FUNCTIONAL IMAGING OF RESPIRATORY SYSTEM USING COMPUTATIONAL FLUID DYNAMICS

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Abstract. *Functional imaging of the respiratory system is a new domain where the respiratory dynamics (such as airflow in the lungs and particle deposition) are studied by means of modern engineering techniques. A three dimensional model of a patient specific bronchial tree is constructed from a computed tomography scan. By segmenting the desired region of air from the set of images in the scan a well defined, smooth geometry of the airway can be extracted, meshed and exported to be used in a computational fluid dynamics (CFD) analysis. Together with the patient specific lung geometry the CFD analysis uses patient specific boundary conditions, extracted from clinical tests, to initialize the airflow in the respiratory system. Two experiments are simulated in this work by means of CFD computations. Careful treatment of the CFD boundary conditions made sure that the experimental circumstances are mimicked as reliable as possible. This leads to a good correlation with the experimental outcome. Not only trends like lung deposition in function of the size of particles but also absolute quantities are predicted well with the CFD computations. The positive outcome of the study is promising for pharmaceutical companies when regarding the development of new respiratory drugs. CFD can give an insight into regional particle deposition and how changes in particle characteristics can influence deposition.*

1 INTRODUCTION

For centuries medicine and engineering have been two completely separated fields where interaction and cooperation was scarce, if not non-existing. However, nowadays engineers and doctors are cooperating more and more intensively to optimize the health care and to increase the patient's welfare. Modern engineering techniques are used in extension to the ancient medical knowledge to meet the modern needs in medicine.

This project combines the modern engineering tools in computed tomography (CT) imaging, computer aided design (CAD) and computational fluid dynamics (CFD) with traditional pulmonology in order to arrive at the best patient specific analysis possible. This is done to attain optimal patient care. The study focuses on the deposition of small particles in the pulmonary system. A matter of great interest for the development of new devices delivering an accurate dose of a drug to a target site in the lungs. Since the lung ventilation and, consequently, particle deposition are greatly influenced by the shape of the (small) airways and most respiratory drugs are developed for patients suffering from lung diseases that affect airway geometry, also these patients are considered within this study.

In section 2 more information on the medical background of this project is given. This is followed in section 3 by a detailed description of the CT imaging tools that are used to capture the patient's lungs and how these images are converted to a well-defined three dimensional (3D) pulmonary CAD model. Subsequently section 4 explains the importance of using patient specific boundary conditions and CAD models to perform the CFD analysis. Section 5 finally shows the results of the CFD simulation of the deposition of particles in the respiratory system together with validation cases provided by clinical tests.

2 MEDICAL BACKGROUND

Most respiratory drugs target patients suffering from lung diseases like chronic obstructive pulmonary diseases (COPD), such as emphysema, and asthma. COPD (emphysema) is characterized by a chronic and slowly progressive airflow limitation causing a gradual decrease of the mass flow rate in the respiratory system. This condition is also known as smoker's lung. Asthma has the same characteristics as COPD with the major difference that asthma is a reversible process. It may abate either spontaneously or as a result of treatment[1]. Both diseases result in an important (sometimes permanent) deformation of the airway branches.

As mentioned before airway geometry is an important factor when considering particle deposition in the respiratory system. Different methods of inhaling require different models. Aerosols are inhaled during multiple breathing cycles at normal breathing volumes, while inhaler devices require mostly one deep inhalation from the patient. Figure 1 shows the lung volume versus time and indicates some special lung volumes.

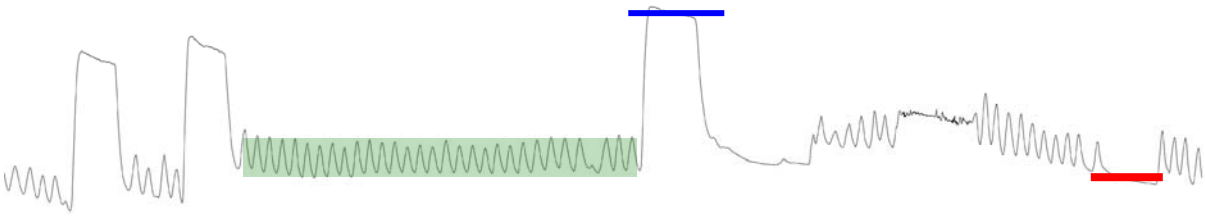


Figure 1 Lung volume versus time (normal breathing = green, total lung capacity (TLC) = blue, functional residual volume (FRC) = red)

To accurately simulate the aimed method of inhalation, the 3D model in the CFD simulation has to correspond well with the lung volume conform to the position in the breathing cycle. For this reason CT scans are taken at different lung volumes. If inhalation during multiple breathing cycles is simulated the CAD model is made from a CT scan taken at functional residual capacity (FRC, red in Figure 1) which corresponds well with the lung volume during normal breathing. If the CFD computation is used to simulate drug inhalation during one deep inhalation the CAD model is made from a CT scan taken at total lung capacity (TLC, blue in Figure 1).

