>
<td>Dichotomous</td>
</tr>
<tr>
<td>Main bronchus diameter</td>
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<td>10-15 mm</td>
</tr>
<tr>
<td>Bronchiole diameter</td>
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<td>&lt;1 mm</td>
</tr>
<tr>
<td>Terminal bronchiole diameter</td>
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<td>0.6</td>
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<tr>
<td>Number of respiratory bronchiole</td>
<td>None</td>
<td>Often 3</td>
</tr>
<tr>
<td>Alveoli diameter</td>
<td>35-80 μm</td>
<td>0.2-0.4 mm</td>
</tr>
</tbody>
</table>

Table 1.1 Lung anatomical differences in rats and humans. Adapted from Irvin and Bates (2003), Fox (2007), and Namati (2009).
Due to the significant difference in the anatomy along with the other histological differences, the flow pattern is not expected to be the same in the bronchial airways of rats and humans. This assumption was confirmed by the findings of Corley et al. (2012) who utilised CFD to simulate a static airflow through an extended airways model of a rat, a monkey, and a human. Although the general laminar flow phenomena was the same in the three models, differences of up to three orders of magnitude were observed when comparing the velocity among the generations.

1.3 Mechanics of breathing

The process of breathing (inspiration and expiration) occurs due to the difference in pressure between the atmosphere and the alveoli. The diaphragm (figure 1.1) is the main muscle of the respiration process assisted by the intercostal muscles, which are located between the ribs. During tidal inspiration, the diaphragm contracts pushing the abdominal contents downward and the intercostal muscles lift the ribs upward and outward. This results in an increment of the volume of the thoracic space that causes a reduction in the pressure inside the airways and hence air is drawn into the lungs. Tidal exhalation, on the other hand, is a passive reaction to inhalation. The lungs and the thorax relax and recoil to their original volume due to the tissue elasticity effects, blowing the air out of the lungs. In case of an exercise or a respiratory disease, where the airflow resistance increases, the intercostal muscles are tensioned to apply extra effort during both inspiration and expiration.
The volume of air inhaled or exhaled during tidal breathing is known as the tidal volume. After a full expiration, a certain volume of air will still be trapped inside the airways, as the lungs do not completely collapse. This volume of air is known as the residual volume. The difference between the tidal volume and the residual volume is known as the expiratory reserved volume. Several other lung volumes were classified based on the volume of air inside the lungs as shown in figure 1.4. The abbreviations and the terminology used for each lung volume are listed in table 1.2.

The lungs are elastic in nature. They are stretched by the rib cage via the pleura layers and deform accordingly. If the lungs are extracted from the body, they collapse immediately to a minimum volume. Thus, during inspiration, the driving pressure must overcome both the resistance induced by the anatomy of the airways and the lung elasticity effects. The elasticity of the lungs depends mainly on the tissue constituents of the lung parenchyma and the surface tension of the liquid that lines the inner wall of the airways and the alveoli. The elastic recoil of the tissue fibre causes the lung to return to its expiratory reserve volume following inspiration. In contrast, the surface tension of the liquid that lines the inner wall of the airways decreases the lung compliance, making the lungs more difficult to inflate.

Figure 1.4 Lung volumes. Adapted from Guyton and Hall (2006)
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV</td>
<td>Residual volume</td>
<td>The volume of air remaining in the lungs after maximum expiration.</td>
</tr>
<tr>
<td>TV</td>
<td>Tidal volume</td>
<td>The amount of air moved in and out of the lungs during tidal breathing.</td>
</tr>
<tr>
<td>ERV</td>
<td>Expiratory reserve volume</td>
<td>The amount of air exhaled by maximum expiratory effort after tidal exhalation.</td>
</tr>
<tr>
<td>IRV</td>
<td>Inspiratory reserve volume</td>
<td>The amount of air inhaled by maximum inhalation effort after tidal inhalation.</td>
</tr>
<tr>
<td>IC</td>
<td>Inspiratory capacity</td>
<td>The maximum volume of air inhaled after a normal expiration.</td>
</tr>
<tr>
<td>FRC</td>
<td>Functional residual capacity</td>
<td>The amount of air volume left in the lungs after tidal expiration.</td>
</tr>
<tr>
<td>VC</td>
<td>Vital capacity</td>
<td>The maximum volume of air exhaled after a maximum inhalation.</td>
</tr>
<tr>
<td>TLC</td>
<td>Total lung capacity</td>
<td>The volume of air occupying the lungs after maximum inhalation.</td>
</tr>
</tbody>
</table>

Table 1.2 Definitions of classified lung volumes and capacities. Adapted from Costanzo (2006), Sarnaik and Heideman (2006), and Rhoades and Bell (2009).

1.4 Modelling the central airways

Interest in the investigation of the flow pattern and distribution within the central airways started in the late 1950s. West and Hugh-Jones (1959) and Dekker (1961) were among the firsts to investigate by experiment the turbulent flow characteristics in the human trachea. Since then, there have been numerous developments in the flow modelling through the central airways. Figure 1.5 gives a schematic of the chronological evolution of the central airway models to date, from the early analytical symmetrical models to the current subject-specific dynamic representation of the central airways.

![Figure 1.5](image-url)
1.4.1 Analytical models

Prior to the availability of constructing realistic subject-specific models of the central airways out of volumetric medical data, many of the flow modelling studies were restricted to simplified analytical models of the central airways. These models were based on generalised anatomical measurements. Early contributions are the symmetric analytical model of Weibel (Weibel, 1963) and the asymmetric analytical model of Horsfield (Horsfield et al., 1971). The flow modelling results obtained by such analytical models are limited to general flow phenomena, since they do not accurately represent any subject-specific geometrical features. Thus, most of the flow modelling studies that utilised such analytical models of the central airways focused on investigating the effect of general anatomical features and the inlet profile on the flow pattern and distribution. For example, the effect of the asymmetry between the daughter branches was investigated by Calay et al. (2002), Liu et al. (2003), and Luo et al. (2004). Comer et al. (2001) investigated the effect of the carinal shape and the rotation angle of the daughter branches on the flow pattern and distribution by imposing deferent shapes of the carinal ridges (rounded and sharp) on symmetrical planar and $90^\circ$ off-planar double bifurcating models of the central airways. Another example is the study of Russo et al. (2008) who investigated the effect of the cartilage rings on the flow within the trachea and the main bronchi. Two separate trachea and main bronchi anatomical models were created; a smooth walled model and a model with cartilage rings protruding into the airways. The dimensions for the size and the geometry of these rings along with the distance between them were taken from a cadaver specimen. Furthermore, the effect of the upper airway on the flow pattern and distribution within analytical models of the central airways was investigated in the study of Zhang and Kleinstreuer (2004). They developed a relatively simple but representative oral airway geometry that comprises the nasal, the oral cavity, the mouth, the pharynx and the larynx, based on a cast replica along with a four generation symmetrical bifurcating airway geometry. Although the structure of the model utilised by Zhang and Kleinstreuer (2004) was simple, the turbulent laryngeal jet, which is the most prominent inhalation flow phenomenon within the upper airway (Lin et al., 2007), was represented in this model at the laryngotracheal region. On the other hand, the effect of the parabolic or oscillating inlet profile on the flow pattern and distribution was investigated in the study of Menon et al. (1984), Heistracher and
Hofmann (1997), Lieber and Zhao (1998), Zhang et al. (2002), and Li et al. (2007a). The findings of these studies generally support the assumption of imposing a quasi-steady inlet profile (see section 1.5). However, they argued the need for more sophisticated model structures in order to obtain more reliable flow results.

1.4.2 Rigid subject-specific models

Early investigations of the airflow through subject-specific models of the central airways tended to prepare airway casts out of a freshly-excited, inflated, frozen cadaver lungs, such as in the study of Briant and Cohen (1989) and Cohen et al. (1993). Advances in medical volumetric imaging techniques then allowed the 3D construction of the first few generations of the central airways for flow analysis. Currently, the imaging modality of choice for the lung tissue is the spiral multi-row detector computed tomography (MDCT) (Burrowes et al., 2008). Magnetic resonance imaging (MRI) was also used in some studies (Wang et al., 2004, Oakes et al., 2012). However, MDCT is more popular because MRI produces a lower number of slices and it takes a longer time for scanning, which may result in distorted images due to the heartbeats and potential subject movement. Both MDCT and MRI produce a series of successive 2D images that cover the full subject thorax. These scans include the bronchial airways lumen of the bronchial airways along with the heart, the vascular tree, and all the constituents of the thorax cavity.

There are several published algorithms for segmenting the bronchial airways put of the acquired images including thresholding, region growing, point clouds and many more. However, this topic is still under active research as none of these algorithms can yet claim complete accuracy due to the insufficient resolution of the CT scans. After the segmentation of the lung lumen, a 3D geometry of the segmented airways is reconstructed and refined. A popular algorithm of the 3D sampling of the segmented airways is the marching cubes of Lorensen and Cline (1987). A comprehensive review of the airways lumen segmentation algorithms and 3D sampling of the bronchial airways out of volumetric medical imaging data can be found in Lee et al. (2008) and Tu et al. (2013).

Due to the radiation dose restrictions for humans, subject-specific studies were limited to one or two CT scans acquired at nearly TLC (Lin et al., 2007, Kim and Chung, 2009,
Kleinstreuer and Zhang, 2010, Vermeulen et al., 2010), or at FRC (De Backer et al., 2008b, Lin et al., 2009, De Backer et al., 2010). The difference in airflow pattern and distribution between a realistic CT-based model and an idealised geometry of the bronchial Airways based on Weibel analytical model was investigated numerically by Nowak et al. (2003). They noted that the airflow in the realistic geometry is much more complex, featuring higher off-axis flow due to the airway curvature and the asymmetric shape of the airway branches, as shown in figure 1.6. Similar flow dissimilarities were observed by Heraty et al. (2008) who experimentally investigated the flow during high-frequency oscillatory ventilation (HFOV) in idealised and subject-specific single bifurcation using particle image velocimetry (PIV). Based on their results, they argued that even though the main flow features were common in both models, the secondary flow velocities were significantly higher in the realistic model due to the irregular wall curvature.

![Image of velocity vectors comparison](image_url)

**Figure 1.6** Comparison of velocity vectors in an axial slice of the tracheal bifurcation of (a) Weibel symmetrical analytical model and (b) CT subject-specific model studied by Nowak et al. (2003).

A significant limitation of subject-specific modelling of the bronchial flow is that the number of the generations in the CT-based airway geometry is limited due to the low image resolution and the small size of the lower generations. To overcome this issue, some studies combined subject-specific models with analytical models in order to predict the flow through a larger number of generations (Gemci et al., 2008, Corley et al., 2012). In addition, Lin et al. (2009) proposed a CFD framework to couple a CT-based 3D model of the central airways to a 1D model that represents the centreline of the missing peripheral airways as shown in figure 1.7. The 1D centreline was generated based on a volume-filling branching algorithm proposed by Tawhai et al. (2004). This algorithm uniformly spreads number of seed points within each lung lobe with a density equals to an estimated number of the terminal bronchioles. The centreline at the
terminals of the CT-based 3D model and the generated seed points are used as a source and a target respectively to fill-in the lobe with branches. Although this method has some subject-specific features, as the shape and the size of the lobe govern the structure of the generated 1D model, the final result does not represent the exact branching pattern of the peripheral airways as the number and the location of the terminal bronchioles are subject-specific.

![3D-1D coupled model and CFD computed pressure distribution](image.png)

Figure 1.7 3D-1D coupled model and CFD computed pressure distribution (red (zero) to blue (large negative) pressure). Adapted from Tawhai and Lin (2010).

1.4.3 Dynamic subject-specific models

The deformation of the bronchial tree during breathing depends on the material properties of the airway wall and the surrounding tissues that vary widely from dorsal to apex. Since most of this information is still unknown, most of the studies to date limited their investigations to rigid models of the central airways, notwithstanding the fact that the central airways are compliant in nature. Studies that investigated the flow through rigid models of the central airways relied on the assumption that the lung volume does not significantly change during normal breathing conditions, and hence airway deformation and lung compliance can be neglected. However, this assumption is invalid when simulating deep breathing conditions.

To date, there is a comparatively little documented research on the effect of the airway deformation and lung compliance on the flow pattern and distribution. Koombua et al. (2008) utilised a fluid-structure interaction (FSI) technique to investigate the airflow...
pattern through a flexible double bifurcated symmetrical model based on the anatomical models of Weibel (Weibel, 1963). A similar approach was adopted by Xia et al., (2010) who investigated the effect of flexible walls on the flow characteristics through a single bifurcated model extracted from a human CT-based bronchial airways geometry. However, the scarcity of the information available on the material properties of the airway wall and of its surrounding tissues makes developing an FSI analysis for the central airways challenging. Alternatively, attempts were made to control the deformation of the airway wall in order to reproduce the observed change in lung volume during the breathing cycle. Hylla et al. (2010) implemented an Immersed Boundary (IB) approach to simulate the airflow through a dynamic bronchial airway model of a swine. In this study, ten surfaces of the airway geometry were constructed from successive CT scans acquired during a controlled breathing cycle. These surfaces were used to update the location of the airway wall during the simulation. One limitation to this algorithm is that it is applicable to research animals only due to the large number of CT scans required. In addition, recurrent freezing of the lung during the breathing cycle for static CT scanning may results in an unstable lung mechanics such as tissue compliance and strain that can affect the computational analysis (Namati, 2009, Burri et al., 2005). Recently, Sera et al. (2013) assumed a sinusoidal expanding and contracting model of the central airways based on a single CT scan. The rate of the expansion was proposed to be equivalent to a typical human adult during tidal breathing. Another attempt to account for the temporal changes of the airway wall during the breathing cycle in the computational domain was made by Yin et al. (2013). They utilised a registration derived deformation algorithm to predict the moving airway geometry at an arbitrary phase between two volumes of the central airways based on a linear voxel to voxel trajectories. However, more than two volumetric CT scans are required for this algorithm to work efficiently due to the non-linearity of the lung deformation. Thus, they used an additional CT-image acquired at mid-point between end-exhale end-inhale to generate a cubic B-spline non-linear deforming model of the bronchial airways for CFD applications.
1.5 Flow modelling boundary conditions

Identifying the correct flow boundary conditions (BCs) that reflect the physical nature of the targeted problem is a key element in order to obtain reliable and useful flow simulation results in CFD. However, the specification of the BCs for the simulation of the flow through the bronchial airways is challenging due to the multi-dimensional complexity of the physiological factors that govern the flow pattern and distribution within the bronchial tree. For example, the existence of the upper airway significantly alters the profile of the air entering the central airways. Other aspects, such as the distensible compliant nature of the lung and the airway wall deformation during the breathing cycle, impose physiological boundary conditions that govern the distribution of ventilation throughout the bronchial airways. Additionally, the flow resistance of the missing peripheral airways must be considered when determining the BCs at the terminal surfaces as the flow domain represents only the first few generations of the bronchial tree. The measurement of such key physiological factors, which govern the flow pattern and distribution within the bronchial tree, is challenging due to the inaccessible nature of the bronchial airways. Therefore, many of the flow modelling studies to date imposed simple steady BCs (velocity, flow, or pressure) on rigid models of the central airways. The effects of imposing subject-specific physiological BCs on the flow pattern and distribution are still under active research. The following is an outline of the efforts made to account for sophisticated physiological BCs that approximate the effect of some of the physiological factors that govern the flow distribution within the bronchial airways.

1.5.1 Oscillating breathing cycle

In a straight tube, the effect of the flow unsteadiness is measured by a dimensionless parameter known as the Womersley number, \( \alpha = r \sqrt{\omega / \nu} \) where \( r \) is the tube radius, \( \omega \) is the angular frequency, and \( \nu \) is kinematic viscosity. If \( \alpha < 1 \), the flow can be classified as a quasi-steady. As the Womersley number increases, the flow pattern tends to deviate from the quasi-steady behaviour (Loudon and Tordesillas, 1998). Based on this assumption, many of the former studies imposed simple steady BCs (velocity, flow, or pressure) for the flow modelling of tidal breathing conditions as the Womersley number during tidal breathing is around 3 (Spence et al., 2010). A representative list of
such studies includes: Schroter and Sudlow (1969), Chang and El-Masry (1982), Zhao and Lieber (1994), Caro et al. (2002), Erbruggen et al. (2005), Gemci et al. (2008), Freitas and Schroder (2008), and Corley et al. (2012).

Li et al. (2007a) numerically investigated the effect of the transient respiration on the flow pattern through an anatomically based model. A laminar parabolic transient inlet profile with a period of 4.3 seconds and a peak flow of 15 l/minute was imposed at the inlet of a 4-generation (G0-G3) off-plane analytical model of the central airways. The Womersley number at the trachea was 2.3. Their results showed almost no difference in the flow pattern obtained by imposing the transient inlet profile to those obtained at the same corresponding Reynolds number (Re) at steady state. However, a stronger secondary profile was predicted at the upper branches during the deceleration phase of inhalation. Their results agreed with the early experimental measurements of Menon et al. (1984) who applied a combination of different frequencies and flow volumes to a 3 generations asymmetric analytical model (G0-G2) of the central airways. Hot-wire probes were used to measure the velocity profiles at several stations through the model. The measurements obtained from the unsteady experiments at low frequencies showed no significant discrepancy to those obtained at steady state experiments ran at the same corresponding Reynolds number. The authors concluded that an unsteady inlet profile could be represented by a steady inlet profile at the corresponding Reynolds number if the peak Reynolds number and the Womersley number do not exceed 8800 and 16 respectively.

