THREE DIMENSIONAL INTEGRATED SOFTWARE DEVELOPMENT FOR AIR-PARTICLE FLOW SIMULATION THROUGH IMAGE-BASED UPPER HUMAN AIRWAYS

MOHD ZAMANI BIN NGALI

UNIVERSITI TEKNOLOGI MALAYSIA

THREE DIMENSIONAL INTEGRATED SOFTWARE DEVELOPMENT FOR AIR-PARTICLE FLOW SIMULATION THROUGH IMAGE-BASED UPPER HUMAN AIRWAYS

MOHD ZAMANI BIN NGALI

A thesis submitted in fulfilment of the
requirements for the award of the degree of
Doctor of Philosophy (Mechanical Engineering)

Faculty of Mechanical Engineering
Universiti Teknologi Malaysia

MAY 2013

To my beloved family,
The lover in you who brings my dreams comes true.

To my beloved wife, Junita Abdul Rahman and our kids, Zinniroh Lubna, Wafi Marina, Muhammad Yusuff Danish and Abdullah Rayyan. Thank you for the never ending support and encouragement. I could not have completed this effort without the invaluable tolerance and enthusiasm from each of you.

ACKNOWLEDGEMENT

"In the name of Allah that the most Gracious, the most Merciful"

Foremost, my greatest gratitude goes to ALLAH SWT for giving me the vigour, strength and spirit to make it possible to complete this thesis under the title of "*Three Dimensional Integrated Software Development for Air-Particle Flow Simulation through Image-Based Upper Human Airways*".

In particular, I wish to express my deepest appreciation to my supervisor, Assoc. Prof. Dr. Kahar Osman from Faculty of Mechanical Engineering, Universiti Teknologi Malaysia (UTM) for encouragement, guidance, advices and motivations. Without his continuous support and interest, this thesis would not have been here.

My appreciation above all goes to Brother Mohd Hazmil Syahidy, Nasrul Hadi, Wan Mohd Basri, Wan Anuar, Ubaidullah, Malik, Syukri, Ishkrizat, Edi, Syira and to all members of Computational Fluid Mechanics Laboratory, FKM, UTM for their consistent support and fruitful discussions and ideas. Finally, I owe an immense compulsion of gratitude to my families for their love and patience. To those who always stay beside me in worse and better times, thanks for your everything, guidance and support.

ABSTRACT

The effort to reconstruct and simulate flow-particle behavior in realistic patient-specific airway system requires multi-software skills. Conventionally, pre-processing, simulation and optimization and post-processing stages are carried out explicitly via a combination of commercial, open source and/or in-house engineering software. The tedious procedure had left more significant medical analysis such as flow pattern classification, patient group-based flow analysis and statistical flow studies at bay. In this work, the focus is on the development of a dedicated software that is capable of performing all the three stages for any patient-specific data set. A novel approach of combining the efficient Immersed Boundary method and Finite Difference Splitting solver within a matrix-based open source programming platform has radically simplified the procedure especially in the pre-processing stage. The air and particle interactions are based on Eulerian-Lagrangian technique with comprehensive validations for each stage of the solvers integration. A non-dimensional convergence error of less than 1×10^{-6} was consistently set for all the validations. An air flow rate of 30 litre / minute was used throughout the analyses representing the normal inhalation condition while a number of 10,000 and 5,000 micro particles were modeled for simplified and image-based airways respectively. The assessment analysis showed that 42.35% of the particles inhaled by female subject managed to reach the end of trachea while male subject with epiglottis blockage recorded only 0.43%. None of the inhaled particles managed to pass through the trachea of the oversized male subject. This work suggests that such pattern analyses are crucial to facilitate medical practitioners in their patient-specific diagnosis and decision making process of airway flow related diseases.

ABSTRAK

Kaedah lazim untuk membentuk semula dan melakukan simulasi realistik tingkah laku aliran zarah dalam sistem saluran pernafasan pesakit tertentu memerlukan kemahiran penggunaan pelbagai perisian. Peringkat pra-pemprosesan, simulasi dan pengoptimuman serta pasca pemprosesan lazimnya dijalankan melalui gabungan perisian kejuruteraan komersil, sumber terbuka dan/atau persendirian. Prosedur yang rumit ini menyebabkan analisis perubatan yang lebih penting seperti pengkelasan corak aliran, analisis aliran berasaskan kumpulan pesakit dan kajian statistik aliran terabai. Tumpuan kajian ini adalah kepada pembangunan perisian khusus yang mampu menyelesaikan kesemua tiga peringkat untuk sebarang set data pesakit tertentu. Satu pendekatan baru menggabungkan kaedah *Immersed Boundary* dan penyelesai *Finite Difference Splitting* dalam platform pengaturcaraan sumber terbuka berasaskan matriks telah mempermudahkan prosedur simulasi secara radikal. Interaksi udara dan zarah adalah berdasarkan keadah *Eulerian-Lagrangian* manakala semua proses pengesahan bagi setiap integrasi penyelesai dilakukan secara menyeluruh. Ralat ketepatan tanpa unit data ditetapkan kurang daripada 1×10^{-6} secara konsisten dalam semua pengesahan. Kadar aliran udara 30 liter/minit telah digunakan sepanjang analisis bagi mewakili keadaan penyedutan biasa manakala 10,000 dan 5,000 zarah mikro masing-masing digunakan bagi model dipermudahkan dan model berasaskan imej perubatan saluran pernafasan. Analisis penilaian menunjukkan bahawa 42.35% daripada zarah dihidu oleh subjek wanita berjaya sampai ke penghujung trakea manakala subjek lelaki dengan sekatan injap nafas mencatatkan hanya 0.43%. Tiada sebarang zarah yang dihidu berjaya melepasi trakea subjek lelaki bersaiz besar. Kajian ini membuktikan bahawa analisis corak aliran adalah penting untuk memudahkan diagnosis dan proses membuat keputusan untuk pesakit tertentu oleh pengamal perubatan apabila berhadapan dengan penyakit berkaitan aliran saluran pernafasan.