3 CT IMAGING AND 3D MODEL GENERATION

3.1 The super slice CT scanner

The first requirement in the generation of high definition, patient specific CAD models is the accessibility to a high resolution super slice CT scanner. For this study the CT images were taken with the General Electric Light Speed VCT scanner. This super slice CT scanner with a minimal slice thickness of 300μm and an in-slice resolution of 512x512 voxels, produces 12-bit gray scale images. A 12-bit gray scale image has $2^{12} = 4096$ different gray values to be stored, which correspond to the tissue electron density (usually expressed in Hounsfield units (HU)), and range on a scale from 1024HU to +3071HU, calibrated so that 1024HU is the attenuation produced by air and 0HU is the attenuation produced by water. With a slice thickness of 300μm a scan of the lungs results in a collection of around 1000 CT images. The display field of view (DFOV) has to be chosen as small as possible in order to get a minimal in-slice voxel size (the DFOV is divided into 512x512 voxels).

3.2 Generating a 3D CAD model

The CT-images are imported in the Materialize MIMICS software package. This software allows the images to be imported with a CT compression filter which sets the Hounsfield unit in all the voxels that have a Hounsfield unit in the region of [1024HU,824HU] to a value of 1024HU. This filtering can be done without any change in the physical properties of the lung since no human tissue produces a Hounsfield unit in this range and has as a purpose to increase the contrast between air and tissue in the small airways pulmonary region. Then the regions of air of interest are carefully segmented into a single mask throughout the collection of CT images. The resulting mask can be converted into a 3D CAD model. Figure 2 shows a

staircasing effect in this original 3D model due to the fact that it is build from a collection of pixels that were given a certain thickness (thickness equals the slice thickness). This model is far from being a smooth surface that can be meshed and used for CFD purposes.

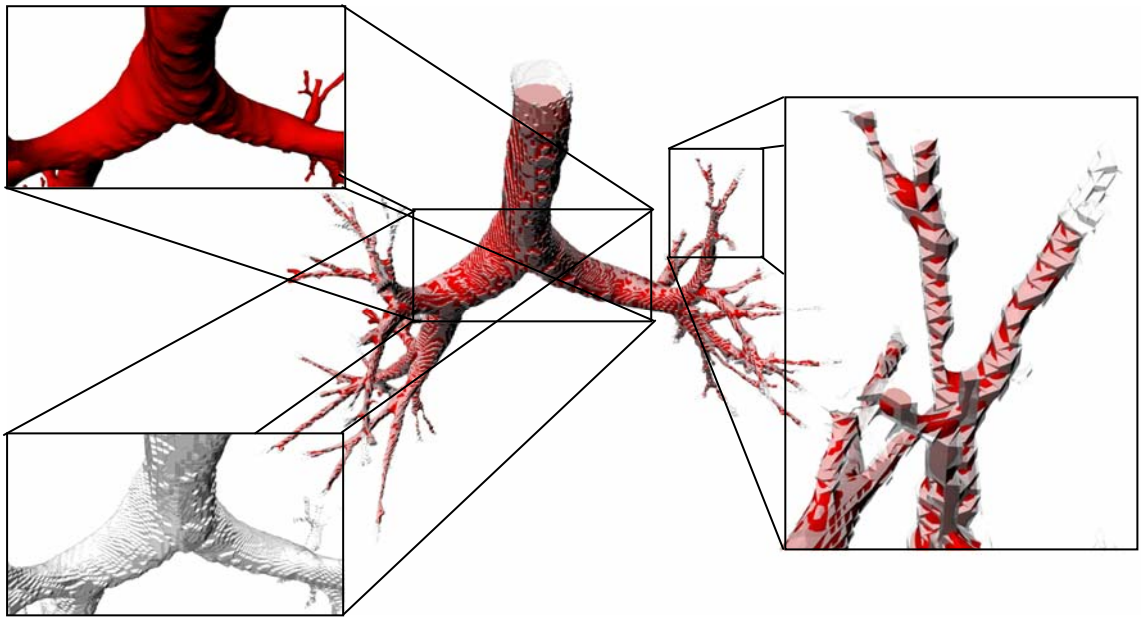


Figure 2 Original 3D model (gray) versus smoothed model (red)

A smoothing algorithm with volume compensation within the Materialise MIMICS software package transforms the staircased first model into a smooth model (red in Figure 2). This smooth model still represents the exact airway geometry and can be exported and meshed.