On the other hand, the oscillating inlet profile was found to have a significant effect on the flow characteristics through subject-specific models of the bronchial airways. Große et al. (2007) used PIV to experimentally investigate the temporal evolution of the flow characteristics within the first bifurcation of a 6 generations (G0-G5) subject-specific model of the central airways during inspiration and expiration. They used several combinations of $\alpha$ (3.3-5.8) and Re (1050-2100) in oscillating flow experiments and a Re range of (1250-1700) for the steady flow experiments. Both the steady and the unsteady flow experiments showed counter rotating vortices at the left bronchia during inspiration. However, increment of Re during steady inspiration was found to have a minor effect on the size and the structure of the depicted vortices. Conversely, the onset
Re (the critical Re) of the vortices at the left bronchia as well as their size and structure was found to be strongly dependent upon the combination of the Womersley number and the Reynolds number during unsteady flow. Nevertheless, the steady and the unsteady flow profiles were almost identical during expiration at this study. Other studies that investigated the effect of oscillating profile on the flow characteristics within subject-specific models of the central airways agreed that the critical Re strongly depend upon the value of α, and the combination of α and Re have a significant effect on the flow structure within the bronchial tree (Eitel et al., 2010, Soodt et al., 2012). Thus, it is recommended that the unsteady flow must be considered since there is a strong impact of the temporal rate of change of the velocity on the development of the flow fields within the airway model. It is important to note the inconsistency between the findings of the studies that utilised analytical models and the conclusion drawn by subject-specific flow modelling studies. Such contradiction highlights the significant effect imposed by the complex structure of the CT-based model on the flow characteristics.

**1.5.2 Truncation of the upper airway**

The intra-thoracic airways (the central and the lower airways) are connected to the atmosphere via the upper airway, which consists of the nasal cavity, the mouth, the pharynx, the glottis, and the larynx (figure 1.1). The structure of the upper airway is complex due to the disordered anatomy of its constituents. Mechanically, the upper airway is often described as a bended tube with several obstructions. Due to the complex structure of the upper airway, the flow in the laryngotracheal region has a wide range of Reynolds number and involves a mixture of various flow types, such as noncircular confined turbulent jet, open cavity flow, shear layer, along with curved and transitional pipe flow (Tawhai and Lin, 2011). Hence, the upper airway has a significant effect on the profile of the flow entering the central airways. Nevertheless, most of the central airways flow modelling studies to date ignored the existence of the upper airway by applying steady or oscillating boundary conditions directly to the tracheal opening. The flow analysis through the upper airway is beyond the scope of this project, a comprehensive review of the flow modelling through the nasal cavity and the upper airway can be found in Strohl et al.,(2012) and Zubair et al.,(2012).
As discussed in section 1.4.1, the work done by Kleinstreuer and Zhang (2003) and Zhang and Kleinstreuer (2004) were one of the firsts to include the upper airway in the computational domain. They developed a simple oral airway geometry with variable circular cross-sections based on a cast replica and a four generation symmetric bifurcating airways geometry based on Weibel (Weibel, 1963). Their results showed a persistent asymmetrical central jet at the laryngotracheal region, known as the laryngeal jet, created due to the constriction in the larynx. They found that the turbulence induced by the upper airway affects the flow pattern down to the 3rd generation.

Lin et al., (2007) investigated the effect of the upper airway on the flow pattern within the laryngotracheal region and the central airways utilising subject-specific models of the bronchial airways. They compared the results obtained from a full subject-specific model extended from the mouth down to the 6th generation of the central airways to those obtained from the same model excluding the upper airway geometry. The same boundary conditions were applied in both simulations to be able to compare the two geometry cases. At the inlet, which is the mouthpiece in the first case and the tracheal opening in the second case, a uniform atmospheric pressure was imposed. At the terminal branches, uniform symmetrical ventilation (320 ml/s) was assumed. The results showed a parabola velocity profile with almost no turbulence at the trachea of the truncated model, while a curved sheet-like laryngeal jet with turbulence intensity of up to 20% was predicted at the trachea of the full model. A similar comparison approach was adopted by Choi et al., (2009) who numerically investigated the airflow through a full subject-specific model extended from the mouth down to the 6th generation, and compared the results to those obtained from truncated airway geometries of the same subject. They truncated the full subject-specific model at three different levels namely: the subglottis, the supraglottis, and the laryngopharynx. They found that as the truncation level increases, the flow pattern tends to deviate from the flow characteristics within the full model as shown in figure 1.8. They concluded that the turbulence induced by the laryngeal jet significantly affects the flow patterns within the central airways, and hence, the upper airway geometry must not be neglected. In case of excluding the upper airway from the flow domain, modifications must be applied to the boundary conditions to accommodate the effect of the truncated upper airway.
1.5.3 Absence of the peripheral airways

As explained in section 1.2.1, the human bronchial airways contain 23 consecutive generations; the first 16 generations are known as the conducting airways, followed by 7 generations known as the respiratory airways (lower airways). Current medical volumetric imaging techniques allow the 3D construction of the first few generations of the conducting airways. A maximum of 7 generations subject specific model was reported in the literature (Choi et al., 2010, Lambert et al., 2011). This is due to the insufficient resolution of the CT scan. Several aspects may affect the CT-scan resolution including the radiation dose restrictions, insufficient scanning time, heartbeats, and possible subject movement. Hence, current subject specific models of the central airways represent only a small portion of the bronchial tree. Nevertheless, most of the flow modelling studies to date assume atmospheric open-ended terminal branches or uniform flow distribution notwithstanding the existence of the peripheral airways. This is due to the inaccessible nature of the bronchial airways that limits the capability of

Figure 1.8 Contours of normalized mean speed (blue (zero) to red (highest positive)) illustrating the effect of truncating the upper airway geometry. The truncation location: (a) trachea (b) supraglottis (c) midpharnx (d) complete geometry. Adapted from Choi et al., (2009).
direct measurement of the pressure-drop or flow distribution within the bronchial airways.

Few efforts were made to account for physiological boundary conditions that approximate the effect of the peripheral airways. De Backer et al., (2008b) referred to the volume change of the left and the right lungs to estimate the pressure values at the terminal surfaces of a subject specific model of the central airways. The volume change was calculated from two CT scans acquired at FRC and TLC respectively. Compared to the conventional atmospheric pressure boundary condition, their proposed boundary condition resulted in a more quantitative agreement to a clinical ventilation assessment of the same subject under the same inlet boundary condition. Yin et al., (2010) applied mass preserving non-rigid image registration technique to calculate regional ventilation from two CT scans acquired at different inflation levels. A 1D airway model (Tawhai et al., 2004) that analytically represents the centreline of the missing peripheral airways was generated and attached to the original 3D model as discussed in section 1.4.2. The registration-derived regional ventilation map was then associated with the coupled 3D-1D model to estimate the flow volume at the 3D model terminal surfaces based on mass conservation. The registration derived regional ventilation was validated by comparing the measured total airway volume change to the registration derived Jacobean value that represents the local tissue expansion. Comparing the predicted results obtained by imposing the image based boundary condition to those obtained by utilising the conventional uniform pressure and uniform flow distribution boundary condition revealed a significant discrepancy in the lobar flow distribution and pressure drop across the airways. Their proposed boundary conditions resulted in CFD predictions of the lobar ventilation that agreed well with the CT measurements of the lobar ventilation with a maximum error of %14.73

1.5.4 Lung compliance and airway deformation

In reality, the distribution of ventilation is regionally dependent and driven by the expansion of the nonlinearly elastic, compressible lung tissue (Lin et al., 2009). However, including the lung compliance and the airway deformation in the computational domain is challenging due to the mysterious nonlinear mechanical properties of the lung tissue and the surrounding parenchyma. Few efforts were made to develop an FSI analysis to
study the effect of the flexible walls on the flow characteristics and wall shear stress (Koombua et al., 2008, Xia et al., 2010). For example, Xia et al., (2010) utilised a triple domain FSI (fluid domain, the structure domain, and the deforming mesh) to investigate the interaction between the flow and the airway wall of a single bifurcation. Their bifurcated model was extracted from the same subject specific model utilised in the study of Lin et al., (2007) who investigated the effect of the turbulent laryngeal jet on a complete model extended from the mouth down to the 6th generation (see section 1.5.2). A parabolic velocity profile (Re= 90-475) was imposed at the inlet of the single bifurcation. The mean velocity at the inlet was equal to that obtained at the same location in the study of Lin et al., (2007). At the outlets, a sinusoidal pressure of 1.0 cmH₂O was assumed. Their results showed that the wall shear stress was decreased by 80% when considering the flexible walls. However, as the material properties of the airway wall and the pressure imposed by the surrounding parenchyma is unknown, developing an FSI analysis to simulate the airway wall deformation is challenging. Alternatively, efforts were made to simulate the deformation of the bronchial tree by means of image registration (Hylla et al., 2010, Ibrahim et al., 2012, Yin et al., 2013). The image registration-derived displacement field obtained from two or multiple lung images at different inflations can be used to deform a CFD mesh by way of linear or higher order interpolation (Tawhai and Lin, 2011). Yin et al.,(2013) adopted a mass-preserving image registration to interpolate the displacement of the airway model between two lung volumes. Three CT scans were acquired from a volunteer at three inflation levels (20%, 60%, and 78% of the vital capacity (VC)) during one scanning session. Based upon image registration, a linear voxel to voxel displacement was adopted for the deformation process. The outlets boundary conditions were imposed using the image based regional ventilation boundary condition proposed by Yin et al., (2010) (see section 1.5.3). A sinusoidal flow with a peak flow rate of 327 ml/s and time period of 4.8 second was imposed at the mouthpiece. The results obtained from the deforming model showed an average pressure drop at peak inspiration of 56 Pascal versus 33 Pascal obtained from a similar rigid model under the same boundary conditions. Thus, the rigid airway model under-predicted the pressure drop at peak inspiration by 40%.
1.6 Validation strategies for numerical modelling of the flow through the central airways

For any CFD simulation, validation is an essential stage of the investigation in order to confirm the validity of the predicted results with respect to the real world observations. This is usually done by comparison with experimental data. Oberkampf and Trucano (2002) describe the validation of the CFD predictions mathematically as

$$\Delta u = (u_{\text{nature}} - u_{\text{exp}}) + (u_{\text{exp}} - u_{\text{PDEs}}) + (u_{\text{PDEs}} - u_{\text{discrete}})$$  \hspace{1cm} (1.1)

where $\Delta u$ represents all the errors and uncertainties of a scalar quantity $u$ between its true value in nature $u_{\text{nature}}$ and the predicted result $u_{\text{discrete}}$. Equation (1.1) can be simplified as

$$\Delta u = E_1 + E_2 + E_3$$  \hspace{1cm} (1.2)

where $E_1$ represents the difference between the true value of $u$ in nature $u_{\text{nature}}$ and the experimental measurement $u_{\text{exp}}$. In other words, it represents how well the physical experiment represents the targeted problem in the real world. $E_2$ represents the modelling errors along with the uncertainties between the experimental measurement and the exact solution $u_{\text{PDEs}}$ of the continuous partial differential equations (PDEs) that numerically represent the experiment. This includes all the errors occurred due to assumptions and simplifications adopted in the simulation modelling setup. $E_3$ represents the error in the CFD calculations as the difference between the exact solution $u_{\text{PDEs}}$ of the governing PDEs and the numerical solution $u_{\text{discrete}}$ of the discrete approximation of the same PDEs provided by the CFD solver.

When validating the CFD predictions of the bronchial flow, the element $E_1$ in equation 1.2 is significant as establishing a physical experiment that accurately represents the flow within a living lung is extremely challenging. This is because most of the physiological boundary conditions that control the flow within a living lung are sophisticated and cannot be represented in a physical experiment. For example, airway deformation during the breathing cycle is classified as inhomogeneous. Such complex non-linear deformation cannot be represented in a physical experiment. Additionally, the physiological flow boundary conditions that govern the flow distribution within the
bronchial airways are not measurable due to the inaccessible nature of the lower airways. As a result, most of the currently available experimental studies were limited to simple flow profiles used to investigate the general flow characteristics within rigid models of the bronchial airways. A representative list of such studies includes: Schroter and Sudlow (1969), Mockros et al. (1970), Chang and El-Masry (1982), Isabey and Chang (1982), Menon et al. (1984), Menon et al. (1985), Briant and Cohen (1989), Cohen et al. (1993), Zhao and Lieber (1994), Lieber and Zhao (1998), Fresconi et al. (2003), Große et al. (2007), Fresconi et al. (2008), Heraty et al. (2008), Kim et al. (2009), Kim and Chung (2009), Vermeulen et al. (2010), and Timmerman et al. (2012). Hence, the vast majority of the experimentally validated numerical studies to date relied on a coarse experimental model of a living lung. This was acceptable to some extent for the application to the early computational models that were limited to simplified geometries and simple flow boundary conditions. However, computational models have since developed to include anatomically accurate geometries and unsteady physiological flow boundary conditions that are more representative of a living lung. As reproducing the same features in physical experiments is difficult, there is a lack of comparative experimental data for CFD validation purposes. To overcome this obstacle, attempts were made to validate the CFD predictions by comparison with clinical data. This is known as in vivo validation. In this case, the modelling errors are evaluated directly with respect to the true nature. Thus, equation 1.1 can be rewritten as:

$$\Delta u = (u_{\text{nature}} - u_{\text{PDES}}) + (u_{\text{PDES}} - u_{\text{discrete}})$$  \hspace{1cm} (1.3)

De Backer et al. (2008b) were one of the firsts to implement an in vivo validation to determine the accuracy of their predicted results. They proposed physiological flow boundary conditions based on CT measured lung volume changes (see section 1.5.3). The flow distribution between the left and the right lung of the same subject under the same inlet boundary condition were measured clinically using 2D gamma scintigraphy. These measurements were then used to validate the CFD prediction by comparison. A similar validation approach was followed by De Backer et al. (2010) who used SPECT 3D image of the regional flow distribution within the lung using a SPECT gamma scanner. They enhanced the regional ventilation image by registration to a CT image of the same subject in order to obtain a clear indication of the location of certain tracer features.
This procedure allowed for global validation of the CFD predictions with lobar tracer concentration. Moreover, some studies proposed the use of CT measured lobar volume change to clinically validate the CFD predictions of the flow distribution (Yin et al., 2010). Unfortunately, in vivo local validation is not yet feasible, as currently available medical imaging techniques are incapable of visualising the respiratory flow within a living lung. However, they can provide regional flow distribution data that can be used to validate some bulk flow quantities. Such significant downside may question the robustness of such validation strategy. However, a combination of an in vivo validation and a good verification assessment may be sufficient to justify the accuracy of the predicted results. An interesting technique for gaining in vivo lung flow was reported by Minard et al. (2006, 2008, 2012). They visualised the flow dynamics within the lung of a living rat using Hyperpolarised helium-3 (HP $^3$He) magnetic resonance velocimetry. The highly polarised inhaled gas emits a MR signal that is adequate for measuring gas flow. To date, this is the only promising clinical procedure that is able to produce velocity vector maps of the gas flow within a living lung. However, one downside of this technique is that constant gas inhalation is required during the imaging time, which limits the validation to steady flow modelling studies.

1.7 Challenges and limitations of modelling the bronchial flow using CFD

Developing computational models to simulate the flow within the bronchial airways using CFD has been significantly improved over the last few years. However, the predicted flow results to date are still far from representing the actual flow characteristics within a living lung. Many of the studies to date treated the bronchial tree as an open-ended network of rigid tubes, while in reality the bronchial tree is a semi-closed network of compliant asymmetrical branches surrounded by several tissues of the thorax constituents. The introduction of subject-specific models has verified the significant effect the airway morphology has on the airflow pattern and distribution. Studies that investigated the flow within subject-specific models have found that different subjects share only the general flow pattern, but the variation in the airway morphology significantly affects the flow between subjects. Hence, the bronchial airway cannot be represented as a network of connected tubes.
Most of the subject-specific studies to date were limited to rigid models of the bronchial airways due to the difficulty of modelling the airway deformation over the breathing cycle. Some efforts were made to account for the airway compliance in the computational domain by developing an FSI analysis. However, airway deformation during the breathing cycle is mainly governed by the deformation of the surrounding tissues, whereas the passing flow has almost no effect on the airway deformation. Furthermore, the material properties of the bronchial airways, in general, are unknown due to the variability in the material properties of the different tissues, the composite nature of the lung constituents, and the subject-specific variability in the thickness of the airway walls. Thus, developing an FSI analysis to account for the airway deformation is not practical. Alternately, the use of non-rigid registration between consecutive CT scans to develop a dynamic airway model was introduced in recent studies. Even though the results of this algorithm were promising, it requires the use of several CT images covering the breathing cycle in order to account for the airway deformation nonlinearity. This downside limits the use of such algorithms to research animals, due to the radiation dose restrictions for human subjects. Thus, current research efforts are focusing mainly on developing simulation algorithms that account for the nonlinear airway deformation using as few CT scans as possible. Furthermore, the currently available airway deformation algorithms have so far been applied to simulate the airway deformation during deep breathing condition. Therefore, it will be interesting to investigate the effect of the airway deformation on the flow characteristics during tidal breathing condition. This will assess the common assumption that airway deformation during tidal breathing condition can be neglected, as the lung volume change is trivial and will have a minor effect on the flow characteristics.

Current CT images allow reconstructing the first few generations of the bronchial tree. Thus, accounting for the airway deformation without the use of physiological flow boundary conditions that reflect the effect of the missing peripheral airways is not sufficient. The number of the studies that proposed algorithms to compute physiological flow boundary conditions is limited and none of them can yet claim complete accuracy, as validating such algorithms is challenging. Measuring the local pressure drop within a living lung is currently not possible due to the inaccessible nature of the lung. Therefore,
research efforts were focused on identifying the volumetric flow rate at each terminal branch based on the volume change of its peripheral branches. A non-rigid registration between successive CT scans is used to map a voxel to voxel volume change of the full lung (regional ventilation). However, it is not yet possible to identify the voxels of the missing peripheral branches distal to each terminal branch due to the low image quality. A mathematically generated 1D model was used to subdivide the lung into several cubic regions where each region includes the voxels associated with each terminal branch. The regional ventilation calculated for each cubic region was then used as a physiological flow boundary condition for its associated terminal branch. Due to the inhomogeneous and asymmetrical airway structure, one can question the accuracy of attributing an appropriate value of bulk flow velocity to each terminal branch using a mathematically generated 1D model as a reference to define the peripheral airway volume change. Therefore, more efforts are required to develop algorithms to account for accurate physiological flow boundary conditions.