TABLE OF CONTENTS

CHAPTER	TITLE	PAGE
	DECLARATION	ii
	DEDICATION	iii
	ACKNOWLEDGEMENTS	iv
	ABSTRACT	v
	ABSTRAK	vi
	TABLE OF CONTENTS	vii
	LIST OF TABLES	x
	LIST OF FIGURES	xi
	LIST OF SYMBOLS	xvi
	LIST OF APPENDICES	xviii
1	**INTRODUCTION**	**1**
	1.1 Overview	1
	1.2 Background of the Problem	2
	1.3 Statement of the Problem	7
	1.4 Objectives	9
	1.5 Scopes of the Study	9
	1.6 Significance of the Study	11
	1.7 Expected Findings and Summary	11
	1.8 Organization of the Thesis	12
2	**LITERATURE REVIEW**	**14**
	2.1 Introduction	14

	2.2	Fluid-Particle Flow in Human Airway System	14
		2.2.1 Human Airway Anatomy	14
		2.2.2 Previous Works on Particle Deposition in Human Airway System	17
	2.3	In-House Air-Particle Flow Algorithm	19
		2.3.1 Three-Dimensional Image Segmentation	20
		2.3.2 Flow Solver	23
		2.3.3 Particle Solver	24
	2.4	Summary of Literature Review	26
3		**METHODOLOGY**	**28**
	3.1	Image Segmentation	28
	3.2	Flow Solver Formulation	32
		3.2.1 Pressure-Velocity Coupling Method	32
		3.2.2 Orthogonal Curvilinear Coordinate Formulation	36
	3.3	Particle Solver Formulation	37
	3.4	Numerical Discretization	39
		3.4.1 Eulerian-Lagrangian Hybrid Scheme	39
		3.4.2 Algorithm structure	42
	3.5	Algorithm validation	46
		3.5.1 Fluid solver validation	47
		3.5.1.1 Two-Dimensional Lid-Driven Cavity Flow	47
		3.5.1.2 Two-Dimensional Multi-Bifurcation Flow	48
		3.5.1.3 Three-Dimensional Immersed Lid-Driven Cube Cavity	51
		3.5.2 Internal Flow Validation	52
		3.5.3 Particle Solver Validation	54
		3.5.4 Fluid-Particle Solver Validation in Complex Geometry	55

4	**RESULTS AND DISCUSSION**	**58**
	4.1 Validation of Two-Dimensional Splitting Velocity-Pressure Coupling via Lid-Driven Cavity Flow	58
	4.2 Validation of Two-Dimensional Segmentation via Simplified Human Airway Multi-Bifurcation Flow	67
	4.3 Validation of Three-Dimensional Immersed Boundary via Lid-Driven Cube Cavity Flow	78
	4.4 Validation of Internal Flow Simulation via Backward-Facing Step Case Study	82
	4.5 Validation of Fluid-Particle Integrated Solver	88
	4.5.1 Two-Dimensional Particle Trajectories in Lid-Driven Cavity Flow	88
	4.5.2 Three-Dimensional Particle Trajectories in Lid-Driven Cube Cavity Flow	90
	4.5.3 Three-Dimensional Multi-Particle Distributions in Lid-Driven Cube Cavity	93
	4.6 Validation of Three-Dimensional Fluid-Particle Solver in Complex Geometry via Simplified Human Airway System	94
	4.7 Air Flow in Image-Based Three-Dimensional Human Upper Airway	101
	4.8 Air-Particle Flow in Image-Based Three-Dimensional Human Upper Airway	107
5	**CONCLUSION AND RECOMMENDATIONS**	**115**
	5.1 Conclusion	115
	5.2 Recommendations	118
	5.2.1 Value Added Expansions	118
	5.2.2 Value Added Improvements	119
REFERENCES		**121**
Appendices A - B		127 - 143

LIST OF TABLES

TABLE NO.	TITLE	PAGE
1.1	Functionality matrix of most common currently available commercial software for image-based air-particle flow analysis in human upper airway system	7
3.1	Characteristics of fifth to seventh generation airway	50

LIST OF FIGURES

FIGURE NO	TITLE	PAGE
1.1	Multi-software usage in conventional patient-specific flow simulation versus fully integrated in-house software developed in this work	5
2.1	Morphological overview of the human respiratory tract	17
3.1	Three-dimensional reconstructed image-based model from medical image data set	30
3.2	A single slice of array segmentation for null nodes (0), fluid nodes (1) and wall nodes (2-7)	32
3.3	Particle displacement in fluid flow region for three time steps	41
3.4	Integrated Algorithm flowchart.	43
3.5	Geometry of the flow domain	49
3.6	Backward-facing step construction based on model by (Armaly et al., 1983)	53
3.7	Visual representation on reattachment length measurement	54
3.8	Three-dimensional reconstruction of simplified human upper airway by (Cheng et al., 1999)	56
4.1	Square geometry of two-dimensional lid-driven cavity	59
4.2	Vertical (left) and horizontal (right) velocity for Reynolds number = 100 (Grid point = 17)	61
4.3	Vertical (left) and horizontal (right) velocity for Reynolds number = 1000 (Grid point = 17)	63
4.4	Vertical (top) and horizontal (bottom) velocity for	