For this project the airway models are generated at different lung volumes as mentioned in section 2. Besides this volume difference also the scanned region changes. Two different regions were defined. The first models were scanned from the trachea down to diaphragm (method A). When a complete simulation of the particle deposition is simulated also the upper airway is included and the CAD model is based on a scan taken from the palatum durum down to the diaphragm (method B).

Figure 3 shows some of the models that were generated for this project. On the left and the middle two models made from scans with method A are shown. These models are shown in blue and red for the same patient. The difference between them is the lung volume at the moment of the scan: the model on the left is taken at TLC while the model in the middle is taken at FRC. On the right a model is shown that was reconstructed from a method B scan at TLC volume. The bronchi in the 3D models end where a collapse is found or where the diameter of the airway becomes too small in order to detect the airway with the CT resolution used (<1mm).

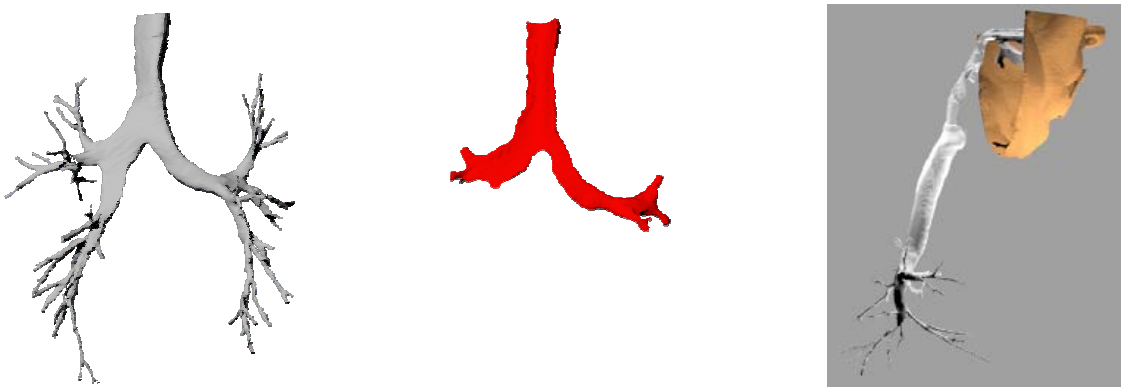


Figure 3 Different CAD models (left = method A at TLC, middle = method A at FRC, right = method B at TLC)

4 PATIENT SPECIFIC BOUNDARY CONDITIONS

A second important factor, next to patient specific geometries, in the simulation of airflows in the human respiratory system is the use of patient specific boundary conditions. The walls of the bronchi are defined as walls (no slip condition). The remaining boundary conditions (inputs) for the CFD simulations are:

- pressure at the pressure inlet (trachea or mouth)
- pressures at the pressure outlets (ends of the bronchi).

The pressure at the pressure inlet is set equal to the atmospheric pressure. This means that the driving force for the airflow is entirely coming from an under pressure at the outlet surfaces, cfr normal tidal breathing. The pressure in small airways is obtained indirectly with an iterative process that matches the mass flow obtained with flow volume curves (see Figure 4).

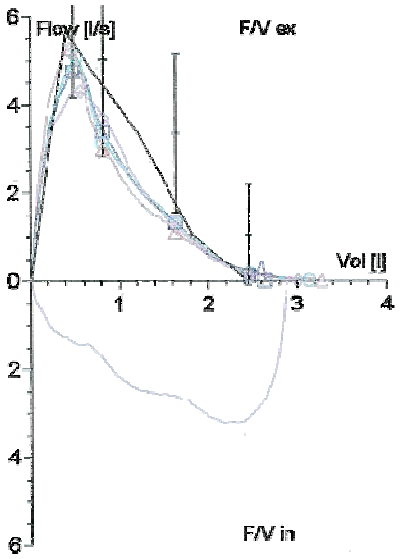


Figure 4 Flow volume curve used to match the mass flow in the CFD computation

5 RESULTS AND VALIDATION

This section gives an overview of the results of the simulations of particle deposition in the human respiratory system. The results are shown for two different situations that correspond with a clinical test. The first CFD simulations that were performed mimic the clinical test know as ventilation scan. The second simulation corresponds with the clinical test that was performed by Usmani et al[2] in 2005. The results are shown and immediately validated with the outcome of the two clinical tests they refer to. All CFD computations are performed with the Fluent software package.