A combination of algorithms that account for the airway deformation nonlinearity and accurate physiological flow boundary conditions will significantly reduce the difference between the predicted results and the actual flow within the living lung. However, validating the flow results predicted with such sophisticated algorithms is challenging. This is because the flow within a living lung cannot be modelled in a physical experiment due to the multi-scale complexity of the airway structure as well as the biological and the physiological aspects that are involved in the process of breathing, which cannot be implemented in a physical experiment. Alternatively, the use of medical data for in vivo validation has been recently introduced. An advantage of such validation strategy is that it provides an accurate subject-specific information of a living lung. However, one downside is that currently available medical imaging devices cannot visualise the flow dynamics within the bronchial tree, but they can provide information on the lung regional ventilation. Such information allows for global validation only, which might not be sufficient to justly the accuracy of the predicted results. It is, therefore, recommended to adopt a good verification study alongside the in vivo validation for a robust discussion on the validity of the predicted results.
1.8 Project aim and objectives

The above literature survey concludes that there are several morphological and physiological factors that govern the flow through the bronchial airways. The vast majority of the research to date concerned mainly on the investigation of the individual factors and their influence on the flow characteristic. Progress is currently limited by the lack of a versatile model, such as from CFD that accurately represents the flow within a living lung during tidal breathing. Hence, the main aim of this project is to develop a dynamic subject-specific model of the bronchial airways that is capable of accurately representing the flow within a living lung during tidal breathing conditions and use the model to advance the understanding of the flow within the bronchial airways. Such a model should account for all the key morphological and physiological factors in order to reduce the difference between the predicted results and the actual flow within the bronchial airways. To achieve this aim, the present study pursues four main specific objectives:

1. Developing a dynamic model that accurately represents the airway deformation during tidal breathing conditions.

2. Developing an algorithm to account for physiological flow boundary conditions that reflect the effect of the missing peripheral airways.

3. Combining the airway deforming model and the physiological flow boundary conditions in a single CFD method.

4. Applying the model to study the effect of the moving walls on the flow through the bronchial tree.

The methodology to achieve the first objective is:

a. Develop a deformation algorithm that is capable of controlling the airway motion between different inflation levels by means of common landmarks.

b. Use the deformation algorithm to interpolate the airway motion during tidal breathing using several airway models reconstructed out of 4DCT data covering the breathing cycle.
c. Develop a deformation algorithm to account for airway motion nonlinearity using only two CT scans acquired at the beginning and the end of the breathing cycle.

d. Validate the proposed deformation algorithms by comparing the interpolated models against the models that were reconstructed out of the 4DCT data.

The methodology to achieve the second objective is:

a. Use the vascular tree as a reference to segment the lung into small sub-volumes, where each sub-volume encloses the peripheral airways of each terminal branch.

b. Develop physiological flow boundary conditions based upon the volume change within each sub-volume.

c. Validate the proposed lung volume subdivision technique using an airway cast model of the examined subject.

d. Validate the computed physiological flow boundary conditions based on CT measured lobar regional ventilation.

The methodology to achieve the third objective is:

a. Develop a computational framework to model the bronchial flow using a dynamic CT data set using the proposed deformation algorithms and the computed physiological flow boundary conditions.

The methodology to achieve the fourth objective is:

a. The evaluation of the effect induced by wall motion on the CFD predictions of the bronchial flow characteristics during tidal breathing.

b. The evaluation of the effect induced by the imposed physiological flow boundary conditions on the flow characteristics compared to the conventional simple boundary conditions.

The findings of this project are expected to enhance the fidelity of the CFD predictions of the bronchial flow compared to the actual flow within a living lung. In addition, the results predicted by the proposed dynamic model will enable to evaluate the common assumption adopted by many studies that airway deformation during tidal breathing conditions has a negligible effect on the flow characteristics.
1.9 Thesis structure

4DCT data set of a laboratory rat was utilised in this study to develop comprehensive methodologies to achieve the project aim and objectives listed in section 1.8. Figure 1.9 illustrates a block diagram explaining the conducted research with reference to the structure of the thesis. The remainder of this thesis is structured as follows.

Chapter 2 presents a deformation algorithm that utilises successive volumes of the bronchial airways to develop a dynamic CFD mesh of the bronchial airways. The successive volumes reconstructed out a dynamic CT data set are used to develop a dynamic CFD mesh of the bronchial airways that accurately represent the airway deformation during tidal breathing. The interpolated mesh was compared against the dynamic CT reconstructed volumes of the bronchial airways at sampled time points for validation. Furthermore, to comply with the radiation dose restrictions for humans and overcome the current limitations of using a dynamic CT data set to develop a dynamic subject-specific model of the bronchial tree, a non-linear interpolation model that utilises two CT lung volumes is proposed in chapter 2. The model was able to capture the non-linear characteristics of the airway motion during tidal breathing.

Chapter 3 proposes an algorithm to derive dynamic subject-specific physiological flow boundary conditions that replace the conventional simple flow boundary conditions. The proposed algorithm relies upon segmenting the lung into small sub-volumes based on the mechanical coupling between the vascular tree and the bronchial tree. The volume change of these sub volumes over sampled time-points over the breathing cycle are then used as flow boundary conditions for the sampled airway geometry. A validation of the lung volume segmentation is presented based upon a registration of a cast model of the bronchial tree of the same animal to a CT based reconstructed vascular tree generated from a CT scan acquired at the same inflation level. Chapter 3 also represents a validation of the proposed dynamic boundary conditions by comparing the calculated volume change against a CT measured lobar volume change.

Building upon the outcome of chapter 2 and chapter 3, A CFD simulation of the flow through a dynamic subject-specific model of the bronchial tree of the laboratory animal during tidal breathing is presented in chapter 4. The computed dynamic subject specific
Figure 1.9 A block diagram of the conducted research with reference to the thesis structure
boundary conditions of chapter 3 are imposed at the terminal surfaces of the deforming model of the bronchial airways of chapter 2. The deforming model was based upon the full data set of the dynamic CT. The predicted flow results are compared to those acquired from a rigid model of the same subject under similar flow boundary conditions, and to the results obtained by a similar rigid model with simple flow boundary conditions.

Chapter 5 illustrates the initial stages of developing dynamic subject-specific models of the bronchial airways for human subject. The deformation algorithm presented in chapter 2 was used to deform the CFD mesh of the bronchial airways of a human subject between the residual volume (RV) and total lung capacity (TLC) in order to approximate the deformation of the bronchial airways during deep breathing conditions. The acquired results were compared to those obtain from a rigid model of the same subject at TLC.

Finally, the outcome and the conclusions of this study along with possible future developments are discussed in chapter 6.
2 MODELLING THE NOTION OF THE BRONCHIAL TREE FOR CFD APPLICATIONS

2.1 Introduction

Modelling the respiratory motion during the breathing cycle is a significant research topic, not only for a computational modelling perspective, but also for a clinical perspective, since it has applications such as the planning of a Radiotherapy treatment for lung cancer patients. Most efforts to date were focussed mainly on developing algorithms to account for the motion of a single point within the lung, usually the trajectory of a cancerous tumour, or the deformation of the entire lung sac over the breathing cycle. However, the deformation of the bronchial tree as a single component, which is essential for the development of dynamic computational fluid dynamics (CFD) models of the bronchial airways, has not been adequately investigated yet. Advances in volumetric imaging techniques such as four-dimensional computed tomography (4DCT) has enabled for a better understanding of the respiratory motion during breathing. 4DCT imaging provides CT images of the thorax constituents at different time points over the breathing cycle. Usually a non-rigid registration between the subsequent CT images is implemented in order to estimate the respiratory motion fields (McClelland et al., 2006, Boldea et al., 2008, Klinder et al., 2008, Eom et al., 2009, Werner et al., 2009, Eom et al., 2010, Staub et al., 2011, Zhang et al., 2013). Hence, 4DCT images in theory can be utilised to develop accurate dynamic CFD models of the bronchial tree following a similar approach. However, one downside is that the quality of the 4DCT images is significantly lower than the conventional static CT images; the acquired dynamic CT images contain inherent distortions that limit the capability of reconstructing large models of the bronchial tree. This is mainly due to the insufficient x-ray exposure time of each shot. Static CT images, on the other hand, have better image quality, which allows the reconstruction of up to 10 generations of the bronchial tree. However, it is not advisable to acquire more than two static CT images of a human subject during one scanning session due to the radiation dosage restrictions. Thus, the development of a dynamic
CFD model of the bronchial tree based on static CT data of a human subject is restricted to a maximum of two CT images, usually acquired at the end-exhale and the end-inhale. This is a challenging task, as the lung deformation during a single breathing phase is significantly inhomogeneous and cannot be simplified as a linear voxel to voxel interpolation between a pair of CT images (Yin et al., 2013).

In this chapter, two dynamic models of the bronchial airways for CFD applications are introduced. The first model utilises a 4DCT data set of a laboratory animal that covers the full breathing cycle. The technique utilises the commercially available solver ANSYS FLUENT (Lebanon, NH, USA). Successive 3D geometries were reconstructed out of the 4DCT data set. The solver was customised to deform the CFD mesh of the starting lung volume and match it with its successive lung volumes in order to compute the deformation of a full breathing cycle. The second model utilises the CT scans at the end-exhale and the end-inhale of the same animal to interpolate the airway deformation during normal breathing condition. This model was capable of approximating the non-linear features of the lung deformation during the breathing cycle using one pair of CT scans. This is a significant achievement as it demonstrates the ability to model the lung motion from only two CT scans, enabling to perform this procedure on human lung geometries generated from static CT scans, which complies with the radiation dose restrictions.

2.2 Developing the deformation algorithm

2.2.1 Animal imaging and airway geometry sampling

The animal data used in this study were supplied by the Biological Sciences division at the Pacific Northwest national laboratory, Washington, USA. The animal use was approved by their affiliated institutional animal care and use committee (Protocol 2010-23). 11 CT images were acquired dynamically (without breath hold) for a 298g male Sprague-Dawley rat with a temporal resolution of 100ms. Hardware setup and imaging procedure are extensively explained in Jacob and Lamm (2011). Briefly, the rat was initially anesthetised by 3% isoflurane in oxygen, then intubated with a 14-gauge catheter tube and connected to the commercial ventilator (CWE Inc. model 830/AP; Ardmore, PA). The ventilator was set to deliver air (30% O₂, 70% N₂) at 54 tidal breaths.
per minute (500 ms inspiration, 600 ms expiration, and \( \sim 6.2 \text{ cmH}_2\text{O} \) Peak Inspiratory Pressure (PIP)). A deep breath (sigh) of 4 Sec (2800 ms inspiration, 1200 ms expiration, and \( \sim 25 \text{ cmH}_2\text{O} \) (PIP) was implemented every 100 breaths to maintain lung recruitment during the long time of the imaging process (\( \sim 90 \text{ min} \)). The ventilator was customised to monitor the pressure change near the trachea and the corresponding flow volumes during the scanning experiment. The rat was scanned supine using the commercial micro-CT scanner (eXplore CT120, GE Health Care Waukesha, WI). Scanning parameters were 80 kVp, 32 mA, 16 ms exposure time, 100 \( \mu\text{m} \) resolution, 360° projection with 1° increment. Figure 2.1 illustrates the CT imaging time points superimposed on a typical flow volume change waveform measured by the ventilator unit.

![Figure 2.1](image.png)

Figure 2.1 A typical waveform of the volume change measured by the ventilator. The position of the bars represents the x-ray exposure time points, the width of the bars represents the 16 ms exposure time, and the height of the bars represents the measured volume standard deviation.

As freezing the lung motion is not required when acquiring the CT images dynamically, lung mechanics (tissue compliance and strain) are maintained stable over the breathing cycle (Burri et al., 2005, Namati, 2009). This is a significant advantage when studying the deformation of the bronchial airway. However, the 16 ms short exposure time used in the dynamic CT image acquisition results in coarse images with low quality that limits the capability of identifying and segmenting large number of generations. Hence, to smooth the boundaries and reduce image noise, a 3D Gaussian filter followed by a 3D median filter (radius = 1) were applied to all images using the free source software ImageJ (NIH, Bethesda, Maryland, USA). A sample of the scanned slices before and after filtering is shown in figure 2.2 (a). The processed images were then imported to the
medical image processing software Mimics (Materialize, Belgium) for image segmentation and 3D CAD sampling. The airway branches were automatically identified and segmented based on their pixels grey-level values by means of the intensity threshold approach. However, this segmentation required some manual adjustments to ensure the surface boundary continuity of the bronchial tree cross-sections. 11 airway 3D geometries were then reconstructed out of the segmented images. The reconstructed geometries were labelled as $G_t$ where $t$ is the acquisition time point of their associated CT image in ms (see figure 2.1). The generated 3D geometries were limited to 4±1 generations as shown in figure 2.2 (b). It was not possible to accurately reconstruct additional generations due to the insufficient image quality.

![Sample slice before and after filtering](image1.png)

![3D reconstructed geometries](image2.png)

Figure 2.2 (a) a sample slice of the dynamic CT data set before (top) and after (bottom) filtering of the Sprague-Dawley rat. (b) an example of the 3D reconstructed airway geometries ($G_0$).

Each airway geometry was then manually cleaned up using the commercial software Magics (Materialize, Belgium). The cleaning-up process was performed to insure that the generated 3D geometries of the bronchial airways are watertight and suitable for generating the CFD mesh. The process includes closing the gaps within the generated
airway geometries along with resolving the intersecting and overlapping wall triangles. Furthermore, to maintain well-defined flow boundaries, the terminal branches at each model were truncated perpendicular to their associated centreline. The centreline of each geometry was generated following the Sequential 3D Thinning algorithm of Palágyi et al. (2001). This algorithm deletes iteratively the border points of the binary until only the skeleton is left. This algorithm was proven to have good results on tubular-like geometries such as the bronchial tree (Tawhai et al., 2004). A defined centreline length was used as a reference to locate the truncation plane for each terminal branch. This step was necessary in order to maintain the morphological consistency between the reconstructed airway geometries.

2.2.2 From geometry samples to affine static CFD meshes
The proposed bronchial tree deformation algorithm is shown in figure 2.3. A set of static structured CFD meshes were produced from the dynamic-CT based geometries of section 2.2.1 using the commercial software ANSYS ICEM CFD (Lebanon, NH, USA). Consider a pair of static CFD meshes of the bronchial airways \((M_t, M_{t+\Delta t})\) that were generated from two successive airway geometries \((G_t, G_{t+\Delta t})\) over the breathing cycle, where \(M_t\) is the static CFD mesh at time \(t\) and \(M_{t+\Delta t}\) is the static CFD mesh at time \(t +\)
For the proposed algorithm to function correctly, three main conditions are required:

- The number of nodes at the wall of $M_t$ must equal to that at the wall of $M_{t+\Delta t}$.
- The spatial sequence of the nodes at the wall of $M_t$ and $M_{t+\Delta t}$ must be equal to avoid geometry violation during the deformation process, i.e. the wall nodes are numbered following the same spatial path.
- Each node at the wall of $M_t$ must be linked to its corresponding node at the wall of $M_{t+\Delta t}$ to prevent intersections.

To satisfy these conditions, a structured mesh $M_t$ was generated for each airway geometry sample $G_t$ over the breathing cycle $0 \leq t \leq 1100$ ms using the same blocking topology so that all geometry meshes $M_t$ have the same number of nodes distributed on their walls with the same node ID labels. Blocking segments were evenly stretched on all $G_t$ at increasing time $t$ in order to gain a consistent distribution of wall nodes. The centreline of each geometry, generated by the Sequential 3D Thinning algorithm of Palágyi et al. (2001), was used to define the initial position of the blocks on each $M_t$ structured mesh. Each branch centreline segment was discretised uniformly by inserting $n \geq 1$ nodes. The locations of these nodes from the bifurcating points of the

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**Figure 2.4** Blocking strategy illustrated on a sample branch. The magnification illustrates the slight manual modification applied to a vertex location.
generated centrelines were used as common landmarks to control the CFD mesh blocking topology as shown in figure 2.4. The positions of the corresponding block vertices on $G_t$ and $G_{t+\Delta t}$ were then manually adjusted in order to improve the mapping result based on visual morphological landmarks, such as the bifurcation region and the morphological characteristics of the individual branches. The appropriateness of the manually selected vertices was evaluated based on the accuracy of the registration between the static mesh $M_t$ deformed to time points $t + \Delta t$ and the reference geometry $G_{t+\Delta t}$ over the breathing cycle as discussed in section 2.3.2. As a result, all meshes $M_t$ had the same number of wall nodes, with the same IDs, distributed at corresponding positions on their walls.

2.2.3 From static affine CFD meshes to a continuous motion model

The proposed deformation algorithm was designed to deform $M_t$ and accurately align it on $M_{t+\Delta t}$ by displacing the mesh nodes at the wall of $M_t$ in small time steps until they match their corresponding position at the wall of $M_{t+\Delta t}$. This algorithm affectively converts $M_t$ into a moving mesh. The deformation of the CFD mesh was performed using the CFD commercial software ANSYS FLUENT v13.0 (Lebanon, NH, USA). Due to the non-linear and inhomogeneous deformation of the bronchial tree during breathing, the CFD solver requires spring smoothing and local remeshing dynamic mesh schemes to handle this kind of deformation. These two dynamic mesh schemes are not available in ANSYS FLUENT 13.0 for simulations that use a structured mesh and can only be used in conjunction with an unstructured mesh. Therefore, the internal hexahedral elements of all meshes were deleted and the wall quadrilateral elements were converted to triangular elements by splitting each trapezoid (quadrilateral) element by its minor diagonal. The number of wall nodes, the node IDs, and the spatial distribution of the wall nodes do not change when converting from quadrilateral to triangular elements and, hence, the wall node correspondence between the geometries is preserved.