	Reynolds number = 100 (Grid point = 65 for splitting and 17 for spectral)	65
4.5	Vertical (top) and horizontal (bottom) velocity for Reynolds number = 1000 (Grid point = 65 for splitting and 17 for spectral)	66
4.6	Comparison on Computing Time to reach steady state condition using different Reynolds number for various numerical splitting methods approaches	67
4.7	Macro views of flow velocities and streamlines from G5 to G7.	69
4.8	Stream slices for Reynolds number ranging from 75 to 350	71
4.9	Different cross-section locations for Axial velocity profile; (a) AA’ (G5), (b) BB’ (G6), (c) CC’ (G7, medial), and (d) DD’ (G7, lateral)	73
4.10	Axial velocity profile at different cross section locations; (a) AA’ (G5), (b) BB’ (G6), (c) CC’ (G7, medial), and (d) DD’ (G7, lateral)	74
4.11	Pressure distribution (normalized) at first bifurcation for all breathing cases	76
4.12	Pressure difference between section CC’ and DD’ for various Reynolds Number	77
4.13	Transient isosurface of 0.13 velocity for lid-driven cube cavity flow with Reynolds number 100	79
4.14	Steady state 0.13 velocity isosurface for Reynolds number 100 between (Zunic et al., 2006) (left and current result (right)	80
4.15	Steady state center lines velocity comparison for Reynolds number 100 between current work, benchmark and previous validation works	81
4.16	Velocity contours obtained using reputable time-independent (top) and current time -dependent (bottom) solvers	84

4.17	Streamwise velocity profiles at location X/S = 5	85
4.18	Streamwise velocity profiles at location X/S = 10	85
4.19	Streamwise velocity profiles at location X/S = 15	86
4.20	Streamwise velocity profiles at location X/S = 20	86
4.21	Streamwise velocity profiles at location X/S = 25	87
4.22	Visual representation on reattachment length measurement	87
4.23	Reattachment length measured between two X-velocity cross sections at ‘0’	88
4.24	Trajectory of one particle in the driven cavity. Comparison of numerical simulation (a) (Kosinski et al., 2009) Solver and (b) Experimental result (from (Kosinski et al., 2009), Fig. 12). (c) Current Solver with experimental parameter (d) Current Solver with particle diameter 0.09 of overall cavity width.	90
4.25	Qualitative comparison between current three-dimensional simulation results (Right) with experimental data (Left) by (Tsorng et al., 2006), (Left figures from (Tsorng et al., 2006) Fig. 11.)	92
4.26	Sand-like particles underneath a reservoir for Re = 470	95
4.27	Transient Velocity contours and particle distributions for Simplified upper human airway system	98
4.28	Velocity contour comparison between (Zhang et al., 2002) at left and current work at right for flow rate equivalent to 30 l/min	100
4.29	Particle deposition comparison between (Zhang et al., 2002) at left and current work at right for flow rate equivalent to 30 l/min and Stokes number 0.08	101
4.30	Three-dimensional upper airway reconstructed images of female, male and oversized male	102
4.31	Center slice velocity contour of image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.2	103

4.32	Center slice velocity contour of image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.4	104
4.33	Center slice velocity contour of image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.6	105
4.34	Center slice velocity contour of image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.8	105
4.35	Center slice velocity contour of image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 1.0	106
4.36	Center slice velocity contour of image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 1.2	106
4.37	Inhaled particle distributions for image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.2	109
4.38	Inhaled particle distributions for image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.4	110
4.39	Inhaled particle distributions for image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.6	111
4.40	Inhaled particle distributions for image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 0.8	112
4.41	Inhaled particle distributions for image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 1.0	113

4.42 Inhaled particle distributions for image-based three-dimensional upper airway of female (left), male (center) and oversized male (right) at time = 1.2 114

LIST OF SYMBOLS

h	-	Grid size
H	-	Non-dimensional height
i	-	Spatial increment in x direction
j	-	Spatial increment in y direction
k	-	Spatial increment in z direction
L	-	Non-dimensional Length
n	-	Current time increment
N	-	Non-linear term in N-S equation
p	-	Non-dimensional pressure
q	-	Iteration index
R_e	-	Reynolds Number
t	-	Non-dimensional time
u	-	X direction velocity
U	-	Reference velocity
v	-	Y direction velocity
w	-	Z direction velocity
x	-	Left to right direction
y	-	Back to front direction
z	-	Bottom to top direction
α	-	Clustering location
β	-	Clustering parameter
λ	-	Height to Length ratio
ρ	-	Non-dimensional density
μ	-	Non-dimensional viscosity

ROI	-	Region of Interest
CGI	-	Critical Gray Intensity,

LIST OF APPENDICES

APPENDIX	TITLE	PAGE
A	Information from associated DICOM images	127
B	List of publications	140

CHAPTER 1

INTRODUCTION

1.1 Overview

The involvement of engineering practices in medical technology has grown substantially over the years due to the advancement in computing power. However, the implementation of Computational Fluid Dynamics, CFD is still considered as a new premature tool for medical practitioners. As non-expert users of CFD tools, a fully integrated CFD software that capable of utilizing raw medical image data up to the visualization of air-particle distribution throughout human airway system is far beyond their reach. Being an establish simulation tool, this great fluid engineering tool happens to be too complicated for medical diagnosis purposes that often deal with specific patient conditions, complex flow boundaries and most importantly the time constrain for the diagnosis procedure. The complexity is even greater when it comes to air-particle distributions within the upper human respiratory system where large computational domain and time dependency are involved. With almost all commercial and non-commercial CFD pre-processing, flow solver and post-processing softwares are intended for engineering applications, it is really a novel challenge to develop a full-blown CFD algorithm which is capable of accurately converting medical 3D image data into numerical flow domain, simulating the time-dependent air-particle flow distributions within the airway system and present the results in a way that medical practitioners could really appreciate.

1.2 Background of the problem

Non-invasive peroral procedure is one of the most common routes of drug administration especially when it comes to respiratory diseases such as Asthma and Chronic Obstructive Pulmonary Disease, COPD. Inhalers or puffers are extensively used to transmit aerosol or powdered drug particles through oral inhalation. With increasing numbers of inhaler types and aerosol particle sizes, there are no practically available *in vivo* or *in vitro* procedures to determine the effectiveness and most appropriate type of inhaler for each patient with unique airway size and shape. Questions on how much the inhaled drug particles actually reach the targeted sections and how the patient should inhale for better effectiveness are always ambiguous for medical practitioners. The common practice of prescribing suitable treatment is only based on the medical practitioners' experience with generalized solutions for most of the cases.