5.1 Ventilation scan

A ventilation scan or ventilation scintigraphy is the traditional clinical test that is used to asses a patient's lung ventilation. During a ventilation scan a patient inhales technogas particles (aerodynamic diameter = 0.02μm) during 4 normal breathing cycles. A gamma camera is used to give a visual as well as a quantitative distribution of particles going to each lung.

The CFD computations were performed in a way to simulate the ventilation scintigraphy as well as possible. A "method A"-scan at FRC was taken to construct a 3D model of the lower airways. Then an injection of technetium particles with a diameter of 0.02μm was superimposed on the CFD results of a steady, laminar[3] airflow for a mass flow rate that equals normal breathing. Table 1 shows that for 5 different patients the CFD computations match the right/left particle distribution well with the results of the ventilation scintigraphy.

Patient	Scintigraphy: R/L ratio	CFD: R/L ratio
DBV	64/36	60/40
JJ	58/42	62/38
GG	58/42	58/42
GP	57/43	60/40
DA	53/47	57/43

Table 1 Right/left particle distribution for clinical testing (ventilation scintigraphy) versus CFD simulation

From the visual output of the ventilation scintigraphy it can be seen that the 3D CAD model used to perform the CFD simulation provides already some information on the possibility of clustering of particles during the deposition. This can be seen from Figure 5 where the 3D lung model is laid on top of the visual results of the ventilation scintigraphy. It can clearly be seen that a clustering of particles occurs at unusual closure point in the bronchi (collapse of the bronchus at the end of expiration corresponding with FRC due to loss of elasticity caused by emphysema).

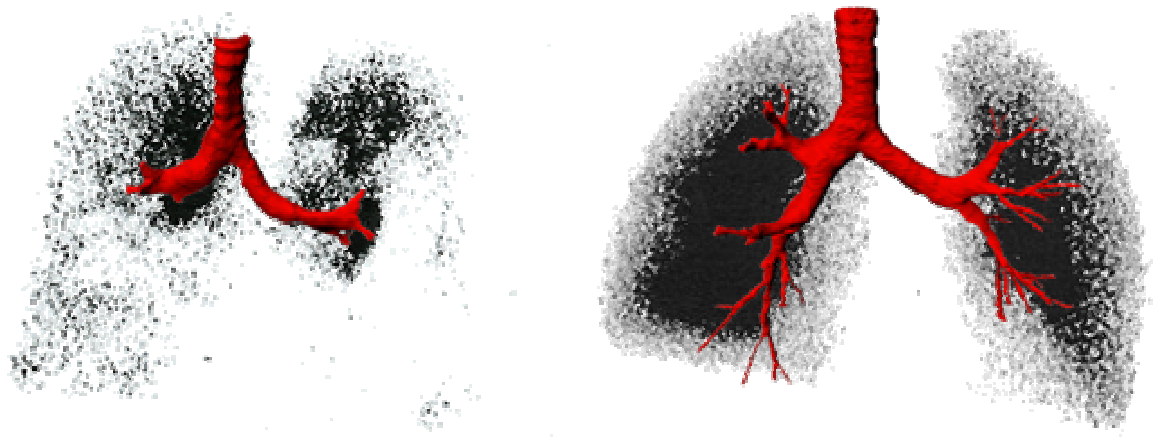


Figure 5 Particle deposition during a ventilation scintigraphy with overlay of 3D FRC model used during CFD computations (left: COPD patient, right: asthmatic patient)

5.2 Lung Deposition in function of the particle size (Usmani et al 2005[2])

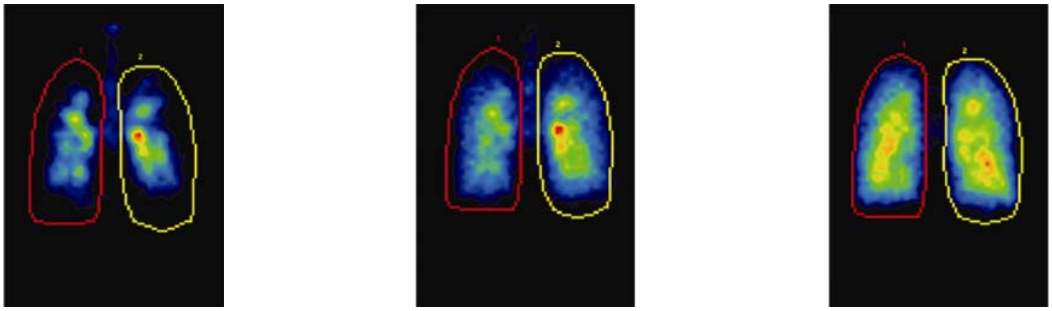
The CFD results of the deposition of particles in the lower airways are validated with a clinical test published by Usmani et al[2]. In this publication Usmani et al. did some experiments to analyze the influence of the particle size on lung deposition in a group of 12 asthmatic patients. During one deep breath these patients inhaled technetium-99m–labeled monodisperse albuterol aerosols with a mean aerodynamic diameter of 1.5, 3 and 6 μm. Again a gamma camera visualization was used to give both a visual and quantitative distribution of particles inside the respiratory system. Usmani presented his results by averaging the results for the 12 patients participating in the study.