Let $\alpha$ be the set of the nodal coordinates defining each triangular element in the wall of the moving mesh $M_t$, and $\beta$ is the set of the wall nodal coordinates of the target mesh $M_{t+\Delta t}$. The wrapping algorithm establishes a correspondence between the wall nodes so that $\forall i \ (i \in \alpha \rightarrow \hat{i} \in \beta)$ where $i$ and $\hat{i}$ are the corresponding node coordinates $(x, y, z) \in \mathbb{R}^3$ at the moving and the target mesh walls respectively. To retain this
correspondence, the Delaunay tetrahedral mesher was utilised to generate the tetrahedral volume mesh elements of the moving mesh $M_t$. This mesher utilises the existing wall surface nodes as a reference to generate the volume mesh elements and does not alter any wall node location. However, as new nodes were added due to the volume elements, the wall node IDs were altered, generating a new set $\gamma$ of the wall nodes for $M_t$. This new set of nodes includes all the elements of $\alpha$ but in a different order so that

$$\forall i \in \gamma \leftrightarrow i \in \alpha, \gamma \times \alpha \neq \alpha \times \gamma$$

(2.1)

Since the node IDs were altered, there is no correspondence between the new set of the moving mesh wall nodes $\gamma$ and the target mesh wall nodes $\beta$. However, as the number and the position of the wall nodes were fixed, a C code was written to generate a new set $\delta$ of corresponding nodes for all $i \in \gamma$ based on the previously established

Figure 2.5 Code flowchart to resequence the nodal positions at $\beta$ as $\delta$. 
mapping $\alpha \rightarrow \beta$. Figure 2.5 illustrates the flow chart of this code. Thus, at the end of the procedure shown in figure 2.3 $\forall i (i \in \gamma \rightarrow \hat{i} \in \delta)$.

### 2.2.4 Deforming the mesh by a User Defined Function (UDF)

A User Defined Function (UDF) was written to enable the solver ANSYS FLUENT to recognise the start and target positions of each node at the wall of the moving mesh, and the deformation type (linear, non-linear) that applies to each node. The solver reads the start position set $\gamma$ of the nodes as well as the target position set $\delta$ by executing the DEFINE_ON_DEMAND macro. These data are saved at User-Defined Node Memory (UDNM) locations. The solver then starts to deform the airway wall by updating the computational grid in small time-steps utilising the DEFINE_GRID_MOTION macro. The position of the wall nodes at each time step is calculated based on a pre-specified equation depending on the deformation type with respect to the breathing time) as shown in the pseudo-code in figure 2.6. The applied deformation type is discussed in details in section 2.3 and 2.4.

### Pseudo-code for Deforming the mesh

1: Read files of wall nodes start and end position $\gamma \& \delta$ <DEFINE_ON_DEMAND>
2: Open file
3: $\forall (i \in \gamma \& \forall (i \in \delta)$
4: Set marker, NODE_MARK($v$) = 1 to all nodes, to make sure each node is only picked once
5: Start node loop
6: Start counting the number of processed nodes
7: If (NODE_MARK($v$) == 1), do
8: save nodes cords to UDMs
9: NODE_MARK($v$) = 0
10: Number of processed nodes +1
11: End if
12: End node loop
13: Close file
14: Display total number of read nodes

15: Define airway wall motion <DEFINE_GRID_MOTION>
16: Start _f_loop
17: If NODE_POS_NEED_UPDATE
18: Read node coordinates
19: Calculate the linear distance between the start and the end position
20: Calculate node position for the current time step based on a pre-defined node velocity equation (Constant velocity in the dynamic CT based deforming model, or the derivative of the normalised lung volume change waveform in the 2-CT based deforming model)
21: End if
22: End _f_loop
23: Update face metrics

24: Define terminal surface motion <DEFINE_GEOM>
25: Define: three surface boundary nodes
26: Ensure the three nodes are not located in straight line
27: Locate corresponding node position at the wall of $M_{\text{wall}}$
28: Calculate the linear distance between the start and the end position of each node
29: Calculate nodes position at the current time step based on a pre-defined equation
30: Calculate plane normal vector based on the calculated nodes position
31: Project the deforming surface nodes on the calculated plane

Figure 2.6 The general structure of the deformation UDF.
The terminal surfaces of the moving mesh must deform consistently with the deformation of the airway-bounded wall. However, as the deformation of the airway wall is non-uniform, it is required to maintain the planeness of the terminal surfaces during the deformation in order to avoid geometrical violation. This was done by defining a plane equation for each terminal surface at every time step based on pre-calculated positions of three nodes located at the surface boundary. The solver then projects the nodes of the deforming terminal surface on the new plane location using the DEFINE_GEOM macro. One limitation of such technique is that the deformation time step size must be small to maintain acceptable mesh statistics near the moving surfaces.

2.3 The dynamic CT based deforming model

2.3.1 The specifications of the moving mesh
This deforming model utilises all the CFD meshes \( M_0, ..., M_{1000} \) of the 11 airway geometries that were reconstructed out of the dynamic CT data set to interpolate the airway motion during the full breathing cycle. The moving mesh is \( M_0 \), which is the CFD mesh of the end-exhale geometry \( G_0 \). This is the geometry reconstructed out of the CT data that were acquired at the beginning of the breathing cycle at \( t = 0 \) ms. The target mesh \( M_{t+\Delta t} \) is determined by the deformation time \( t \). The solver was customised to

![Figure 2.7](image)

Figure 2.7 The dynamic CT based deforming mesh at different inflation levels over the breathing cycle (0 < t < 1100 ms). (a) Inspiration (b) expiration.
select the subsequent mesh $M_{t+\Delta t}$ as a target mesh based on the current deformation time. The deformation between the subsequent meshes was assumed linear. Figure 2.7 illustrates the airway deforming mesh during inspiration and expiration.

2.3.2 Validation of the dynamic CT based deforming model

In order to validate the accuracy of the proposed dynamic CT based deforming model, the registration between the deformed CFD mesh and the dynamic CT based reconstructed geometries was investigated as shown in figure 2.8. 3D CAD models were reconstructed out of the deformed CFD mesh at the same time-points over the

Figure 2.8 Maximum computed Hausdorff distance of the deformed mesh at (a) inspiration, and (b) expiration. The histograms represent the distribution of the computed Hausdorff distance.
breathing cycle used for the CT imaging i.e. every 100 ms. The alignment of each 3D CAD model to its corresponding dynamic CT based geometry was then inspected by computing the Hausdorff distance. Figure 2.8 shows that the deformed CFD mesh aligned very well with its corresponding dynamic CT based geometry over the breathing cycle. The mean of the computed Hausdorff distance was \( \mu = 0.0 \) mm for all the inspected models. Additionally, 99.96 % (±0.01 %) of the computed Hausdorff distance values were within the range of ±0.01 mm. This range is small compared to the typical mesh deformation between \( t \) and \( \Delta t \) of ∼0.2 mm. Limited discrepancies with a maximum Hausdorff distance of approximately ±0.025 mm were observed on some models mainly around the bifurcating zones or on branches with highly irregular morphology. Such a small error is not expected to affect the CFD predictions. Figure 2.8 illustrates the computed Hausdorff distance for the models with the largest observed discrepancy at inspiration and expiration along with their associated data distribution. Hence, the deformed CFD mesh accurately approximates the deformation of the bronchial airways within a living lung during the breathing cycle, which indicates the robustness of the proposed deforming algorithm.

2.4 The 2-CT based deforming model

2.4.1 The displacement vector of the moving nodes
To develop a general understanding of how the bronchial tree deforms during the breathing cycle, the trajectories of 25 landmarks located mainly at the bifurcating zones were extracted from the dynamic CT based deforming model. The locations of the selected landmarks are illustrated in figure 2.9 (a) by red dots. The initial positions of the landmark at \( M_0 \) were defined first. Then, their corresponding positions on every subsequent mesh \( M_{0+\Delta t} \) were acquired from the dynamic CT-based deforming model of section 2.3. The trajectories of the landmarks were interpolated by connecting the acquired positions of the landmarks on the progressive time sequence of meshes using B-spline curves. Two trajectories were built for each landmark as shown in figure 2.9 (b), an inspiration trajectory and an expiration trajectory. The inspiration trajectory starts from the initial landmark position \( P_0 \) at \( M_0 \) passing through its corresponding positions on the progressive mesh sequence \( (M_{100}...M_{400}) \) and terminates at its corresponding position \( P_{500} \) on the end-inhale mesh \( M_{500} \). On the other hand, the expiration trajectory
starts from the P500 landmark position on M500 and terminates at its initial position P0 on M0 passing through all its corresponding positions on the intermediate meshes (M600...M1000).

The trajectories of the landmarks did not follow the same path during inspiration and expiration. This result was expected due to the lung motion hysteresis (Escolar and Escolar, 2004, Boldea et al., 2008). Since most of the studies to date assumed a deformation in a straight line between the corresponding nodes at the end-exhale and the end-inhale meshes (Ibrahim et al., 2012, Yin et al., 2013), it was necessary to

Figure 2.9 (a) locations of the landmarks illustrated on a sample geometry. (b) the calculated trajectory of a sample landmark (Pt), where t is the deformation time. (c) the distribution of the calculated perpendicular distance of each landmark at the intermediate meshes to its associated straight trajectory between end-exhale and end-inhale.
investigate the effect of the lung motion hysteresis on the airway wall deformation. To do that, the corresponding positions of each landmarks at the end-exhale and the end-inhale meshes were connected by a straight line as shown in figure 2.9 (b) and the perpendicular distance \( d \) of each landmark position on the intermediate meshes from their associated straight line was then calculated. Figure 2.9 (c) illustrates the distribution of the calculated perpendicular distances. The statistics showed that more than 90% of the landmarks at the intermediate geometries are located within 0.1 mm from their associated straight line, with a standard deviation of 0.0368 mm. Such a small shifting is not expected to significantly alter the geometrical characteristics of the deforming geometry and hence the CFD predictions. Therefore, lung motion hysteresis can be neglected and the deformation in a straight line might be sufficient when developing a dynamic CFD model of the bronchial airways.

### 2.4.2 The velocity of the moving nodes

In Yin et al. (2013), the displacement of the wall nodes in a straight line with a constant velocity between the corresponding node positions at the end-exhale and the end-inhale meshes was implemented using a human model of the bronchial airways. To evaluate this assumption, they compared an interpolated mesh at the middle of the inspiration phase to a 3D geometry reconstructed from a CT scan acquired at the same time-point on the breathing cycle. Their results showed a significant discrepancy between the interpolated mesh and the CT-based geometry. The interpolated mesh overestimated the anatomical positions at that specific time point on the breathing cycle. This indicates that moving the airway wall nodes between end-exhale and end-inhale in a straight line with a constant velocity is a broad approximation and a more reliable deforming model is required.

To develop an understanding of how the airway wall deforms with respect to time during the breathing cycle, the corresponding landmarks on the intermediate meshes as calculated in section 2.4.1 were projected on their associated straight-line trajectory between their corresponding positions at the end-exhale \( M_0 \) and the end-inhale \( M_{500} \) meshes. The linear distance of each projected landmark from its initial position at \( M_0 \) was then calculated and normalised with respect to the total distance between the landmark positions at \( M_0 \) and \( M_{500} \). Figure 2.10 (a) and 2.10 (b) show the calculated
distances of the projected landmarks during inhalation and exhalation respectively plotted against the breathing time. It can be noticed that the scatter of the calculated linear distances followed a distribution similar to the form of the lung volume change waveform that was measured by the ventilator unit shown in figure 2.1. This suggests that there is a significant correlation between the velocity of the moving airway wall nodes and the lung volume change rate. To evaluate this correlation, the calculated linear distances data sets were fitted to the normalised waveform of the measured lung

![Graph](image)

Figure 2.10 Normalised lung volume change waveform and a straight line fit superimposed on the landmarks projection at the straight line trajectory between end-exhale and end-inhale during (a) inspiration and (b) expiration. The linear fit represents the displacement in a constant velocity
volume change of figure 2.1. For comparison, a straight-line fit was also applied to the calculated linear distances data sets, which represents the deformation at a constant velocity. As shown in figure 2.11 (a) and 2.11 (b), the residuals from fitting to the normalised lung volume change waveform were mainly concentrated around zero, whereas negative residuals were observed for much of the data range in the case of the straight-line fitting. This indicates that the straight-line fit poorly describes the data sets. Hence, using constant velocity to deform the airway wall nodes will result in an inaccurate interpolation. On the other hand, a significant correlation between the lung volume change rate and the velocity of the moving airway wall nodes was observed. The normalised lung volume change waveform better describes the data set. This result suggests that such correlation can be used as a reference to control the velocity of the moving nodes and hence a more reliable dynamic CFD model of the bronchial airways can be developed. The relationship between the volume change and the landmark displacement is somewhat unexpected. Specially, from simple dimensional arguments, the volume change of a spherical sack is proportional to the cube of the envelope displacement. The volume change of a dilating cylinder is proportional to the square of the envelope radial displacement. The linear relationship between the normalised displacement of the landmarks and the normalised volume change suggests a unidirectional expansion of the bronchial tree that is yet to be explained.

Figure 2.11 Residuals from fitting the normalised displacements of the landmarks (a) to the normalised lung volume change waveform from figure 2.1 and (b) to a straight line.
2.4.3 The specifications of the moving mesh

The proposed deforming model utilises the CFD mesh of the end-exhale $M_0$ and the end-inhale $M_{500}$ geometries to develop a deforming CFD model that accurately interpolates the airway deformation during normal breathing conditions. The moving mesh is $M_0$ and the target mesh is $M_{500}$. The trajectory of the wall nodes between the wall of $M_0$ to the wall of $M_{500}$ was assumed to be in a straight line. The derivative of the normalised lung volume change waveform from of figure 2.1 was used to control the velocity of the moving wall nodes between end-exhale and end inhale. Figure 2.12 illustrates the airway deforming mesh using the proposed 2-CT based model.

![Figure 2.12](image)

Figure 2.12 The 2-CT based deforming mesh at different inflation levels over the breathing cycle (0<\(t<1100\) ms). (a) inspiration and (b) expiration.

2.4.4 Evaluation of the 2-CT based deforming model

In section 2.3.2, it was shown that the deformed CFD mesh using the dynamic-CT based deforming model accurately represents the deformation of the lung over the breathing cycle. Thus, a comparison between the mesh deformed using the 2-CT based deforming model and the dynamic-CT based deforming model can be used to evaluate the capability of the 2-CT based deforming model in capturing the non-linear deformation features of the lung utilising only a pair of CT images. To do so, the distance between the node positions at the wall of the deformed CFD mesh using the 2-CT based
deforming model to their corresponding positions at the wall of the deformed CFD mesh using the dynamic-CT based deforming model was computed. Furthermore, a linear deformation (node displacement in constant velocity) between end-exhale and end-inhale was implemented on the same CFD mesh, and the distance between the nodes positions at the wall of the linearly deformed CFD mesh to their corresponding positions at the wall of the deformed CFD mesh using the dynamic-CT based deforming model was also computed. Figure 2.13 and 2.15 illustrates the computed distances at the same

Figure 2.13 The distance between the deformed wall nodes to their corresponding anatomical positions at different inflation levels during inspiration ($0 < t < 500$ ms). The nodes were deformed using (a) the proposed 2-CT based deforming model and (b) linear deformation between end-exhale and end-inhale. The anatomical positions of the landmarks were extracted from the dynamic CT based deforming model of section 2.3. The positive and the negative values represent respectively the overestimation and the under estimation of the nodes anatomical positions.
time points over the breathing cycle that were used in the validation of the dynamic-CT based deforming model during inspiration and expiration respectively. The positive and the negative distance values denote the overestimation and the underestimation of the expected node position respectively.

From figure 2.13, it can be noticed that during inspiration, no significant discrepancy can be observed between the linearly deformed CFD mesh and the result of the proposed deformation model. This is because the change in the lung volume was approximately linear during most of the inspiration phase and, hence, the velocity of the deforming nodes was almost constant at inspiration. Therefore, both models showed good agreement to the reference CFD mesh. To clarify the difference between the 2-CT based deforming model and the linearly deformed model, the distribution of the computed wall node distances was plotted as shown in figure 2.14. The statistics showed that the 2-CT based deforming model resulted in a greater proportion of nodes located within a distance of ±0.1mm from their expected anatomical positions at $M_{100}$ and $M_{200}$. This is due to the slight concavity that occurs on the curve of the lung volume change at the

![Graphs showing distribution of computed distances](image)

Figure 2.14 The distribution of the computed distances between the deformed wall nodes to their corresponding anatomical locations at inspiration.
beginning of inspiration at $0 < t < 300$ ms (See figure 2.1). However, when the lung volume was varying constantly with time at $300$ ms $< t < 500$ ms, no significant difference was observed between the distributions of the computed wall node distances for the two models. It is important to note that an error of up to 0.1 mm is acceptable, as the spatial resolution of the dynamic CT images on which the models are based was 0.1mm.