Although there are few high-end diagnosis tools such 4D Magnetic Resonance Image and Ventilation-Perfusion Scan, time dependent in vivo analysis of air-particle flow distribution within human upper airway is still practically impossible with present technologies. While in vivo human airway flow pattern is way out of topic, few in vitro, experimental setups of human airway models were established with the aim of analyzing the actual flow pattern throughout the upper airway system. Although the efforts are noble and proven to be capable of simulating the actual flow phenomena, the experimental setups are excessively complicated and acquires handsome amount of time to generate multiple image-based reconstructed model analyses.

Moreover, Medical practitioners are now well aware of the physical differences of human airways between genders, age groups and medical conditions. Instead of running the experimental setup for each type of airway profile uniqueness, numbers of commercial software developers have expanded their effort to introduce CFD into biomechanics applications. The efforts however are more universal towards converting medical image data into three-dimensional model and utilizing common engineering tools. In most CFD commercial software, three-dimensional models are often required to be in tetrahedral mesh, triangular surfaces or other specific mesh generated formats. Unfortunately, mesh generation functionality is not offered in most image segmentation software. Such advantage is currently found in AMIRA (Mercury Systems, MA, USA), Simpleware (Simpleware Ltd., UK) and MIMICS (Materialise, NJ, USA) which are capable of converting medical image data into reconstructed model format that can be transported into other commercial software such as ADINA (ADINA R&D, Inc., USA), ABAQUS (Dassault Systèmes, FR.), ANSYS (ANSYS, Inc., USA), cfd++ (Metacomp Technologies, Inc., USA) COMSOL (COMCOL, Inc., USA) and LS-DYNA (LSTC, USA) for various engineering purposes.

In academic field, quite a number of CFD researchers had offered their expertise in analyzing flow behaviors in human respiratory system via sets of commercial software. With majority of the works were done in all three different pre-processing, flow solver and post-processing phases, weeks or even months were needed to establish all the objectives for any single medical data image. Literature review shows that the reconstructed 3D model from a medical image data sets were established using commercial pre-processing software such as MIMICS, Simpleware and AMIRA. Fluid-particle flow analyses were then launched using few other commercial CFD software such as ADINA, ABAQUA, ANSYS and LS-DYNA before the employment of another commercial post-processing software such as AMIRA, MatLab or Tecplot to visualize and analyze the resulting data. Obviously, these previous works were expensive in terms financial, time and efforts.

One of the most recent researches on the same interest of simulating flow behavior on patient-specific intranasal cavity was the award winning research by Gengenbach at al., (2011) at Karlsruhe Institute of Technology, Germany. Being an outstanding and one of the most modern computational research centers, this effort however was still utilizing commercial pre-processing MIMIC software and ParaView open source visualization software as necessary complement of their own in-house flow solver. The schematic diagram of the simulation procedure constructed by the research team is compared head-to-head with the current integrated procedure in Figure 1.1. This figure clearly illustrates the novelty of the current effort relative to the conventional procedures that is still widely utilized at present. This current developed software is not only more economic being an entirely open source software but also higher in efficacy as it does not require any data conversion between processes.

Apart from the use of commercial CFD software, algorithm development is also considered as another unpopular CFD procedure which is utilized for specific purposes including human airway flow analysis. The complexity of the works involved however had left only few CFD researchers courageously pulling their efforts to introduce dedicated CFD algorithm for human airway flow analysis. The tediousness of algorithm development had also limited the previous studies to concentrate only on the medical image-based meshing algorithms, air / air-particle flow analysis or the post-processing of collected flow data.