To mimic the results of the experiments the CFD were performed on a 3D model generated from a method B CT scan taken at TLC. This means that the scan includes the upper airway and that the particles are injected from the plain between the lips. The laminar flow computations are performed for one patient with unsteady boundary conditions injecting the particles (3 different sizes: 1.5, 3 and 6μm) superimposed on the flow at the peak flow values.

Figure 6 shows a comparison between the deposition sites for both the experiment (top) and the CFD simulation (bottom) for all three particle sizes. The experimental results show the particle density as visually given by the gamma camera. Red areas indicate a high particle density, blue areas a low particle density. The CFD results show particle paths colored by residence time. Red corresponds with slow moving particles, blue with fast moving particles. Particles paths in the CFD results end where particles hit the wall.

It can be seen from Figure 6 that the results of the CFD simulation correspond well with the experimental results by Usmani et al. Larger particles (6μm, figure 6 (a)-(d)) do not enter the lungs farther then the large airways (experiment: high particle density, CFD: particle paths stop in the large airways). As the particles become smaller (3μm and 1.5μm, figure 6 (b)-(e) and (c)-(f)) they deposit less in the larger airways but reach farther into the lungs. 3μm particles reach the level of small airways and 1.5μm particles deposit mainly in the peripheral

airways.



(a) 6µm (b) 3µm (c) 1.5µm

(d) 6µm (e) 3µm (f) 1.5µm

Figure 6 Particle deposition: experiment (top) versus CFD (bottom)

Also regarding the total lung deposition (particles within the red and yellow circles in Figure 6) the CFD simulation is in good correlation with the experimental results. This can be seen from Figure 7. Most importantly the CFD results show the same trend in lung deposition versus particle size as was retrieved from experiments by Usmani et al.

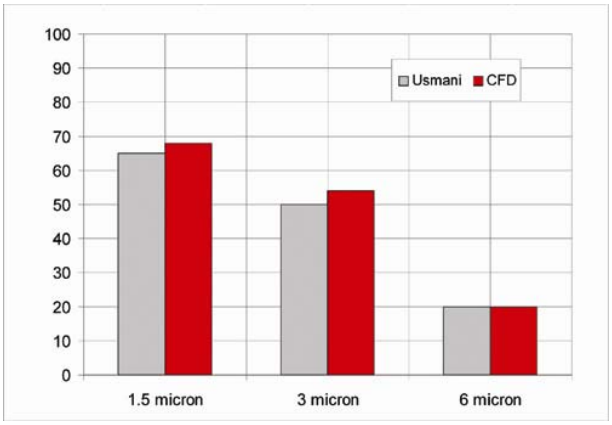


Figure 7 Total lung deposition

6 CONCLUSION

It has been shown in this paper that by using patient specific boundary conditions and geometries during CFD simulations of the deposition of particles in the human respiratory system, the results of an experiment is predicted well. For this purpose the CFD computations are set up to mimic the experiment as well as possible. The patient specific model is build from CT scan taken with a high definition CT scanner and the patient specific boundary conditions come from standard clinical tests (lung function test, full body plethysmography). Validating the results of the CFD computation with two experiments (ventilation scintigraphy and particle deposition in function of particle size (Usmani et al.[2])) shows that the CFD computations predict well the behavior of particles in the lungs. Trends are found to be similar with experiments and even absolute quantities lay within an acceptable range of the experimental results.

These new techniques in studying the particle deposition in the human respiratory system can be used by pharmaceutical companies in the development of new drugs where they can assist in different matters. They can help the companies understand during the testing phase of an inhaled drug why it has an effect or not (particles do/do not reach the desired region). Furthermore these techniques can lead to a situation where drug inhalers can be designed in such a way that each patient receives the right dose of drug at the right location in the respiratory system.

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