Study of flows in physiologically realistic patient specific airway models

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ABSTRACT

The paper presents the development of techniques to study flows in human conducting airways aimed at improving understanding of underlying mechanisms in asthma and Chronic Obstructive Pulmonary Disease (COPD). The models developed are made through additive layer manufacturing (ALM) of segmented lung Computed Tomography (CT) scans. The flow dynamics in these models are studied using time-resolved stereo PIV. Results are presented for various lung models including different geometries as well as different material properties to allow differentiating between flow effects due to geometry and wall compliance.

INTRODUCTION

Asthma and COPD are widespread, serious health problems with asthma affecting 300 million people, while 80 million people have moderate-to-severe COPD worldwide. They impose serious health risks with asthma estimated to cause approximately 239,000 deaths worldwide per year and COPD predicted to be the 3rd leading cause of death in the world by 2030 [1]. In people with COPD and asthma damaged, inflamed or obstructed airways are common, hindering breathing. Although targeted approaches to treatment are being developed, often it has been unknown how to match these to specific patients since current methods to detect and treat these conditions do not consider individual differences between airways. Thus, people suffering from these conditions may not get the optimal treatment. The EU-funded programme AirPROM (www.airprom.eu) aims to develop models of the airways to assess how air flows through the lungs and why this flow becomes obstructed in people with asthma and COPD. This will enable development and testing of new individually tailored therapies, through linking the characteristics of different airways to particular treatments. Furthermore, this will aid monitoring future risks to patients by helping predictions regarding the effect on the airways and the progression of the diseases. The work presented here is focused on enabling investigation of flow modifications seen in asthma and COPD.

As part of this project, techniques are developed to study flows in human conducting airways to improve understanding of underlying mechanisms in asthma and COPD. For this, realistic patient-specific physical models of the conducting airways are created through additive layer manufacturing (ALM) of segmented lung CT scans, which allow the airflow in lungs to be studied to understand how lung-conditions affect the patients’ breathing.

The paper will discuss the use of Additive Layer Manufacturing (ALM) techniques to develop high order (typically up to 7th) airway models, and the use of particle image velocimetry (PIV) to investigate flow characteristics in these models.

FLOW IN LUNGS

Understanding flows in human airways is vital for combating respiratory complications. Issues include aerosolised drug delivery, high frequency ventilation and pulmonary disease diagnosis and treatment [2]. The work presented here is focused on flow modifications seen in asthma and COPD. Patients suffering asthma have inflamed airways, making them swollen and very sensitive. When the airways react, mucus production increases and the muscles around airways tighten, narrowing them and thus causing less air to flow into the lungs. COPD typically involves two separate lung conditions: chronic bronchitis and emphysema. In chronic bronchitis, the airways (bronchi) become inflamed, congested with mucus, and narrowed, resulting in obstructed air flow. In emphysema, the walls of the air sacs (alveoli) are destroyed, leading to fewer but larger alveoli, making them less efficient in transferring oxygen from the lungs to the bloodstream.

Flows in lungs have been studied extensively over the past decade, both numerically and experimentally. Most of these studies are of generic geometries. However, one of the most important factors influencing the flow field is the geometry of the lung airways. Furthermore, airway deformation needs to be taken into account for realistic flow patterns, as the
airways are compliant and will deform over the breathing cycle. The dynamics and effect of this airway deformation is currently unknown, as typically CT scans are only captured for full expiration and inspiration, whilst MRI currently lacks resolution for airway segmentation.

Flows in human airways have been studied using silicone models based on typical (generic) airways geometries [3] derived from data from e.g. Horsfield et al [4] and Weibel [5], as well as using patient-specific silicone optically transparent ALM models based on CT-data, generally aimed at improving artificial ventilation (e.g. [6-8]).

The flow in the trachea and upper bronchi has been found to be highly three-dimensional and asymmetric with counter-rotating vortices in the bronchi (e.g. [8,9]). There is no consensus on the influence of different inflow conditions on the flow in the subsequent bifurcations, e.g. to what extent the upstream flow conditions have an impact on the flow field in sub-branches as a function of the local Reynolds number. Ball et al [10] showed strong vortex shedding in numerical simulation of the flow from the laryngeal region with flow impact up to 8D. Van Erbruggen [11] found highly three-dimensional flow in numerical simulations, showing the importance of non-fully developed flows in the branches due to their relatively short lengths. Thus physically relevant studies require realistic models of the lung geometry, including effects from the laryngeal region (e.g. [12]). Studies to date have shown a quantitative evaluation of volumetric flow will require time-resolved three-dimensional measurements.

Most investigations were conducted using planar 2C PIV in non-compliant, rigid models presenting either a generic or a complex geometry. More recently three-dimensional PIV has been presented in a low generation lung model [7]. In the experiments described here these techniques are investigated further to study the flow dynamics in different models of conducting human airways using 3C-3D PIV. Furthermore, the effect of compliance is investigated by developing ALM models with material properties mimicking those of realistic airways.