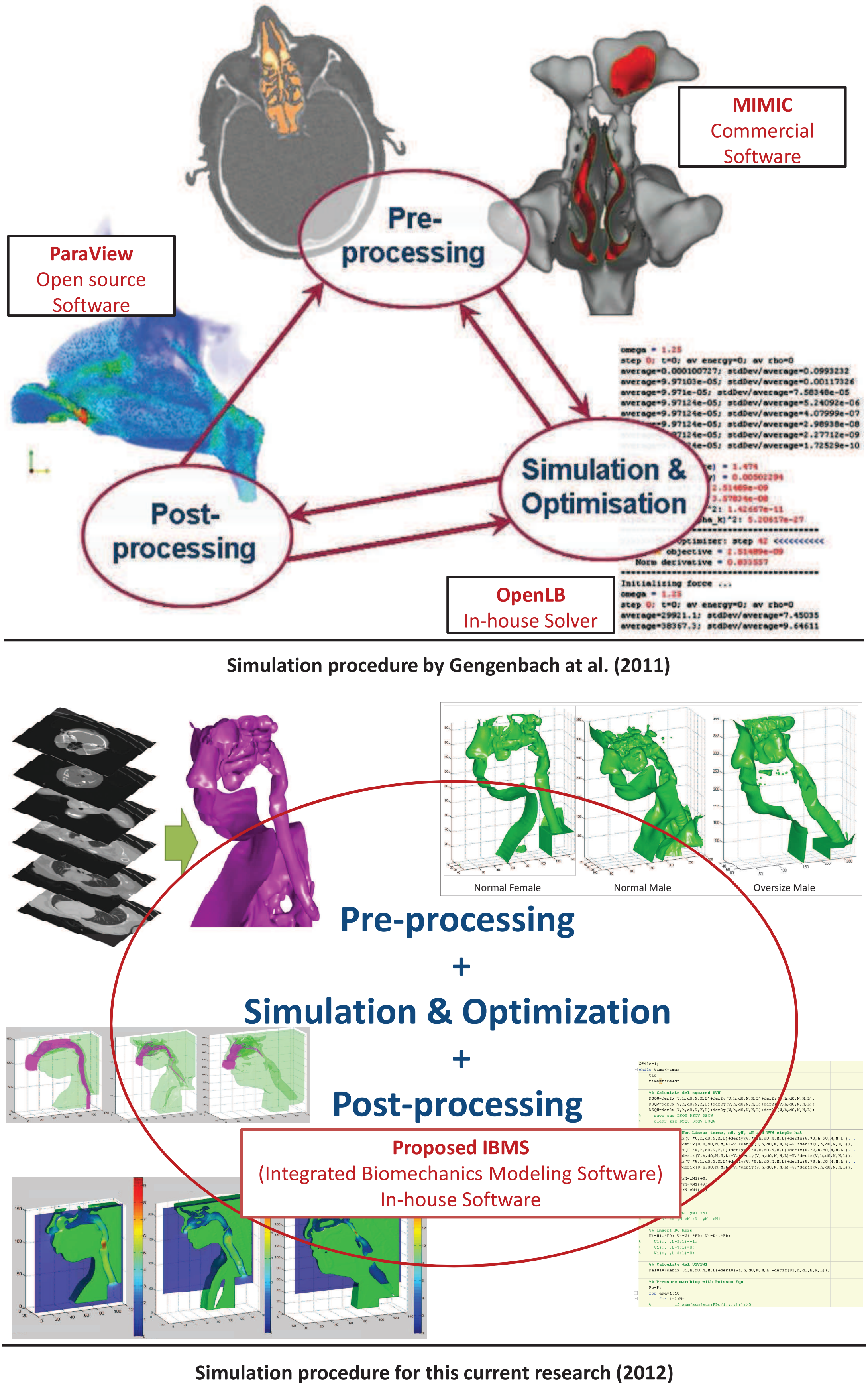

Figure 1.1 Multi-software usage in conventional patient-specific flow simulation versus fully integrated in-house software developed in this work.

The focal uniqueness of the present effort is that there is no exertion as far as the current work progresses has integrated the capability of reconstructing medical image into 3D model, introducing the air and particle throughout the air passage and time dependently visualizing the results for flow pattern analysis. Table 1.1 illustrates the broad figure of current scenario for air-particle flow analysis in image-based human upper airway system. The distribution shows that none of the existing commercial software is truly intended for specific application of image-based human airway flow analysis whereby all simulation phases are taken into account. With the aim of having algorithm architecture that suit well with all three simulation phases, the other challenges are to make sure that the algorithm is practical enough to be used in a daily basis by non-CFD experts and without consuming too much time for patient-specific model optimizations and results crunching.

The main motivation of the current work is the advancement of computing capability which enables us to explore more efficient and accurate CFD solver integrations. There are great numbers of CFD methods and solvers introduced by researchers even before the evolution of computational power but the developments were stranded due to the computing constrains of that era. The conflict had left researchers resorted into the use of accuracy-compromised flow solvers and widely used until now. The current computing power however has allowed us to reevaluate and reshuffle the ideas of having an all-in-one application with better accuracy and efficiency. Air-particle solver for instance was considered as a highly computational-consuming multi-phase flow solver.

Although the idea of multiphase flow was introduced back in 1970's, the implementation is only feasible in the past few years since the multiphase computational consumptions are considerably enormous. At present, there are only few relatively expensive commercial CFD software that capable of simulating both fluid and particle distributions with respect to time and these software are not specifically intended for biomechanics applications.

Table 1.1: Functionality matrix of most common currently available commercial software for image-based air-particle flow analysis in human upper airway system

Software		MicroDicom	Osirix	RadiAnt	MIMIC	Simpleware	AMIRA	ADINA	ABAQUS	LS-DYNA	ANSYS CFX	COMSOL	cfd++	Current Work
Phase	Features													
Pre-processing	3D Image data conversion	/	/	/	/	/	/	X	X	X	X	X	X	/
	3D Image segmentation	/	/	/	/	/	/	X	X	X	X	X	X	/
	3D Image-based Grid generation	X	X	X	/	/	/	X	X	X	X	X	X	/
CFD solver	3D Fluid solver	X	X	X	X	X	X	/	/	/	/	/	/	/
	3D Particle solver	X	X	X	X	X	X	X	X	X	/	/	/	/
Post-processing	3D Volume visualization	X	X	X	X	X	X	/	/	/	/	/	/	/
	Temporal visualization	X	X	X	X	X	X	/	/	/	/	/	/	/

1.3 Statement of the problem

The focal dilemma which has driven the exertion of this work is the need of having an all-in-one CFD algorithm for medical practitioners during the diagnosis of upper human respiratory diseases. As the question of how far the drug being delivered during non-invasive peroral procedure is still unanswered, the accuracy of any prescribed treatment is still uncertain. The ability to assess the air flow behavior during inhalation of any individual patient and the possibility to simulate the particle distribution of different types of inhalers are believed to be beneficial for the diagnosis of related respiratory diseases. Another notable issue in medical practice is the effectiveness of surgeries involving the respiratory system. Nasal surgery for instance is mainly to improve airflow but the exclusion must be kept nominal to minimize the side effects such as nasal drainage, septal perforation, numbness of facial structures or even alteration of smell and taste senses. A clear-cut post-surgery flow simulation to optimize the surgical outcome is expected to come in handy.

On the CFD side, the most common way to-date for biomechanics application is by the use of traditional commercial engineering CFD software which is tedious and impractical. As the diagnosis of respiratory diseases are way more critical and urgent than a malfunctioning vehicle, an efficient, specific single algorithm which is proficient of manipulating medical image data up to the air-particle analysis is simply a must. The option to alter the airway geometry is a bonus especially for post-surgical simulations.