Figure 2.15 The distance between the deformed wall nodes to their corresponding anatomical positions at different inflation levels during expiration ($500$ ms $< t < 11100$ ms). The nodes were deformed using (a) the proposed 2-CT based deforming model and (b) linear deformation between end-exhale and end-inhale. The anatomical positions of the landmarks were extracted from the dynamic CT based deforming model of section 2.3. The positive and the negative values represent respectively the overestimation and the under estimation of the nodes anatomical positions.
During expiration, the deformed mesh using the proposed deforming model showed good agreement to the reference mesh, whereas significant discrepancies were observed between the linearly deformed mesh and the reference mesh as shown in figure 2.15. The linearly deformed mesh overestimated the nodes anatomical positions at all the inspected time points with a maximum error that exceeds 0.4 mm at $M_{900}$. Figure 2.16 illustrates the distribution of the computed wall nodes distances during expiration. The results showed that the discrepancy between the linearly deformed mesh and the reference mesh intensifies as the deformation time increases. For

![Proposed model](#)

![Linear deformation](#)

**Figure 2.16** The distribution of the computed distances between the deformed wall nodes to their corresponding anatomical locations at expiration.
example, at $M_{500}$, a portion of 79.1% of the wall nodes were located within $\pm 0.1$ mm from their expected anatomical positions. At $M_{700}$, this percentage was fallen to 46.9%. The largest discrepancy was observed at $M_{900}$ which has only 42.1% of its wall nodes located within the deviation of $\pm 0.1$ mm. On the other hand, more than 91.1% of the deformed nodes using the proposed deforming model were located within a distance of $\pm 0.1$ mm from their expected anatomical positions at all the inspected time points. This excludes $M_{600}$ which 86.1% of its wall nodes were located within $\pm 0.1$ mm. This indicates that the proposed model was capable of interpolating the deformation of the airway walls over the breathing cycle to a good extent and, hence, it has a significant advantage over the linearly deformed model.

2.5 Lung User Defined Function software

Lung User Defined Function software (LUDF) is a home built software intended to prepare the appropriate UDF code and its necessary files for any lung deformation case that uses the proposed deformation models. Specifically, this software was designed to:

- Generate the set of the rearranged wall nodal coordinates $\delta$ as described in section 2.2.3.
- Generate a UDF with macros to extract and read wall nodal coordinates according to the pseudo code in figure 2.6.
- Generate a UDF with a macro to control the velocity of the deforming wall nodes. The user is capable of selecting one of the following options:
  - Constant velocity
  - Velocity corresponding to the lung volume-change
  - User defined
- Generate a UDF with macros to control the motion of the terminal surfaces in accordance to the selected option of the wall node deformation.

This software generates a UDF that is ready to use and, thus, it does not require previous knowledge in writing or dealing with UDFs for ANSYS FLUENT. Furthermore, since the number of the terminal surfaces is usually large and these surfaces deform in different directions, this software saves a significant amount of time and effort with respect to developing a separate UDF for each terminal surface. The UDF controlling the
deformation of the dynamic airways model proposed in this chapter were generated using this software. Furthermore, the UDF used to control the mesh of the human bronchial airways in chapter 5 was also generated using this software. Finally, it is important to note that this software and hence the proposed deformation algorithm of section 2.2 are not limited to the modelling of the bronchial airway deformation. They can be used in other engineering problems with a deforming/moving object as long as a node-to-node mapping is established between the start and the target positions along with the equation that controls the velocity of the moving wall nodes is known.

2.6 Summary

This chapter addresses the development of dynamic CFD models that accurately represent the inhomogeneous deformation of the bronchial airways within a living lung during the normal breathing cycle. A node-to-node deforming algorithm was developed to allow the CFD solver ANSYS FLUENT to deform the bronchial airway mesh between consecutive positions over the breathing cycle. This algorithm was applied to a set of consecutive geometries reconstructed out of a dynamic CT data set that cover the breathing cycle of a laboratory animal. The deformation between the consecutive positions was assumed to be linear and in a constant velocity. The deformed mesh using the proposed deformation model was compared against the CT based reconstructed geometry at intermediate positions over the breathing cycle and showed good agreement. Furthermore, a new deformation model of the bronchial airways that utilises a pair of CT images, acquired at the end-exhale and the end-inhale of the breathing cycle, was introduced. The proposed 2-CT based model links the velocity of the deforming nodes between the end-exhale and the inhale locations to the change in the lung volume. The results of the proposed 2-CT based deformation are found to be good approximation to the deformation of the bronchial airways in a living lung. The significant output from this research is the availability of a new non-linear dynamic model of the bronchial tree that requires just one pair of CT images as input, which therefore complies with radiation dosage limits for human subjects.
3 DYNAMIC SUBJECT-SPECIFIC BOUNDARY CONDITIONS

3.1 Introduction

A significant obstacle to obtain accurate and reliable computational fluid dynamics (CFD) predictions of the flow through the bronchial airways is the difficulty of imposing accurate flow boundary conditions derived from the actual flow within a living lung. Imposing accurate boundary conditions at the tracheal inlet is possible from the measurements of the lung volumes or the tracheal pressure using currently available ventilation units. However, imposing accurate boundary conditions at the terminal surfaces has always been challenging. This is mainly due to the complex and inaccessible nature of the lung. The spatial resolution of the currently available imaging techniques allows the segmentation and 3D sampling of a limited number of generations of the bronchial tree. Thus, the effect of the missing peripheral airways on the flow pattern and distribution must be accounted for by the boundary conditions imposed at the terminal surfaces. Nevertheless, most of the studies to date have used simple flow boundary conditions. Usually, atmospheric pressure is assumed at the terminal surfaces, while a volumetric flow rate or a velocity profile is imposed at the tracheal inlet. A representative list of such studies includes Li et al. (2007b), Lin et al. (2007), De Backer et al. (2008a), Freitas and Schroder (2008), Gemci et al. (2008), Russo et al. (2008), Choi et al. (2009), Hylla et al. (2010), Corley et al. (2012), Sera et al. (2013), and (Qi et al., 2014). Since the lung is classified as a partially closed system, assuming that the terminal branches are open-ended and, hence, ignoring the effect of the missing peripheral airways is a broad approximation.

Few attempts were made to calculate and impose physiological boundary conditions on the terminal surfaces as reported in section 1.5. De Backer et al. (2008b) imposed two different pressure values at the terminal surfaces of the left and the right lungs based on CT measurements of the lung volume change in order to approximate the flow distribution between the left and the right lungs. De Backer et al. (2010) iteratively...
imposed different pressure values at the terminal surfaces until the predicted lobar flow distribution reflected the lobar flow distribution measured from CT scans of the same subject. Another attempt was made by Yin et al. (2010) and Yin et al. (2013) who used a 3D-1D coupling model associated with a ventilation map computed by an image registration technique applied to two CT images acquired at the residual volume (RV) and the total lung capacity (TLC) in order to approximate the flow volume at each terminal surface.

Recently, several methods were developed to measure the regional ventilation and the deformation of the lung using medical imaging techniques. For example, the inhalation of contrast agents such as hyperpolarised gas in magnetic resonance imaging (MRI) and xenon in computed tomography (CT) were used by several researchers to build a volume-change map of the lung (Kreck et al., 2001, McMahon et al., 2006, Holmes et al., 2007, Lam et al., 2007). Another technique is the implementation of non-rigid registration between static CT images to compute the volume-change map of the lung (Guerrero et al., 2005, Reinhardt et al., 2007, Reinhardt et al., 2008, Yin et al., 2009). However, such methods are unable to generate a dynamic volume change map of the lung, since they require breath hold during the imaging process and are controlled by radiation restrictions (Jacob et al., 2013a). Hence, using such methods to drive dynamic subject-specific boundary conditions for the CFD simulations of the flow through the bronchial airways is challenging. Alternatively, successive CT scans acquired dynamically (without breath hold) over the breathing cycle using four-dimensional computed tomography (4DCT) could be used to compute global and local dynamic volume change maps of the lung (Guerrero et al., 2006, Yamamoto et al., 2011, Jacob et al., 2013a). In theory, such dynamic volume change maps could be used to develop dynamic subject-specific boundary conditions for the CFD simulations of the flow through the bronchial airways. However, a current challenge is the poor spatial resolution of the dynamic CT images, which limits the ability of estimating with good accuracy the exact volume of the missing peripheral airways associated to each terminal branch. To overcome this limitation, this study introduces a new technique for sectioning the 3D volume of the lungs reconstructed out of successive dynamic CT images covering the breathing cycle into several smaller volumes, where each volume accommodates the missing peripheral
airways associated to each terminal branch. The aim of the proposed technique is to approximate the volume change of the missing peripheral airways distal to each terminal branch during the breathing cycle and, hence, obtain estimates of the specific time-dependant volumetric flow rate at each terminal surface to be used as boundary conditions in the CFD model of chapter 4.

3.2 The mechanical coupling between the bronchial tree and the vascular tree

Together with the bronchial airways, the pleural cavity encloses the vascular tree, which is responsible for conducting the blood between the heart and the alveolar sacs where gas exchange takes place. The deoxygenated blood is pumped from the right ventricle of the heart through the pulmonary arteries, which continue to divide into smaller arteries until they form the capillaries around the alveolar sacs. The oxygenated blood, on the other hand, is transported from the capillaries to the left atrium of the heart through a network of pulmonary veins. The pulmonary arteries run alongside the airways and the pulmonary veins show a similar branching pattern to the arteries, though separated from them (Hislop, 2002). The topology of the pulmonary veins divides the lung lobes into several segments known as the bronchopulmonary segments. These segments are separated from each other by connective tissue septa that cannot be identified in low-resolution CT images. Each segment is supplied by a segmental bronchus and its accompanying pulmonary artery branch (Drake et al., 2010). This pulmonary artery and its peripheral arteries are tethered to the surface of their adjacent airways and to the lung parenchyma via a connecting tissue (Townsley, 2011). In the conducting zone of the lung, the pulmonary arteries that accompany the conducting airways tend to retain their shape during breathing. They contain a number of smooth muscles and a large volume of blood passing through them, however, they stretch and displace in accordance to their adjacent airways during breathing as a result of that tethering (Benjamin et al., 1974, Kalk et al., 1975, Lai-Fook, 1979). In the respiratory zone of the lung, where most of the lung volume change takes place during breathing, more of the adventitial surface of the arteries (and veins) is tethered to the surrounding lung parenchyma (Townsley, 2011) and the smooth muscles surrounding the blood vessels are less present. Hence, the overall structure (position, diameter and length) of
the arteries (and veins) in the respiratory zone varies in accordance to the change in the lung volume during breathing (Culver and Butler, 1980, Mansell et al., 1992, Albert et al., 1993, Rhoades, 2009). This indicates a mechanical coupling between the lung tissues and the pulmonary arteries and veins in the pleural cavity. By this mechanical coupling, the deformation of the vascular tree in accordance to the change in lung volume during breathing can be used to approximate the volume change of the missing peripheral airways distal to each terminal branch.

In this chapter, a sectioning technique is proposed to segment a time sequence of 3D volumes of the lung reconstructed out of successive dynamic CT images covering the breathing cycle of a laboratory animal into several segments, where each segment encloses the volume of the missing peripheral airways distal to each terminal branch. The corresponding segments are defined based on the mechanical coupling between the 4 tree and the lung tissues. The computed volume change of the segments is then used to drive dynamic subject-specific boundary conditions for the CFD simulations of the flow through the bronchial airways. The proposed sectioning technique is evaluated on a cast geometry of the bronchial airways of the same animal coupled to a CT based reconstructed vascular tree. Additionally, the accuracy of the proposed technique in approximating the volume change of specific segments within the lung during breathing is validated by comparing the CT measurements of the lobar regional ventilation to that obtained following the proposed sectioning technique.

### 3.3 Non-uniform bronchial ventilation model by vascular segmentation

#### 3.3.1 The framework of developing the dynamic subject-specific boundary conditions

The block diagram of figure 3.1 illustrates the overall process of detraining the dynamic subject-specific boundary conditions. The proposed technique was implemented on the same dynamic CT data set of the 298g male Sprague-Dawley rat used in chapter 2. The ethical approval of the animal use and the animal imaging process are discussed in section 2.2.1. The acquired dynamic CT data set consists of 11 CT-images covering the
breathing cycle of the rat during tidal breathing (figure 3.1 (a)). The CT acquisition time points over the breathing cycle are illustrated in figure 2.1.

To compute the dynamic subject-specific boundary conditions, lung volume-masks (figure 3.1 (b)) were computed from the successive CT data set that cover the lungs and zones from the extra-alveolar blood vessels (the pulmonary arteries and the pulmonary veins). 3D geometries of the computed lung volume-masks were then reconstructed out of the generated volume masks as shown in figure 3.1 (c). In addition, 3D geometries of the vascular tree were reconstructed out of the dynamic CT data set. The generated vascular tree geometries were then synchronised to the lung volume geometries and the blood vessels of interest were extracted from the vascular tree. This includes the veins that define the bronchopulmonary segments of the lung and the arteries running alongside the outer branches of the missing airways distal to each terminal branch. Since the vascular tree follows the same branching pattern of the bronchial tree, a midline was generated between the opposing arteries using their centreline. Next, the centreline of the extracted veins and the generated midlines were used to define the bronchopulmonary segments of the lung by generating sweep surfaces. Each bronchopulmonary segment was further refined into smaller segments following the midlines between the opposing arteries until each segment encloses the volume of the missing peripheral airways distal to each terminal branch, as shown in figure 3.1 (d). The

Figure 3.1 Block diagram of deriving the dynamic subject-specific boundary conditions.
volume change of these segments was eventually used to develop the dynamic subject-specific boundary conditions for their associated terminal surface.

3.3.2 Computation and 3D sampling of the lung volume

A mask covering the lungs and a small zone of the extra-alveolar vessels was generated for each CT image following the steps proposed by Jacob et al. (2013a). First, a Gaussian 3D filter (radius = 1) was applied to the image slices. Then, the 3D Toolkit plugin within the free source software ImageJ (NIH, Bethesda, Maryland, USA) was used to generate the lung volume-mask for each CT-image by inserting a seed point within the lung. Finally, the 3D Dilate and the 3D Erode functions, also available within the 3D toolkit of ImageJ, were applied to the generated masks in order to fill the missing voxels and smooth the boundaries. Figure 3.2 (a) illustrates the calculated mask on a sample slice. 3D geometries were then reconstructed out of the generated masks using the commercial software Mimics (Materialize, Belgium). The volume change of the generated lung volume-mask geometries was calculated and compared to the lung volume change measured by the ventilator unit as shown in figure 3.2 (b). It can be seen that the change in volume of the lung volume-mask geometry well matches the lung change.

![Original image](image1)

![Volume-mask](image2)

Figure 3.2 (a) the computed lung volume-mask illustrated on a sample slice. (b) a comparison of the average ventilator-measured lung volume change and the total volume change measured from the lung 3D geometries. The error bars represent the standard deviation of the ventilator measurements.
volume change measured by the ventilator unit. Thus, it can be assumed that the volume change within a specific segment of the lung volume-3D geometry reflects the volume change of the corresponding segment within the living lung.

3.3.3 Segmentation and 3D sampling of the vascular tree

Unlike the bronchial airways, the vascular tree has a distinguishable X-ray opacity comparable to that of the bones, which makes it visible almost down to the capillaries in CT scans with high resolution. However, identifying and segmenting the vascular tree in dynamic CT data is more challenging due to the low image quality of the 4DCT. The dynamic CT images contain inherent blurring that limits the ability of identifying and segmenting small arteries in the respiratory zone. Hence, it was necessary to enhance the contrast of the vascular tree for an easier segmentation process. To do this, the lung was extracted from the CT images by adding the lung volume-masks generated in the previous step to their originating CT images using the image calculator tool in ImageJ. An enhance contrast function was then applied to the digitally masked lung cross-section images. Finally, a tubeness filter (Sato et al., 1998), available within ImageJ, was applied to the contrast enhanced images. This filter examines the connectivity between the pixels within the data set based on the eigenvalues of the Hessian matrix. A sample of the resulting images is shown in figure 3.3 (a). 3D geometries of the vascular tree were then reconstructed by assembling the tubeness-filtered cross-sections. Some manual processing of the 3D surfaces was required to repair open vessel walls and properly connect smaller vessels to their distal larger vessels and remove the incomplete geometries of the smaller vessels. A sample geometry of the reconstructed vascular tree superimposed on its associated airway geometry is shown in figure 3.3 (b). It can be seen that the generated 3D geometry of the vascular tree adventitial surface in figure 3.3 (b) is coarse. This is mainly due to the low spatial resolution of the dynamic CT data set (0.1 mm). However, only the centreline of the blood vessels will be used to segment the 3D volumes of the lung and, hence, the roughness of the adventitial surface can be neglected.
3.3.4 Sectioning of the lung volume geometry

To define the boundaries of the desired lung volume segments, the veins that outline the bronchopulmonary segments of the lung and the arteries running alongside the outer branches of the missing airways distal to each terminal branch were extracted from the vascular tree geometries as shown in figure 3.4 (c). The extracted veins and arteries were referred to as the blood vessels of interest. Following the extraction process, centreline segments were generated for the blood vessels of interest using the 3D thinning algorithm of Palágyi et al. (2001).

Let $C_v$ be the centreline segments of the extracted veins and $C_a$ be the centreline segments of the extracted arteries as shown in figure 3.4 (d). Due to the low resolution of the dynamic CT data set, some of the small veins and arteries at the tips of the

Figure 3.3 (a) CT image pre-processing for the segmentation and 3D sampling of the vascular tree out of the dynamic CT data set. (b) 3D rendering of a sample vascular tree superimposed on its associated airway geometry.
vascular tree geometries were lacking. Therefore, the connection between the vessels of interest and the visceral pleura is missing and has to be approximated. This was done by projecting the end-points of $C_v$ and $C_a$ on the wall of the visceral pleura. These points were then used to bridge the gaps between the centreline segments and the visceral pleura by connecting the end-points of $C_v$ and $C_a$ to their corresponding points at the wall of the visceral pleura using straight lines. Additionally, as the structure of the arteries within the vascular tree follow the same branching pattern of the bronchial tree, midline curve segments $C_m$ were generated between the opposing arteries within the vessels of interest based on the structure of their centreline segments $C_a$.