**ALM CREATION OF PATIENT-SPECIFIC ANATOMICAL MODELS**

To enable study of the airflow inside the lungs of a specific patient, hollow models of the airways are created based on an *in vivo* CT-scan of the patient. The x-ray absorbance information in the 3D CT data (e.g. Figure 1) is used to extract (segment) the contiguous 3D shape of the inner surface of the airways using e.g. Mimics (Materialise BV). For a CT data-set, airways can typically be identified down to 6/7th order (with trachea being 0th order); beyond this airways are too small to be reliably resolved from CT. The resulting geometry (in stl format) can then be used to create a 3D physical model that accurately represents the anatomical shape of the airways using additive layer manufacturing. The same geometry may also be used for numerical flow simulations, allowing CFD-experimental comparisons to be made.

![Figure 1](image.png) 3D CT data of a patient's lung (left) and segmented 7th order airways as used for creating ALM model (right).

To create a hollow model of the airways to enable study of airflows, the geometry is thickened and then hollowed in software leaving an open geometry where the inside accurately represents the inner shape of the airways. This geometry can then be used as direct input for 3D printing. In a second approach, the original CT-based stl geometry can be printed directly. In this case a hollow model can be produced by casting a material around this model and subsequent removal of the core.

To enable optical measurement techniques to be used the models developed here are made out of optically transparent materials. In the measurements presented three types of anatomical model have been used: a generic rigid geometric model, a high (7th) order rigid CT-based model based on a hollowed geometry produced through standard ALM techniques and a low-order compliant CT-based model made by casting an optically clear elastomer around a CT-based, ALM produced core, which is subsequently removed. The elastomer used in the latter model (Clear Flex® 50 water
clear urethane rubber, Smooth-On Inc) possesses a level of elasticity similar to that of the cartilage in the trachea and left and right bronchial tubes (Young's modulus ~2.47MPa vs. averages ranging from 2.5-7.7MPa for trachea [13]), thus allowing flow study at near-realistic compliance.

The rigid model provides a full airway geometry up to 7th order, enabling study of the effects of the various branches on total and local flow dynamics.

EXPERIMENTS

For measurements shown here the flow was generated using a peristaltic pump rig providing a controlled input flow rate. Distortions due to refractive index differences were minimised by using oil as flow medium, enabling visualisation in the complex airway geometries by matching refractive index of the models (~1.49) to that of the flow (~1.47 [14]). To enable velocity measurements the flow was seeded with reflective polyamide particles of 50 µm diameter. A light sheet was generated using a 200mW green laser diode (SD-301) or double-pulsed Nd:YAG laser and used to illuminate a 2D plane or thin volume in the geometry. A novel hybrid PIV system was designed based on the use of three to five synchronised (high-speed/PIV) cameras for simultaneous capture of PIV data from a thick light sheet. Depending on the configuration used this enables (quasi) time-resolved 3C volumetric measurements allowing study of different aspects of flow behaviour including flow development inside the airways (Figure 2).

![Figure 2 PIV systems: 3-camera arrangement (left); Hybrid 3C/high-speed system (right).](image)

The anatomical ALM phantoms used were mounted on a traversing system allowing fully automated accurate scanning of the flow region of interest throughout the airway models. Thus, by effectively scanning the light sheet different parts of the airways can be investigated and the turbulent flow distribution through the complete airway geometry can be built up.

RESULTS

Preliminary results were obtained for the three configurations discussed here. Figure 3 shows a mean result for the geometric model, aimed at CFD validation. Clear recirculation regions can be identified in the region just behind the bifurcation.

![Figure 3 Geometric model representing basic airway configuration (left), instantaneous 3C velocity map (centre) and mean 3C velocity based on PIV.](image)
Results for the CT-based patient-specific rigid 7th order and compliant 2nd order models are shown in Figures 4 and 5, respectively.

Figure 4 7th order CT-based airway model used for PIV measurements (centre); example instantaneous flow in section through centre and left branch (right); time resolved PIV in section through 6th order bronchi (left).

Figure 5 2nd order CT-based compliant airway model used for PIV measurements (left); example instantaneous 3C flow in section through centre (right).

CONCLUSIONS
A measurement system capable of high-speed 3C PIV has been designed for measurements in optically transparent airway models of realistic configuration and compliance. Preliminary results have been presented, with further data being processed. Issues being investigated include the creation of realistic inflow conditions by using CT-based upper airway models (Figure 6) and generating realistic breathing patterns.

Figure 6 CT-based ALM models of upper airway used to generate realistic inflow conditions for airways.
Furthermore, attention is focused on creating on ALM models that are not only anatomically correct but also in terms of mechanical behaviour, thus allowing e.g. realistic airway movement over the breathing cycle to be investigated. For this, novel multi-material ALM techniques are developed that allow creation of models combining different materials providing sections with different compliance depending on the tissue that is represented (e.g. muscle and soft tissue in trachea). By comparing flow dynamics for different models the respective roles of different physiology and geometry can be studied individually providing insight into their relevance.

The measurements obtained will serve to study flow dynamics in airways under different lung conditions as well as allow validation and development of CFD models and in vivo MRI velocimetry.

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