In order to develop a full-blown algorithm, proper planning on how the three simulation phases should be integrated must be given priority. Since the accuracy of the simulation is a life-threatening issue, algorithm validation must be carried out in the best of interest. The algorithm consists of flow solver and particle solver which act as internal flow within an immersed boundary. Five phases of validations are underlined to make sure that the solver integrations are irrefutable. The first validation is on the fluid flow solver which is the most critical part of the simulation. The second is the validation of fluid flow solver within an immersed boundary. The third is the validation of particle trajectory deep in the fluid flow within an immersed boundary. The final validation is on the fluid-particle flow in immersed complex geometry equivalent to the actual medical image-based upper human airway model.

Once the algorithm is fully validated, the final hurdle is to assure the feasibility of the developed algorithm. Actual medical image data need to be applied and a trial analysis is to be selected. With respect to the available sets of medical CT scan image data, courtesy of Department of Radiology, Hospital Universiti Sains Malaysia, Kubang Kerian, analyses of flow patterns and particle distributions in upper airway passages of a male adult, a female adult and an obese patient are chosen. A good amount of image data set is not an option since all contributed data is not intentionally taken on patients with respiratory diseases.

.

1.4 Objectives

Based on the problem statements brought up in previous section, the objectives of this research are:

i. To develop an algorithm which is capable of reconstructing upper airway passage from medical image data, introducing air and particle distributions throughout the passage and visualize the results as a supplementary tool for the diagnosis of respiratory diseases.
ii. To optimize the developed algorithm as a single, efficient and easy-to-use tools for medical practitioners both for diagnosis and post-surgery simulation.
iii. To fully validate the developed algorithm with fluid phase, immersed-fluid phase, immersed-fluid-particle phase and immersed-fluid-particle in complex boundary phase validations.
iv. To demonstrate the flow patterns and particle distributions in different upper airway passage geometrical conditions of male, female and oversized patients.

1.5 Scopes of the study

Simulation of particle inhalation is a vast field of study. A thorough development of such algorithm requires a life-long effort from not only a single expert. This study is expected to be a wide but elementary platform for further development of more complete, multi-optional software that suit the needs of more CFD, biomechanics applications. The scope of this study is based on the time constrain and the current computing power accessible to the most of the intended target group. List of the scopes are as follows.

i. The developed code is expected to produce 4 dimensional simulations with x, y and z directions plus the variations with time. The coordinate system chosen is arguably the most efficient, Cartesian coordinate system. The selection is also based on the fact that the structure of medical image data and finite difference flow solver are fully matched and require zero conversion algorithm that may lead to initial conversion errors.
ii. Eulerian Incompressible finite difference Navier-Stokes fluid flow solver is selected for this work. The fluid flow solver is chosen correspond to the original structure medical image data to assure the efficiency of post-processing algorithm.
iii. The particle solver is based on the Lagrangian solid sphere particle equation of motion. As the corresponding particles under considerations are relatively small while a single calculation is adequate to represent a cloud of imaginary particles, solid sphere particle equation of motion is expected to serve the requirements comparable to more complex particle solvers.
iv. As the implicated particles are relatively small and almost conform to the fluid flow, one-way-coupling between fluid flow and particle flow is opted for. The particle flow in this manner is directly a function of collocated fluid flow but has negligible effect on the fluid behavior.
v. The selection of programming platform is also based on the nature of all related materials. A matrix based programming platform is believed to be the most fitting with finite difference solver and orthogonal nature of most medical image data structure.
vi. Code validations are expected to be comparable with benchmark experimental and numerical data which is carefully selected from reputable scientific articles and procedures.
vii. Algorithm feasibility verification is based on the capability of the developed algorithm to exploit several patient-specific medical image data for flow pattern and particle distribution analysis.

1.6 Significance of the study

A successful development of a full-blown algorithm with the capabilities of 3-dimensional reconstruction model based on medical image data, simulation of air-particles distributions and visualization of the resulting time dependent flow patterns will definitely benefit not only medical practitioners in diagnosis of patients with respiratory diseases but also to biomechanics researchers in their related studies. The developed algorithm is expected to offer more than the traditional tedious CFD engineering procedures which normally only practical for analysis of any single medical image data set. The simplicity, feasibility and efficiency of the developed algorithm will open the possibilities of further analyses of flow patterns and particle distributions of various patient categories, derivations of related coefficients for multi-conditional flow distribution, predictions of surgical practices on flow patterns and many other air-particle distribution related analysis.

1.7 Expected findings and summary

The possible outcomes of the research project are:-

i. A fully developed algorithm with capabilities of medical image based reconstruction of upper airway passage model, introduction of air and particle distributions throughout the passage and visualization of results as a supplementary tool for research analysis anddiagnosis of respiratory diseases.
ii. An optimized algorithm as all-in-one, efficient and easy-to-use tools for medical practitioners both for diagnosis and post-surgery simulation.
iii. Comparable validation results for fluid phase, immersed-fluid phase, immersed-fluid-particle phase and immersed-fluid-particle in complex boundary phase with benchmark results of two-dimensional lid-driven cavity flow, two-dimensional symmetric bifurcation flow, lid-driven cube cavity fluid flows, particle

trajectories in immersed lid-driven cube cavity fluid flows, internal flows through backward facing step channel and air-particle distributions through simplified model of human upper respiratory system respectively.

iv. Variations and comparisons of flow patterns and particle distributions in upper airway passages of a male adult, a female adult and an obese patient.

1.8 Organization of the thesis

This thesis is organized with the aim of conveying the idea of an all-in-one algorithm for air-particle distribution throughout the image based human airway system. The first two chapters discuss the problem statements from the medical practitioners' point of view, the previous works done on the matters and the objectives of the current effort. The third chapter discusses on how the work is carried out while the fourth chapter resembles the results obtained throughout the research period. The final chapter concludes the outcomes of the research with a list of suggested further works.