Sectioning of the lung volume 3D geometries was performed following two main steps. First, the bronchopulmonary segments of the lungs were identified by generating surfaces that define the boundaries of each bronchopulmonary segment. Then, the defined bronchopulmonary segments were further sectioned into smaller segments when necessary until each segment involves the lung volume associated with its enclosed terminal surface. The specific steps of sectioning the lung volume-mask geometries were as follows: First, the tips of the curve segments of $C_v$ and $C_a$ were connected to the visceral pleura via straight lines. Then, the curve segments of $C_v$ were used sweep surfaces across the 3D lung volume geometries that define the bronchopulmonary segments of the lung. Since the airway geometry used in this study consists of 4±1 generations as shown in figure 3.4 (a), the generated bronchopulmonary segments were sufficient to account for the lung volume associated with many of the terminal surfaces. However, some of the generated bronchopulmonary segments enclosed the lung volume associated with two or more of the terminal surfaces. In this case, $C_m$ curve segments were connected to the visceral pleura via straight lines, and then used to section the bronchopulmonary segments further into smaller segment until the lung volume associated with each terminal surface was defined. This was done by generating bisecting surfaces guided by $C_m$ that separates each segment belong to the different terminal surfaces within the bronchopulmonary segments, and finally bridge the gap to the defined boundaries of the bronchopulmonary segments. Figure 3.5 illustrates the segmentation of a sample geometry of the lung volume-mask following the proposed technique.
Figure 3.4 Extraction of $C_v$, $C_a$, and $C_m$ illustrated on a sample terminal branches. (a) the sample terminal branches (b) the vascular tree portion associated to the sample terminal branches (c) extraction of the vessels of interest (d) generation of the centrelines defining the sectioning surfaces.
Figure 3.5 The terminal surfaces of the bronchial airway geometry. (b) The generated segments associated to each terminal surface. The terminal boundaries were labelled in accordance to their accommodating lobe (RCR: right cranial, RM: right middle, RCA: right caudal, A: accessory, and L: left) and numbered with respect to the flow direction during inspiration.
Due to the tethering of the vascular tree to the bronchial airways and the lung parenchyma, it was assumed that the shape and the position of the generated segmental boundaries vary in accordance to the change in the lung volume during breathing. Thus, the volume change of the individual segments reflects the volume change of their enclosed airways. Hence, the volume change of the individual segment was used to drive flow volume boundary condition for their associated terminal surfaces using the following equation

\[ Q = \frac{d(V_S - V_G)}{dt} \]  

(3.1)

Where \( Q \) is the volumetric flow rate, \( V_S \) is the volume of the lung segment associated to a given terminal surface, \( V_G \) is the volume of the airway geometry enclosed within the same lung segment, and \( t \) is the breathing time.

### 3.4 Evaluation of the proposed sectioning technique on an airway cast geometry

To evaluate the accuracy of the proposed technique in defining the lung volume associated to each terminal surface, the proposed sectioning process was applied to a cast geometry of the bronchial airways extracted from the same laboratory animal post-mortem. The cast geometry was coupled to a vascular tree geometry of the animal reconstructed out of a CT image acquired at approximately the same inflation level as the cast geometry. Airway casting and animal imaging were performed by a research group at the at the Pacific Northwest national laboratory, Washington, USA. Animal use ethical approval was previously discussed in section 2.2.1. The animal imaging process and airway casting are extensively explained in Jacob et al. (2013b). Briefly, the rat was subjected to euthanasia using CO\(_2\) asphyxiation, and then intubated with a 14-gage catheter tube. A ventilator unit was then used to inflate the rat lungs to TLC at \( \sim 25 \) cmH\(_2\)O. At that time, the lungs were scanned using the commercial micro-CT scanner (eXplore CT120, GE Health Care Waukesha, WI). Scanning parameters were 90 kVp, 40 mA, 16 ms exposure time, 50 \( \mu \)m resolution, 360° gantry rotation with 900 projections. Following the scanning process, an in-situ rigid cast of the rat bronchial tree was made following the methodology of Phalen et al. (1973). The lungs were degassed and held
inflated at $\sim 30 \text{ cmH}_2\text{O}$. A pre-calculated lung volume of $\sim 2.3 \text{ mL}$ of a casting agent was then injected slowly into the lungs in-situ via the intubated catheter tube. The casting agent mix consisted of 10 g Dow-Corning 734 flowable sealant, 3.7 g Dow-Corning 200 fluid, and 1.3 g of Ultravist (iopromide, Bayer HealthCare), and an iodine-based CT contrast agent. Finally, a CT image of the rat thorax was acquired using the same scanning parameters used for imaging the lung at TLC.

The vascular tree of the animal was segmented and reconstructed out of the TLC image following the same steps discussed in section 3.3.3. Additionally, a geometry of the bronchial airways was generated from the same image set following the method discussed in section 2.2.1. This geometry was used to attach the 3D airway cast geometry to the geometry of the vascular tree. On the other hand, the 3D geometry of

![Figure 3.6 3D geometries of (a) the bronchial airways reconstructed from the TLC CT image and (b) the airways cast.](image)
the airway cast was automatically segmented and reconstructed out of the cast images. The segmentation process did not require any pre-processing steps. This is due to the CT contrast agent that was added to the cast materials which makes it distinguishable in the CT image. However, a Gaussian blur filter (radius=1) was applied to the cast image to smooth the boundaries and reduce the noise. The reconstructed cast geometry included airway generations that are significantly beyond the resolution of the CT and MRI imaging of living animals. However, the exact proportion of the reconstructed cast geometry compared to the actual bronchial tree of the animal cannot be easily quantified. Figure 3.6 (a) gives a 3D representation of the reconstructed airway geometry generated at TLC and figure 3.6 (b) shows the corresponding geometry from

![3D representation of the reconstructed airway geometry](image)

Figure 3.7 Alignment between the airway cast geometry and the airway geometry at TLC (a) before and (b) after registration.
the lung cast. Comparing the two images shows the lower number of generations resolved by the TLC scan.

To attach the cast geometry to the vascular tree geometry, the cast geometry was aligned to the TLC airway geometry following the steps proposed in Jacob et al. (2013b). A centreline was generated for the cast model using the sequential 3D thinning algorithm by Palágyi et al. (2001). The generated centreline was then used as a skeleton to manually control the rigid transformation and rotation of the cast geometry in order to align it on the TLC airway geometry. This process was done using the skeleton tools within the commercial software Maya (Autodesk, USA). Since the casting procedure may have resulted in altered bifurcating angles, a minor rotation and transformation of the individual branches was implemented to improve the accuracy of the registration. Figure 3.7 illustrates the alignment between the cast geometry and the TLC geometry before and after registration. Figure 3.8 illustrates the attachment of the cast geometry to the vascular tree of the animal as a result of the registration process.

The airway cast geometry was pruned to represent the geometry of the bronchial airways with a reduced number of generations similar to that obtained from the dynamic CT scans. The sectioning technique was then applied to the pruned cast geometry in order to estimate the sections of the lung volume associated to each terminal branch. The actual section of the lung associated to each terminal branch was determined by referring back to the unpruned airway cast geometry. Figure 3.9 illustrates the sectioning process applied to the right cranial lobe of the animal lungs. It can be seen that the proposed sectioning technique was able to successfully define segments within the lung volume that wrap and separate the missing peripheral airways of the terminal surfaces. However, minor geometrical violations were observed on some of the generated segments the animal lungs similar to that shown in in the magnification window in figure 3.9. The volume of the misinterpreted airway geometries within the lung volume segments was less than 2% compared to the volume of the enclosed airway branches. Such small error is not expected to significantly affect the accuracy of the resulting CFD boundary conditions.
Section 3.4 provided a validation test for the non-uniform bronchial ventilation among the terminal branches of one lobe, the right cranial lobe. This section attempts the model validation by evaluating the non-uniform ventilation distribution among the five lobes. Figure 3.10 illustrates the comparison between the lobar volumes at different time points computed following the proposed sectioning technique using the dynamic CT scan data to that measured from the CT scans. The CT measurement of the lobar volume was done by segmenting the lobes from the CT images following the fissure lines. The purpose of this comparison was to validate the accuracy of approximating the time dependant volume of a specific lobe within the lung using the proposed technique.
No significant discrepancy was observed between the computed and the measured volume at 10 time points over the breathing cycle. The proposed technique was able to accurately predict the lobar volume at different times with a maximum error of less than

Figure 3.9 Implementation of the sectioning technique of section 3.3 to a cast model of the right carinal lobe of the Sprague-Dawley rat. (a) the lobe position in the pleural cavity. (b) the bronchial airways related to each terminal surfaces of the right carinal lobe coupled to the blood vessel within the lobe. (c) extraction of the vessels of interest. (d) the generation of the boundary surfaces of each segment. (e) the generated segments. the magnification window illustrates a minor geometrical violation observed between the RCR3 segment and the RCR2 segment.
2.5%. Since this section does not provide a validation of the non-uniform bronchial ventilation for the individual terminal surfaces, it is important to note that the lobes are the smallest morphologically defined segments of the lung in a CT scan since the fissure lines separate them. Therefore, validating against the change in the lobes volume is a good indication of the accuracy of the proposed technique. However, the lung volume segments associated with the terminal branches in most of the CFD simulations are usually smaller than the volume of the lung lobes. Therefore, limiting the validation to the measurements of the lobar volume change may not be sufficient. However, most of the currently available lung ventilation imaging techniques such as phase contrast MRI and Xenon CT scanning are unable to provide dynamic measurements of the ventilation within corresponding segments of the lungs. Hence, comparing the computed results to the CT measurements of the lobar volume change to date is the most reliable validation method.

3.6 Discussion and limitations

The proposed sectioning technique provides the ability of obtaining dynamic subject-specific boundary conditions for the CFD simulations of the flow within the bronchial airways depending mainly on a refined biological information extracted from the lungs. This is different to the previously proposed algorithms, which relied on the volume change of the overall lungs, or individual lobes (De Backer et al., 2008b, De Backer et al., 2010) or on a generalised mathematical model of the bronchial airways (Yin et al., 2010, Yin et al., 2013) to approximate the boundary conditions at the terminal surfaces. Hence, the proposed technique is expected to result in more reliable CFD predictions of the flow within the bronchial airways. However, a couple of limitations and uncertainties have to be addressed. Firstly, the proposed sectioning technique of the lung volume depends on the mechanical coupling between the vascular tree and the lung tissues. This mechanical coupling has not been extensively investigated yet. Although the arteries are accompanying the bronchial airways down to the alveolar sacs, the amount of their adventitial surface that is tethered to their adjacent airways vary widely from dorsal to apex (Townsley, 2011). Similarly, the tethering between the veins and the lung tissues is complex and inhomogeneous. Additionally, the volume of the smooth muscles surrounding the arteries and the veins vary widely from dorsal to apex and the volume
of the blood flowing through each vessel is unpredictable. All these elements may affect the elasticity and, hence, the deformation pattern of the blood vessels during breathing with respect to the change of the lung volume. Since most of these effects have not been systematically investigated yet and due to the limitation of the currently available validation strategies, assuming that the vascular tree deforms in accordance to the change in the lung volume during the breathing cycle cannot be precisely evaluated.

Figure 3.10 Comparison between the lobar ventilation measured using the proposed sectioning technique to that measured from the dynamic CT data set.
Another limitation affecting the accuracy of the proposed sectioning technique and, hence, the reliability of the driven dynamic subject-specific boundary conditions, is the ability of identifying and segmenting the lower vessels of the vascular tree (the arterioles, the venules, and the capillaries) out of the CT images. This limitation manifests particularly when dealing with low-resolution CT data sets similar to that of the dynamic CT imaging. The missing blood vessels are likely to affect the accuracy of the lung volume sectioning since the coupling between the segmented vascular tree and the inner pleural membrane (the visceral pleura) has to be estimated. Additionally, the lung volume contained by the peripheral airways that are adjacent to the missing arteries cannot be accounted for when sectioning. This may results in imprecise but still acceptable dynamic subject-specific boundary conditions. However, it is important to note that the uncertainty due to such limitation is likely to increase as the number of the terminal branches increases. This is because the sectioning technique would rely more on the arteries accompanying the peripheral airways of the terminal branches if the number of the terminal branches is large. Thus, it is important to ensure the segmented vascular tree represents the most possible number of blood vessels to reduce the sectioning error.

3.7 Summary

This chapter aims to develop dynamic subject-specific boundary conditions for CFD simulations of the flow within the bronchial airways. The proposed technique utilises the vascular tree as reference to section the lung volume into several segments where each segment encloses the missing peripheral airways associated to each terminal branch. The volume change of the generated segments is then used to develop the dynamic flow boundary conditions for their associated terminal surfaces. This technique was applied to the dynamic CT data set of the same laboratory animal of chapter 2. Since the vascular tree is tethered to the bronchial airways and the lung parenchyma via a connecting tissue, the shape and the position of the vascular tree vessels vary in accordance to the change in the lung volume during breathing because of that tethering. This mechanical coupling was used to define the corresponding segments of the lung in the sequence of the dynamic CT images. The proposed sectioning technique was evaluated on a cast geometry of the bronchial airways extracted from the same animal
representing most of the animal’s bronchial tree at TLC. The cast geometry was coupled to a vascular tree of the animal extracted from a CT image acquired at almost the same inflation level of the cast geometry. The results showed that the proposed technique was able to successfully determine the volume of the peripheral airways associated to each terminal branch at total lung capacity. Furthermore, the ability of the proposed technique in approximating the volume change associated with specific segments of the lungs was validated by comparing CT measurements of the lobar volume change to that computed following the proposed technique. The maximum observed discrepancy between the measured and the computed lobar volume change was less than 2.5%. The measured volume change of each lung segment is used to determine the volumetric flow rate boundary condition for its enclosed terminal surface.

The significant output from this research is the availability of dynamic subject-specific boundary conditions that depend on biological information obtained from the lung deforming constituents. This is different to the previously published algorithms that use the global lung (or lobes) volume change or generalised mathematical models of the bronchial airways to account for the volume change of the missing peripheral airways. Thus, the dynamic subject-specific boundary conditions acquired following the proposed technique is expected to result in more reliable CFD predictions of the bronchial flow.
4 THE DYNAMIC SUBJECT-SPECIFIC MODEL OF THE RAT BRONCHIAL AIRWAYS

4.1 Introduction

In chapter 2, a deformation algorithm was proposed to deform the computational fluid dynamics (CFD) mesh of a geometry of the bronchial airways in small time-steps to approximate the motion of the bronchial tree within a living lung during breathing. The proposed deformation algorithm based on a node-to-node correspondence between the walls of subsequent airway geometries reconstructed out of successive dynamic CT images covering the breathing cycle of a laboratory animal. In chapter 3, dynamic subject-specific boundary conditions were computed for the terminal surfaces of the deforming mesh based on a sectioning technique of the total airway volume at sampled time points over the breathing cycle. In this chapter, the proposed deforming airway model and the computed dynamic subject-specific boundary conditions were integrated into one model in order to simulate the flow within the bronchial airways using CFD. The aim of this chapter is to evaluate the ability of the proposed deforming airway model in capturing the flow within a living lung compared to the conventional rigid models with simple flow boundary conditions. For the first time, the effect of the wall motion on the flow pattern and distribution within the bronchial airways during normal breathing conditions are investigated in this chapter. The outcome of this research will evaluate the arbitrarily assumption adopted by many previous studies that airway deformation during normal breathing conditions is trivial and has a negligible effect on the flow characteristics.

4.2 Study cases and boundary conditions

The 3D geometries of the bronchial airways of the laboratory rat used to develop the dynamic CT based deforming model in chapter 2 were used in all the simulation cases in this chapter. Section 2.2.1 discusses the animal use ethical approval, the animal imaging process, and the 3D sampling of the bronchial airway geometries out of the acquired dynamic CT data set. Three simulation cases were carried out in order to investigate the
effect of wall motion and the dynamic subject-specific boundary conditions on the flow pattern and distribution. In the first case (Case A), the flow within a dynamic subject specific model of the bronchial airways during normal breathing conditions with dynamic subject-specific boundary conditions was investigated. The second case (case B) investigates the effect of imposing the dynamic subject-specific boundary conditions of chapter 3 on a rigid model of the bronchial airways reconstructed from the CT image acquired at end-exhale. The third case (Case C) is similar to case B but with the imposition of simple boundary conditions on the terminal surfaces of the rigid model. The exact specifications and boundary conditions used in each simulation case are summarised as follows:

**Case A: A deforming model with dynamic subject-specific boundary conditions**

The dynamic-CT based deforming model proposed in section 2.3 was used in this simulation case to govern the deformation of the CFD mesh of the bronchial airways. The deforming model setup and specifications are discussed in section 2.2 and 2.3.1 respectively. The CFD mesh of the airway geometry \( G_0 \) reconstructed from the CT image acquired at end-exhale (t=0ms) was used as the moving mesh \( M_0 \), and the CFD mesh of the subsequent airway geometries \( G_{100} - G_{1000} \) were used as the reference mesh in order to approximate the deformation of the bronchial airways during the breathing cycle.