Chapter 1 initiates with the explanation of the current measure of CFD involvement in the study of air-particle flow in human airway system. The current work is then justified by comparing the issues raised by medical practitioners with what were offered by previous works. As the need of having a single algorithm that capable of simulating air-particle flow in multi-patient sets of medical image data is found to be the prime upshot of this work, the objectives, scopes of study, significance of study and expected outcomes of the study are thoroughly prearranged.

Chapter 2 contains the justifications of scopes of study, selected numerical methods, validation criteria and simulation setups. These rationalizations are based on literature reviews on related previous works. Major references are clarified in more details to give a clearer view on what is expected from the current effort.

Chapter 3 describes the methodology of this research. The first section describes the code structure for the segmentation process. Once the process of converting the medical image data into the form most suitable for matrix manipulation, the second section will take place with the flow solver development is explained. The third section is meant for the particle solver formulation while the fourth section explains discretization issues. Section five describes the validation methods employed in this work while the sixth section discusses on the simulation setups for trial analysis. The final section is reserved for the post-processing methodology.

Chapter 4 exemplifies the simulation results from the procedures explained in chapter 3. Discussions on all validation case studies are first constructed before the view on the trial case study takes place. The validation analyses consist of experimental and simulation results comparisons.

Chapter 5 concludes the whole achievement of this novel masterpiece. The fulfillment of the outlined objectives are justified with results and analyses customized in chapter 4. Long list of suggestions for further studies implies that there are plenty of rooms for improvement for this work with focus on the solvers improvements and alternatives for existing features.

REFERENCES

Armaly, B. F., Durst, F., Pereira, J. C. F., Schonung, B. (1983). Experimental and theoretical investigation of backward-facing step flow. *J. Fluid Mech.* vol. 127: pp. 473-496.

Asgharian, B., Hofmann, W., and Bergmann, R. (2001). Particle deposition in a multiple-path model of the human lung. *Aerosol Sci. Technol*. 34, pp. 332-339.

Balásházy, I., Hofmann, W. (1993). *J. Aerosol Science*, 24: pp. 745-772.

Balásházy, I., Hofmann, W., Heistracher, T. (1999). *J. Aerosol Sci.* 30, 2: pp. 185-203.

Barragy, E., Carey, G. F. (1997). Stream Function-Vorticity Driven Cavity Solutions Using pFinite Elements. *Computers and Fluids*. 26: pp. 453-468.

Blacker, T. (2001). Automated conformal hexahedral meshing constraints, challenges and opportunities. *Eng. Comput*. 17: pp. 201–210.

Broday D. M. (2004). Deposition of ultrafine particles and gaseous pollutants at carinal ridges of the upper bronchial airways. *Aerosol Sci. Technol*., 38: pp. 991-1000.

Calay, R.K., Kurujareon, J., Holdo, A.E. (2002). Numerical simulation of respiratory flow patterns within human lung. *Respiratory Physio. Neurobiology.* 130: pp. 201-221.

Canuto, C., Hussaini, M.Y., Quarteroni, A., Zang, T.A. (1988). Spectral Method in Fluid Dynamics. *Springer-Verlag.*

Chen, Y. K., and Yu, C. P. (1993). Particle deposition from duct flows by combined mechanism. *Aero. Sci. Tech*. 19, 389–395.

Cheng, Y. S., Zhou, Y., Chen, B. T. (1999). Particle deposition in a cast of human oral airways. *Aerosol Science and Technology.* 31: pp. 286–300.

Choi, S. K., Nam, H. Y., Lee, Y. B., Cho, M. (1993). An Efficient Three-Dimensional Calculation Procedure for Incompressible Flow in Complex Geometries. Numerical Heat Transfer, Part B. 23: pp. 387-400.

Comer, J. K., Kleinstreuer, C., Kim, C. S. (2001). Flow structures and particle deposition patterns in double-bifurcation airway models. Part 2. Aerosol transport and deposition. *Journal of Fluid Mechanics* 01/2001; 435.

Courant, R., Isaacson, E., Rees, M. (1952). On the solution of non-linear hyperbolic differential equations by finite difference. *Commun. Pure Appl. Math*. 5: pp. 243–255.

Dunbar, C. A., Hickey, A. J. (2000). Evaluation of probability density functions to approximate particle size distributions of representative pharmaceutical aerosols. *J. Aerosol Sci*. 3: pp. 813–831.

Dunbar, C., Concessio, N., Hickey, A. J. (1998). Evaluation of atomizer performance in production of respirable spray-dried particles. *Pharm. Dev. Tech.* 3: pp. 433–441.

Gengenbach, T., Heuveline, V., Krause, M. J., Mayer R., Zimny S., (2011). A Preprocessing Approach for Innovative Patient-specific Intranasal Flow Simulations. *Preprint Series of the Engineering Mathematics and Computing Lab (EMCL),* ISSN 2191–0693, No. 2011-07.

Ghia, U., Ghia, K.N., Shin, C.Y. (1982). High-Re solutions for Incompressible Flow using the Navier-Stokes Equations and a Multigrid Method, *J. Comp. Phys*. 48: pp. 387-411.

Gong, Y., Tanner, F. X. (2009). Comparison of RANS and LES Models in the Laminar Limit for a Flow Over a Backward-Facing Step Using OpenFOAM. *Nineteenth International Multidimensional Engine Modeling Meeting at the SAE Congress.*

He, C., Ahmadi, G. (1999). Particle Deposition in a Nearly Developed Turbulent Duct Flow with Electrophoresis. *J. Aerosol Science*. Vol. 30: pp. 739-758.

Hidy, G. M. (1984). Aerosols, An Indusrrial and Environmental Science. *Academic Press*. New York.

Hinds, W. C. (1982). Aerosol Technology: Properties, Behavior and Mensurement of Airborne Porricles. *John Wiley & Sons*. New York.