In addition, the dynamic subject-specific flow boundary conditions computation technique proposed in chapter 3 were used to compute a volumetric flow rate boundary condition for each terminal surface of the deforming model. Figure 4.1 illustrates the volumetric flow rate profiles imposed at each terminal surface. On the other hand, the tracheal pressure change measured by the ventilator unit was used as a boundary condition of the tracheal inlet. However, as discussed in section 2.2.1, the rat was connected to the ventilator unit by a 4 cm long 14-gauge catheter tube. Thus, to impose an accurate boundary condition at the tracheal inlet, the pressure loss due to the flow through the catheter tube was evaluated using equation 4.1.

\[
\Delta P = 4f \cdot \frac{l}{D} \cdot \frac{\rho V^2}{2}
\] (4.1)
Figure 4.1 The dynamic subject-specific boundary conditions imposed at the terminal surfaces of case A and case B.
Where $f$ is the catheter tube friction factor, $L/D$ is the ratio of the length to the diameter of the catheter tube, $\rho$ is the density of the flowing air, and $V$ is the mean velocity. Since the maximum flow volume measured by the ventilator unit was $\sim 7.3$ cc/s at $t=575$ ms (figure 4.4), and the density and the dynamic viscosity of air at 37°C is 1.1385 kg/m³ and 1.9E-5 kg/m.s respectively, the maximum expected Reynolds number at the catheter tube was $\sim 350$. This Reynolds number is much less than the turbulence limit. Therefore, the friction factor $f$ was calculated as $f = 16/Re$. Figure 4.2 illustrates the calculated pressure boundary condition for the tracheal inlet with respect to the pressure loss across the catheter tube superimposed on the original ventilator unit measurement of the tracheal pressure.

**Case B: A rigid model with dynamic subject-specific boundary conditions**

The geometry reconstructed from the CT scan acquired at end-inhale ($t=500$ ms) was adopted for the simulation process in this case. The wall of the model was assumed rigid with non-slip conditions. The boundary conditions imposed at the tracheal inlet and the terminal surfaces were similar to those used in case A. Therefore, the CFD predictions of the flow through the bronchial airways in this case were acquired from a rigid geometry of the bronchial airways, but with the imposition of the dynamic subject-specific boundary conditions of chapter 3. This will allow the evaluation of the effect of wall motion on the flow predictions by comparing the acquired prediction results to those acquired by case A.

![Figure 4.2 Ventilator measurements of the tracheal pressure and the calculated boundary condition imposed at the tracheal inlet of case A and case B.](image-url)
Case C: A rigid model with simple boundary conditions

This case is similar to case B but with the imposition of simple flow boundary conditions. The static airway geometry reconstructed from the CT image acquired at end-inhale (t=500 ms) was used in this simulation case as the flow domain. The airway walls were assumed rigid and non-slip. Additionally, the volumetric flowrate waveform measured by the ventilator unit shown in figure 4.4 was used as a flow boundary condition on the tracheal inlet, whereas an atmospheric pressure was assumed at the terminal surfaces. This simulation case resembles the conventional CFD modelling strategy adopted by most of the previous studies to investigate the flow through the bronchial airways.

4.3 CFD setup and mesh independence

All the conducted CFD simulations were carried out using the commercial CFD solver ANSYS FLUENT (Lebanon, USA). Since the maximum expected Reynolds number at the catheter tube was ~350, the flow was assumed laminar and the airflow predictions were based upon the laminar three-dimensional incompressible Navier-Stokes equations. Unlike the previous studies, air at 37°C was used as the flowing medium, with a density of 1.1385 kg/m³ and dynamic viscosity of 1.9E-5 kg/m.s. This was an attempt to account for the effect of the body temperature on the flow characteristics in the flow modelling process. The flow was considered transient, and the time step size used in each simulation case was 1.0e-06 s. All simulations in this study were carried out using the High Performance Computing (HPC) service at the University of Leicester (Leicester, UK).

The generation of the mesh of the deforming model in case A is discussed in section 2.2.2 and 2.2.3. For the rigid geometry of case B and C, a tetrahedral unstructured mesh was generated using the commercial software ANSYS ICEM CFD (Lebanon, USA). The generated meshes of the simulation cases were iteratively refined by a factor of ~0.3 until mesh independence was achieved. Table 4.1 lists the meshing information and the meshing parameters of the most reliable three meshes of each simulation case labelled as coarse, medium and fine mesh. The mesh sensitivity test was conducted at t=575 ms as the maximum Reynolds number at the catheter tube is expected at this time point. As shown in figure 4.3, the difference in the CFD prediction of the velocity magnitude at a section located close to the first bifurcation
was used for the mesh sensitivity test. Since the flow stream at t=575 ms is moving towards the tracheal inlet, the flow prediction at the first bifurcation zone is significantly sensitive to the mesh resolution of the peripheral airways. Thus, conducting a sensitivity test study in a station close to the first bifurcation at this sampled time point is reliable to evaluate the effect of the mesh resolution in the flow prediction.

![Station position diagram](image)

Figure 4.3 The velocity magnitude predictions at station located close to the first bifurcation using three different resolutions of CFD meshes as listed in table 4.1. (a) the location of the station used to check for mesh independence (b) the velocity magnitude results of case A, (c) the velocity magnitude results of case B, and (d) the velocity magnitude results of case C.

<table>
<thead>
<tr>
<th></th>
<th>Case A</th>
<th></th>
<th></th>
<th>Case B/C</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coarse</td>
<td>Medium</td>
<td>fine</td>
<td>Coarse</td>
<td>Medium</td>
<td>fine</td>
</tr>
<tr>
<td>Number of cells</td>
<td>1.5M</td>
<td>2.1M</td>
<td>2.9M</td>
<td>2.3M</td>
<td>3M</td>
<td>3.9M</td>
</tr>
<tr>
<td>Cell size (mm$^3$)</td>
<td>0.014-0.14</td>
<td>0.012-0.12</td>
<td>0.011-0.11</td>
<td>0.014-0.14</td>
<td>0.012-0.12</td>
<td>0.01-0.1</td>
</tr>
<tr>
<td>Maximum skewness</td>
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<td>0.6-0.9</td>
<td>0.65-0.92</td>
<td>0.63</td>
<td>0.6</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Table 4.1 The information of the CFD meshes used in the mesh independence study. The number of cells and the cell size of the meshes in case A were acquired from the airway mesh at the beginning of the breathing cycle t=0 ms. The skewness of the meshes at case A varies as the mesh deforms.
4.4 Results

4.4.1 Evaluation of the dynamic subject specific model of the bronchial airways

Figure 4.4 illustrates the CFD predictions of the tracheal inlet volumetric flow rate predicted by the dynamic model of case A compared to the ventilator measurements of the lung volumetric flow rate. It can be seen that the CFD predictions of the tracheal volumetric flow rate agreed well with the ventilator unit measurements except at the beginning and the end of each breathing phase. This is mainly due to the limited number of the intermediate dynamic CT images that cover the breathing cycle. Additional intermediate imaging points concentrated at the beginning and the end of the breathing phases are expected to decrease the discrepancy between the CFD predictions and the ventilator measurements of the tracheal volumetric flow rate.

![Figure 4.4 Comparison between the CFD predictions of the tracheal volumetric flow rate in case A to the ventilator measurements of the tracheal volumetric flow rate.](image)

On the other hand, the CFD predictions of the lobar volumetric flow rate distribution acquired by the dynamic model of case A was compared to the actual lobar ventilation of the living lung measured from the dynamic CT data set as shown in figure 4.5. It can be seen that the CFD predictions of the distribution of the lobar volumetric flow rate well match those measured from the dynamic CT data set at all the inspected time points with a maximum error of less than 3%. In addition, the capability of the deforming CFD mesh of the dynamic model in capturing the non-linear deformation characteristics of the bronchial airways within a living lung during the breathing cycle is discussed in
section 2.3.2. In summary, the airway CFD mesh deformation and the CFD predictions of the lobar volumetric flow rate distribution acquired by the dynamic model of case A are of a good approximation to those measured experimentally from the living subject at ten time points over the breathing cycle. This indicates that the resultant CFD predictions are expected to be significantly relevant to the actual flow within the living lung. However, due to the absence of algorithms to visualising the dynamic flow within a living lung during breathing, only a global validation against CT measurements of the lobar ventilations is possible for the CFD predictions of the bronchial flow.

4.4.2 Effect of the dynamic subject specific boundary conditions

Figure 4.5 illustrates the lobar volume flow rate measured from the CT scans by means of lobar volume change compared to that obtained by the CFD predictions in each simulation case. The lobar flow volume rate obtained by the CFD models of case A and B agreed well with the CT measurements. The maximum error obtained in the simulation case A and B, where the proposed dynamic subject specific boundary conditions were imposed at the terminal surfaces, was less than 3% at all the measured time points. This indicates the robustness of the proposed dynamic subject-specific boundary conditions. On the other hand, the results predicted by the rigid model with the simple atmospheric pressure at the terminal surfaces and volume flow rate at the tracheal inlet of case C show a significant discrepancy to the lobar flow volume rate measurements. For example, CT measurements indicate that approximately 7%-10% of the inspired air feeds the rat’s accessory lobe, while the CFD predictions of case C illustrate that almost 25% of the inspired air feeds the accessory lobe of the rat.

The pressure drop predictions across the examined airway geometry computed by the CFD model of each simulation case at a midpoint on the inspiration and the expiration phases (t=300 ms, and t=800 ms respectively) are illustrated in figure 4.6. The results show that the pressure predictions at the trachea and the main bronchi are almost identical at the dynamic and the rigid model with subject specific boundary conditions (i.e. case A and B). However, at the lower generations, where the cross sections of the airways of the dynamic model are smaller compared to that of the rigid model, the predictions of the dynamic model show a slightly lower pressure compared to the pressure of their corresponding airways of the rigid model of case B. This indicates that
as the number of the generations increases, the effect of wall deformation on the flow pattern and distribution intensifies. During expiration, higher pressure was predicted by the rigid model at the left lung compared to the CFD predictions by the dynamic model. Nonetheless, both models illustrate the physiological non-uniform ventilation distribution feature of a living lung. This feature is not visible on the pressure prediction obtained by the rigid model with the simple flow boundary conditions of case C.

Figure 4.5 Lobar flow volume rate obtained by the CFD simulation cases (A, B, and C) compared to the CT measurements of the lobar volume change. The measurements were normalised with respect to the tracheal flow rate.
Figure 4.6 Gauge pressure contours in (Pa) across the examined airway geometry at (a) t=300 ms and (b) t=700 ms. Left: case A, middle: case B, and right: case C.

4.4.3 Effect of wall motion on the flow characteristic

The effect of wall motion on the CFD predictions of the bronchial flow pattern is defined by observing the velocity magnitude at several sections across the deforming model of case A and the rigid model of case B that share the same dynamic subject-specific boundary conditions. Figure 4.7 illustrates the observed velocity magnitude at the mid of the inspiration phase, t=300 ms. It can be seen that there is no significant discrepancy between the CFD predictions of the velocity magnitude acquired from the dynamic and
the rigid model at the trachea and the main bronchi. However, as the flow progresses downstream, a significant discrepancy was observed between the CFD predictions of the velocity magnitude across each model. This can be clearly seen at section C-C’ and E-E’ in figure 4.7 which are located within the feeding branch of the right carinal lobe and the accessory lobe respectively. The maximum velocity magnitude observed at section C-C’ was 2.4 m/s and 1.6 m/s at the dynamic and the rigid model respectively. At section E-E’ the maximum observed velocity at the dynamic and the rigid geometry were 0.84 m/s and 0.68 m/s. This indicates a discrepancy of up to 50% between the dynamic and rigid models.

At mid expiration, a discrepancy of up to 50% was also observed between the CFD predictions of the velocity magnitude across the dynamic and the rigid model as shown in figure 4.8. Unlike inspiration, the predicted velocity magnitude across the trachea and the main bronchi are not identical. The dynamic model shows higher pack velocity entering the trachea as shown in section A-A’. This is probably due to the contracting airways that reduce the geometry volume pushing more air out of the lungs. The observed discrepancy between the CFD predictions of the velocity magnitude across the dynamic and the rigid models during inspiration and expiration indicates that wall motion has a significant effect on the CFD predictions of the bronchial flow characteristics during normal breathing conditions and, hence, it must not be neglected. This conclusion dissent the widely used assumption adopted by many previous studies that airway wall motion could be neglected when simulating the flow of tidal breathing due to the trivial change in lung volume during normal breathing.
Figure 4.7 Contours of velocity magnitude (m/s) at several cross section at t=300 ms. The locations of the cross sections are illustrated on the top left corner. The contours to the left were acquired from the deforming model of case A, while the contours to the right were acquired from the rigid model of case B.
Figure 4.8 Contours of velocity magnitude (m/s) at several cross section at t=700 ms. The locations of the cross sections are illustrated on the top left corner. The contours to the left were acquired from the deforming model of case A, while the contours to the right were acquired from the rigid model of case B.
4.5 Summary

Building upon the outcome of chapter 2 and 3, this chapter integrates the computed dynamic subject-specific boundary conditions and the dynamic mesh of the bronchial airways in order to investigate the effect of wall motion on the flow characteristics during normal breathing conditions. The acquired CFD predictions of the dynamic airway model were compared to those computed by a rigid model with the imposition of the dynamic subject-specific boundary conditions and to the CFD predictions acquired by a rigid model with simple flow boundary conditions. The rigid models were generated from the geometry of the CT scan at end-inhale. The results show a significant discrepancy between the lobar ventilation obtained by the dynamic model and the rigid model with simple flow boundary conditions. The dynamic model and the rigid model with dynamic subject boundary conditions predicted a non-uniform lobar ventilation that agreed well with CT measurements. However, the simple flow boundary conditions imposed on the rigid model result to a uniform ventilation across the airways. The pressure drop predicted by the three models showed a somewhat higher pressure drop across the dynamic model compared to the other two rigid models. To identify the effect of wall motion on the flow characteristics, the velocity magnitude across the dynamic model and the rigid model with the dynamic subject-specific boundary conditions was evaluated. The results show a higher peak velocity predicted by the dynamic model. A discrepancy of up to 50% was observed at the lower branches between the CFD predictions of the velocity magnitude across the dynamic model and the rigid model that share the same dynamic subject-specific boundary conditions.

Two main findings are concluded from this research. First, the imposition of philological and dynamic subject-specific boundary conditions is essential in order to obtain airway ventilation predictions close to that of a living lung. Second, airway wall motion has a significant effect on the CFD predictions of the flow characteristics within the bronchial airways during normal breathing conditions. This finding dissents the widely used assumption adopted by many previous studies that airway wall motion can be neglected when simulating the flow of normal breathing conditions due to the trivial change in lung volume during normal breathing.
5 DYNAMIC SUBJECT SPECIFIC MODEL OF THE HUMAN BRONCHIAL AIRWAYS

5.1 Introduction

In chapter 2 (section 2.2), a deformation algorithm is introduced to deform the CFD mesh of the bronchial airways between consecutive CT-based subject-specific volumes of the bronchial airways in order to approximate the deformation of the bronchial airways within a living during breathing. This algorithm is used in this chapter to control the deformation of a subject-specific airway model of a human subject between the residual volume (RV) and total lung capacity (TLC). The aim of this chapter is to investigate the effect of wall motion on the flow pattern and distribution through a dynamic subject specific model of the human bronchial airways. These results have been published in Ibrahim et al. (2012)

5.2 Acquiring patient-specific airway geometries

This study was approved by the University of Leicester ethics committee. The data used in this study were acquired from a 65 years old non-smoking female subject suffering from mild asthma. CT scans were acquired during breath hold at RV and TLC. The acquisition of the CT data was performed utilising a 16-detector Siemens Sensation scanner (Siemens, Germany). The CT scanning was conducted at the Institute of Lung Health, Glendfield Hospital (Leicester, UK). The scanning parameters were 120 KVp, 40 mA, pitch 1.5, slice thickness of 0.75 mm, and slice interval of 0.5 mm. The main steps to construct the computational models of the central airways are shown in figure 5.1. The segmentation and 3D sampling procedure of the airway geometries was similar to that discussed in section 2.2.1. Two 3D geometries were reconstructed out of the acquired CT images using the threshold technique available in the commercial software Mimics (Materialise, Belgium). The generated geometries were evenly truncated to the 4th generation.
5.3 Mesh preparation for the deformation process

Figure 5.2 illustrates the framework of the airway wall deformation process. The mesh preparation process is similar to that discussed in section 2.2.2. To allow a direct control on the number and the distribution of the mesh wall nodes distributed in the RV and the TLC model, a structured mesh was generated for both geometries so that both meshes have the same number of nodes distributed on their walls. To retain the wall node IDs, the same blocking topology utilised to generate the structured mesh for the RV model was used to generate the TLC model structured mesh. Blocking segments were evenly stretched on both models in order to gain a consistent distribution of nodes between the wall of the RV geometry and that of the TLC geometry. A centreline was generated for each geometry using the 3D Thinning algorithm of Palágyi et al. (2001) applied to the
continuous polygonal surface data of each geometry. The block start and end points were selected based on the bifurcating points of the airway tree geometry centreline as shown in figure 5.3. Each branch centreline segment of the RV and the TLC geometry was then discretised uniformly by inserting \( n \geq 1 \) nodes. These nodes were selected as common landmarks for generating the numerical mesh in each block. As a result, the two meshes share the same number of wall nodes and node IDs, located in corresponding locations at the wall of the RV and TLC geometries.

As the deformation between RV and TLC is large, spring smoothing and local remeshing dynamic mesh schemes are both required to handle this amount of deformation. These two dynamic mesh schemes are not available for simulations that use a structured mesh and can only be used with an unstructured mesh. Therefore, the internal hexahedral elements of both geometries were deleted and the wall quadrilateral elements were converted to triangular elements. Similar to the rat case of chapter 2, the Delaunay Tetra mesher was then utilized to generate the volume mesh elements for the deforming mesh (RV). The Lung User Defined Function (LUDF) software discussed in section 2.5 was used to retrieve the node-to-node correspondence between the wall boundary nodes of the RV geometry and that of the TLC geometry. The LUDF software was also used to generate the User Defined Function (UDF) used to enable the solver ANSYS FLUENT (Lebanon, USA) to recognise the start and target positions of each node at the wall of the moving mesh (RV), and the deformation manner of each node. The nodes trajectories in this study were assumed to be in a straight line. The nodes displacement between and RV and TLC was assumed to be harmonic so that:

\[
A = \hat{i} \in \delta - i \in \gamma \quad (5.1)
\]

\[
\Delta i = A \sin(\omega \cdot t) - A \sin[\omega (t - \Delta t)] \quad (5.2)
\]

\[
i_t = i_{t-\Delta t} + \Delta i \quad (5.3)
\]

where \( i \) and \( \hat{i} \) are the corresponding node coordinates \((x, y, z) \in \mathbb{R}^3\) at the wall of the moving mesh (RV) and the wall of the target mesh (TLC) respectively. \( \delta \) and \( \gamma \) are the set of the nodal coordinates defining each triangular element in the wall of the moving mesh and the target mesh respectively, which are generated as discussed in section
2.2.3 using the LUDF software discussed in section 2.5. \( i_t \) is the position of the moving node at the current breathing time \( t \). \( \Delta t \) is the time step size, and the angular frequency \( \omega \) is calculated with respect to the breathing time. It is important to note that lung motion is non-linear in nature as shown in chapter 2, especially at the lower generations, thus equation (5.1-5.3) is a broad approximation of the lung motion.

![Airway geometry blocking](image)

Figure 5.3 Airway geometry blocking for generating the structured meshes for (a) the Residual volume (RV) geometry, and (b) the Total Lung Capacity (TLC) geometry.

### 5.4 CFD simulation and boundary conditions

For comparison purposes, a rigid model of the bronchial airways of the same subject was developed in addition to the deforming airway model of section 5.2. The rigid model was generated using the non-deforming (static) geometry of the bronchial airways generated from the CT image acquired at TLC. A harmonic inflow/outflow boundary condition shown in figure 5.4 (a) was imposed at the tracheal inlet of the rigid as well as of the dynamic model with a maximum Reynolds number of 1250 measured at peak flow velocity. The inspiration time was set to approximately 2.3 seconds, which gives a Womersley number of 3.3. The terminal surfaces were set to atmospheric pressure and a non-slip boundary condition was assumed on the walls of both models. It is important
to note that the technique introduced in chapter 3 to impose non-uniform flow boundary conditions was not implemented in this study.

Figure 5.4 (a) inlet boundary condition, with phase angles sampling time. (b) cross-sections A-F

The meshed geometries were imported into the commercial CFD solver ANSYS FLUENT (Lebanon, USA). The utilised air density and kinematic viscosity were 1.2 kg/m³ and $1.7 \times 10^{-5}$ m²/s respectively. The flow was assumed to be incompressible with constant density and temperature Large Eddy Simulation (LES) approach was employed to capture the transitional and turbulent flow characteristics within the deforming and the rigid model. The Smagorinsky-Lilly model (Smagorinsky, 1963, Lilly, 1966) was adopted in this study as the subgrid-scale turbulent model with a Smagorinsky constant $C_s$ of 0.1. The SIMPLE scheme was selected to solve the discretised Navier-Stokes equations. To
achieve grid independence, three meshes were generated for each model with 30% incremental mesh refinement: a coarse mesh, a medium mesh, and a fine mesh. Solving the airflow on the three meshes, it was found that the results obtained by the medium mesh (820k and 950k elements for the rigid and the dynamic model respectively) predicts the airflow properties with a sufficient accuracy with a maximum error of less than 2.5%. The simulations were performed using 8-core Intel i7 (3.0 GHz) processor with 8GB of RAM. Each mesh was divided into 8 partitions for message passing interface (MPI) parallel computation. The adopted time step size was $1 \times 10^{-6}$ seconds for all the conducted simulations. Figure 5.4 illustrates the time points and the position of the cross-sections where the flow behaviour was examined. The time points are based on the phase angle ($\Phi$) of the inlet sine wave.

5.5 Mesh deformation validation

The elasticity and other material properties of the airway walls and the surrounding tissues vary widely from dorsal to apex. This results in a non-linear deformation of the airway walls during breathing. Hence, developing an accurate mathematical lung motion model is currently not possible. Boldea et al., (2008) utilised four-dimensional CT to examine lung motion nonlinearity by tracking landmarks on lung consecutive scans. According to their records, the upper part of the lung showed a nearly linear deformation while lower regions showed less linearity. Hence, as current CT scan resolution allows the construction of only the first few generations of the respiratory tree, it was assumed that the inflation and deflation of the current model are elastic and linear, similar to an ideal spring motion.

The volume change acquired by the proposed deformation algorithm was compared to the experimental measurements by Tokuda et al. (2009). They acquired dynamic 3D images from a volunteer using fast magnetic resonance imaging (Fast-MRI) and recorded the volume change during deep breaths. The volunteer in this study and in Tokuda et al. (2009) have approximately the same Residual Volume and Total Lung Capacity Volume. Given the RV and the TLC 3D geometries of the airways, the proposed algorithm was able to interpolate the bronchial volumes for a complete breathing. As shown in figure 5.5, the interpolated volume change is in good agreement as compared to the MRI measured volume change. The largest discrepancy was observed at the beginning of the
inspiration. However, this phase of inspiration depends mainly on the patient effort and, therefore, some variability in the volume change is expected.

![Graph](image)

Figure 5.5 (a) Tokuda et al. (2009) MRI lung volume change (b) comparison between the volume change predicted by the proposed model and that from MRI measurements of Tokuda et al. (2009).

### 5.6 Deforming mesh stability

Figure 5.6 (a) illustrates the deformed airway mesh at several phase angles during the breathing cycle. The applied deformation scheme involved both smoothing (Spring Analogy) and local remeshing that allows the solver to add or remove nodes and cells to preserve the mesh statistics. As shown in figure 5.6 (b), cell skewness was maintained below 0.9 during the deformation process. Cell skewness tends to increase as the deformation advances. The maximum cell skewness was detected at nearly end-inspiration. Although a 0.9 skewness is a considerably high value, it is an acceptable value for the deformation of a complex geometry such as that of the bronchial tree.
5.7 Effect of wall motion on the CFD predictions of the bronchial flow

5.7.1 Flow distribution

Predicting the mass flow distribution among the lung lobes is important to enhance the understanding of lung diseases. Figure 5.7 illustrates the mass flow rate distribution of each lung lobe predicted by the dynamic and the rigid models at several phase angles.

Figure 5.6 (a) 3D representation of the deforming mesh (b) Deforming mesh skewness statistics.
during inspiration. A significant discrepancy can be seen between the dynamic model and the rigid model mass flow distribution. This is due to the original difference in volume and the dynamic change in diameter and length that are resolved by the dynamic model compared to the rigid model. For example, at peak inspiration (Φ=90°), the rigid model predicts a mass flow rate that is 30% higher than that from the dynamic model at the Left Lower Lobe (LLL). At the third quarter of the inspiration phase (Φ=135°), the lower airway lobe branches feature an up to 25% expansion in length and diameter compared to a 15% increment in the upper lobes branches, causing redistribution of flow. This change is not predicted by the rigid model. The discrepancy between the dynamic model and the rigid model predictions exceeds 45% at the Right Lower Lobe (RLL) at Φ=135°.

Figure 5.7 Flow distribution among lung lobes during inspiration at phases (a) Φ=45°, (b) Φ=90°, (c) Φ=135°.

5.7.2 Airway resistance
The airway resistance, which describes the obstruction to the airflow, is an important factor that controls the airflow through the lungs. The airway resistance is defined as $R = \Delta P/Q$ where $\Delta P$ is the pressure drop across a branch, and $Q$ is the volumetric flow rate. The branch airflow resistance depends mainly on its geometrical characteristics in addition to the density and the viscosity of the fluid. Figure 5.8 shows the variation in the flow resistance through each branch during inspiration for the dynamic and the rigid models. Both models show an increment in the airflow resistance as the branch cross-section decreases with increasing bronchial tree branching. The dynamic model predicts airflow resistance that is higher than the rigid model for every phase of the breathing cycle. The left and right bronchia do not experience a significant change in the cross-section. Therefore, the airflow resistance is approximately identical between the
dynamic and the rigid model. The discrepancy tends to increase downwards from the second generation (L2→L7, R2→R7). The dynamic model shows approximately three times higher airflow resistance at branches L5, L6, R5 and R6 due to the change in the branch cross section with Φ, as well as the change in the bifurcation angle between L5-L6 and R5-R6 due to the airway motion. At the phase angle 135°, the rigid model shows an airflow resistance similar to that predicted at the phase angle 45°, particularly for the left lung branches, while the dynamic model shows a considerably higher airflow resistance.

Figure 5.8 The CFD predicted resistance of the airway branches during inspiration. (a) branch L1-L7 (b) branch R1-R7
5.7.3 Flow velocity

The velocity magnitude at several cross-sections (see figure 5.4 (b) for cross-sections locations) was studied to evaluate the effect of the moving walls on the flow pattern. During inspiration, the fluid enters the trachea and splits at the first bifurcation to the left and right lungs. When the Reynolds number exceeds a certain level, the flow in the left bronchia tends to skew toward the inner wall forming a recirculating flow zone next to the upper wall. Figure 5.9 (1) shows the velocity contours at cross-section A-A' located at the entrance of the left bronchia where the recirculating flow regions starts to develop. The discrepancy in the velocity magnitude between the dynamic model and the rigid model at this cross-section is not large, as both models predicted a maximum velocity of approximately 0.9 m/s at peak inspiration ($\Phi=90^\circ$). However, the instantaneous streamlines showed two counter rotating vortices in the rigid model, while only one vortex predicted by the dynamic model. This discrepancy in the cross-sectional flow pattern is most likely due to the reduced cross sectional area of the left bronchia and the slightly higher flow rate that reduces the zone of the strongly

![Velocity Contours](image)

Figure 5.9 Cross-sections of velocity magnitude (m/s) (a) Dynamic model (b) Rigid model
reduced velocity at the outer wall of the left bronchia in the dynamic model. The cross-section B-B' which is located at the end of the right bronchia also showed a similar velocity magnitude but different secondary flows between the dynamic and the rigid models, as shown in figure 5.9 (2). Across the lower branch L2, the flow pattern displayed two inplane recirculations in the dynamic wall model, where only one spiral motion is predicted by the rigid wall model as shown in figure 5.9 (4). This is due to the static nature of the rigid model boundaries. As the flow continues downwards, the discrepancy in velocity magnitude and secondary flow pattern between the dynamic and the rigid models tends to increase.

5.6 Summary

A new subject-specific moving wall CFD model of the human bronchial airways was developed in this study. The deforming algorithm discussed in section 2.3 was used to deform the mesh of the start airway geometry at the residual volume to the target airway geometry at total lung capacity based on a node-to-node correspondence between the mesh walls. The change in lung volume predicted by the deformation algorithm was compared to a MRI measured volume change study and showed good qualitative agreement. It was found that the wall motion has a significant effect on the flow pattern and distribution. The CFD predictions of the rigid model gave a mass flow rate distribution among the airway lobes that was up to 30% different to that predicted by the dynamic model. Furthermore, the dynamic model showed an up to three times higher branch resistance during the inspiration phase. In addition, the predicted velocity magnitude was roughly similar within the dynamic and the rigid models. Nevertheless, the secondary flow results showed different profiles. The discrepancy in the predicted results (pressure, velocity profiles) between the rigid and dynamic models tends to increase as the number of generations increases. In summary, the wall motion alters significantly the predicted airflow and should not be neglected to achieve a more reliable CFD simulation of the airflow through the central airways.

It is important to note that this is a preliminary attempt to investigate the effect of wall motion on the flow characteristics within a dynamic subject specific model of the human bronchial airways. The mesh nodes displacement vectors were assumed linear (in a straight line) with a sinusoidal deformation between the residual volume and the total
lung capacity, similar to an ideal spring. In addition, simple flow boundary conditions were implemented in this study. Thus, the proposed technique to impose non-uniform flow boundary conditions on the terminal surfaces to obtain reliable CFD predictions of the bronchial flow was not implemented in this study. Hence, the implementation of the proposed computational framework to predict the bronchial flow within a human airway model using CFD will be carried out in the near future. This includes the dynamic 2-CT based deforming model of chapter 2 and the dynamic subject specific boundary conditions algorithm of chapter 3.
6 CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

6.1 Conclusions

This research introduces new dynamic subject-specific CFD models of the bronchial airways with dynamic flow boundary conditions derived from the actual flow within the living lung. The proposed dynamic CFD models were used to investigate the effect of wall motion on the CFD predictions of the flow characteristics.

1. The development of dynamic CFD models that are capable of capturing the non-linear deformation features of the bronchial tree during breathing:
   a. A new deformation algorithm is introduced, which establishes a node-to-node correspondence between the walls of the CFD meshes of the subsequent airway geometries generated from CT scans acquired at different time points during the breathing cycle. The proposed deformation algorithm is not limited to the deformation of the bronchial airways and can be used in any engineering simulation problem that requires homogeneous or non-homogeneous deforming mesh. A home-built software was established in order to facilitate the case setup in the future.
   b. The proposed deformation algorithm was used to develop a dynamic model of the bronchial airways based on a dynamic CT data set of a laboratory animal acquired over normal breathing conditions. Compared to the CT-based reconstructed geometries at mid-points over the breathing cycle, the deforming CFD mesh was capable of capturing the airway motion non-linearity during normal breathing conditions.
   c. In addition to the dynamic CT based deforming model of the bronchial airways, a novel non-linear dynamic CFD airway model based on a pair of CT images acquired at end-exhale and at end- inhale is introduced. This dynamic CFD model was capable of approximating the airway motion
non-linear deformation features based on a ventilator measurements of the total lung volume change. The deforming CFD mesh was validated against airway geometries at mid-points over the breathing cycle generated from the dynamic CT data set and showed good agreement.

d. The significant output from this research is the availability of a new non-linear dynamic model of the bronchial tree that requires just one pair of CT images as input, which therefore complies with radiation dosage limits for human subjects.

2. The imposition of dynamic subject specific boundary conditions derived from the actual flow within a living lung.

e. A sectioning technique of the subsequent 3D volumes of the lung generated from a dynamic CT data set covering the breathing cycle of a laboratory animal was introduced in order to approximate the volume change of the missing peripheral airways distal to each terminal surface over the breathing cycle.

f. The proposed lung 3D volume sectioning technique was based on the mechanical coupling between the vascular tree and the bronchial airways within the pleural cavity. Since the vascular tree is tethered to its adjacent airways and to the lung parenchyma via a connecting tissue, the vessels of the vascular tree are expected to deform in accordance to the change of the lung volume during breathing. The proposed sectioning technique was validated on a cast geometry of the bronchial airways at total lung capacity that includes most of the bronchial airways beyond the resolution of the conventional CT or MRI imaging of a living lung.

g. The proposed sectioning technique was also used to compute the lobar volume change of the bronchial airways for validation. Compared to the dynamic CT measurements of the lobar volume change, the proposed sectioning technique was able to approximate the lobar volume at different time-points over the breathing cycle.

h. The proposed lung volume sectioning technique was used to segment the subsequent 3D volumes of the dynamic CT data set into several sub volumes, where each volume encloses the missing peripheral airways.
distal to each terminal surface. The volume change of each segment over the breathing cycle was then used to drive the volumetric flow rate boundary conditions for their associated terminal surfaces.

i. The significant output from this research is the availability of dynamic subject-specific boundary conditions that depend on biological information obtained from the lung deforming constituents.

3. The computed dynamic subject-specific boundary conditions were imposed at the terminal branches of the dynamic airway mesh to develop a CFD model of the bronchial airways to investigate the effect of the airway wall motion on the flow characteristics during normal breathing conditions.

a. This is the first assessment of the effect of wall motion on the CFD predictions of the flow pattern within the bronchial airways during normal breathing conditions.

b. The CFD predictions of the proposed dynamic model was compared to those acquired from a rigid model with dynamic subject-specific boundary conditions, and a rigid model with simple flow boundary conditions. Both of the rigid models were based on the CT image of end-inhale.

- Compared to the flow predictions acquired by the rigid model with the dynamic subject-specific boundary conditions, a discrepancy in velocity magnitude and flow pattern was observed downstream. The results showed that this discrepancy intensifies as the generation number increases.

- The flow distribution within the rigid airway model with the simple flow boundary conditions were uniform across the airway geometry, while a non-uniform ventilation was predicted by the proposed dynamic CFD model that resembles the non-uniform ventilation of a living lung.

c. The results suggest that even at normal breathing conditions, airway motion has a considerable effect on the CFD predictions of the flow pattern within the bronchial airways, particularly at the lower generations. This finding
dissent the common assumption of neglecting the airway motion when simulating the flow at normal breathing conditions.

4. An attempt was made to investigate the effect of wall motion on the flow pattern and distribution within a human model of the bronchial airways
   a. This is a preliminary attempt to investigate the effect of wall motion on the flow characteristics within a dynamic subject specific model of the human bronchial airways. The airway deformation was assumed linear and sinusoidal between the residual volume and the total lung capacity similar to an ideal spring. Furthermore, simple flow boundary conditions were imposed at the terminal surfaces of the human airway geometry. Thus, the proposed dynamic 2-CT based deforming model of this study and the proposed dynamic subject-specific boundary conditions were not used to model the flow within the human airway geometry.
   b. Although the imposed boundary condition profiles and the airway wall deformation pattern were simple, wall motion was found to have a significant effect on the CFD predictions of the flow characteristics and airway resistance.

6.2 Future Work

1. With the availability of the new 2-CT based deforming model of the bronchial airways it will be interesting to investigate the effect of wall motion on the CFD predictions of the flow within the human bronchial airways during normal breathing conditions.

2. Evaluate the capability of the proposed 2-CT based deforming model in capturing the airway deformation within a diseased lung.

3. Development of a technique to visualise the flow dynamics within a living lung. This is important for a better validation of the flow predictions acquired by sophisticated CFD models of the bronchial airways.
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