Hofmann, W., Golser, R., Balashazy, I. (2003). Inspiratory deposition efficiency of ultrafine particles in a human airway bifurcation model. *Aerosol Science and Technology*. 37: pp. 988-994.

Iaccarino, G., Kalitzin, G., Khalighi, B. (2003). Towards an Immersed Boundary RANS Flow Solver. *AIAA.* pp. 0770

Jin, H. H., Fan, J. R., Zeng, M. J., Cen, K. F. (2007). Large Eddy Simulation of Inhaled Particle Deposition within the Human Upper Respiratory Tract. *Journal of Aerosol Science.* 19: pp.157-168.

Karniadakis, G. E., Israeli, M., Orszag, S. A. (1991). *J. Comput. Phys.* 97: pp. 414–443.

Katz, I. M. & Martonen, T. B. (1996). T. B. flow patterns in three-dimensional laryngeal models. *Journal of Aerosol Medicine*. 9: pp. 501-511.

Keyak, J.H., Meagher, J.M., Skinner, H.B., Mote Jr., C.D. (1990). Automated three dimensional finite element modelling of bone: a new method. *J. Biomed. Eng.* 12: pp. 389–397.

Kim, S., Jaques, P. A., Chang, M. C., Froines, J. R., Sioutas, C. (2001). Versatile aerosol concentration enrichment system (VACES) for simultaneous in vivo and in vitro evaluation of toxic effects of ultrafine, fine and coarse ambient particles Part I: Development and laboratory characterization. *J Aerosol Sci.*, 32: pp. 1281–1297

Kosinski, P., Kosinska, A., Hoffmann, A.C. (2009). Simulation of solid particles behaviour in a driven cavity flow. *Powder Technology journal*. 191: pp. 327–339.

Li, A., Ahmadi, G. (1992). Dispersion and Deposition of Spherical Particles from Point Sources in a Turbulent Channel Flow. *Aerosol Science Technology*. Vol. 16: pp. 209-226.

Li, A., Ahmadi, G. (1995). Computer simulation of particle deposition in upper tracheobronchial tree. *Aerosol Science and Technology.* 23: pp. 201-223

Li, C.W., Wang, L.L. (2004). An immersed boundary finite difference method for LES of flow around bluff shapes. *Int. J. Numer. Methods Fluids*. 4685–107.

Li, Q. T., Cheng, T., Tsang, T. T. H. (1995). Transient solutions for three-dimensional lid driven cavity fows by a least-squares finite element method. *Int. J. Numer. Math. Fluids.* 21: pp. 413-432.

Liao, S. J., Zhu, J. M. (1996). A Short Note on Higher-Order Streamfunction-Vorticity Formulation of 2-D Steady State Navier-Stokes Equations. *Int. J. Numer. Methods Fluids*. 22: pp. 1:9.

Lorensen, W., Cline, H. (2000). Marching cubes: a high resolution 3D surface construction algorithm. *Computer Graphics.* 21(4): pp. 163–9.

Martonen, T.B., Zhang, Z., (1993). Deposition of sulfate acid aerosols in the developing human lung. *Inhal. Toxicol*. 5: pp.165-187.

McLaughlin, J.B. (1989). Aerosol Particle Deposition in Numerically Simulated Channel Flow. *Phys. Fluids A.* Vol. 7: pp. 1211-1224.

Müller, R., Rüegsegger, P. (1994). Morphological validation of the 3D structure of non-invasive bone biopsies. *10th Int. Workshop on Bone Densitometry. Bone Miner*. 25: pp. 8.

Nowak, N., Kakade, P. P., Annapragada, A. V. (2003). Computational fluid dynamics simulation of airflow and aerosol deposition in human lungs. *Annals of Biomedical Engineering*. 31: pp. 374-390.

Oldham, M. J., Phalen, R. F., and Heistracher, T. (2000). Computational Fluid Dynamics Predictions and Experimental Results for Particle Deposition in an Airway Model. *Aerosol Sci. Technol*. 32: pp. 61–71.

Ounis, H., Ahmadi, G. (1990). Analysis of Dispersion of Small Spherical Particles in a Random Velocity Field. *ASME J. Fluid Eng*. Vol.112: pp. 114-120.

Ounis, H., Ahmadi, G., McLaughlin, J.B. (1993). Brownian Particle Deposition in a Directly Simulated Turbulent Channel Flow. *Phys. Fluids A*, Vol. 5: pp. 1427-1432.

Papavergos, P. G., Hedley, A. B. (1984). Particle Deposition Behavior from Turbulent Flow. *Chem. Eng. Des*. 62: pp. 275-295.

Patankar, N.A., Joseph, D.D. (2001). Modeling and numerical simulation of particulate flows by the Eulerian-Lagrangian approach. *International Journal of Multiphase Flow*. 27 (10): pp. 1659-1684

Peng, Z., Asaro, R.J., Zhu, Q. (2010). Multiscale simulation of erythrocyte membrane. *Phys. Rev. E.* 81: 031904.

Tsorng, S. J., Capart, H., Lai, J. S., Young, D. L. (2006). Three-dimensional tracking of the long time trajectories of suspended particles in a lid-driven cavity flow. *Experiments in Fluids*. 40: pp. 314–328

Satpathi, D. K., Kumar, B. V. R., Chandra, P., (2003). Unsteady-State Laminar Flow of Viscoelastic Gel and Air in a Channel: Application to Mucus Transport in a Cough Machine Simulating Trachea. *Mathematical and Computer Modelling*. 38: pp. 63-75.

Sheu, T.W.H., Wang, S.K., Tsai, S.F. (2002). Finite element analysis of particle motion in steady inspiratory airflow. *Comput. Methods Appl. Mech. Engrg.* 191: pp. 2681-2698.

Smith, S., Cheng, Y. S., Yeh, H. C. (2001). Deposition of Ultrafine Particles in Human Tracheobronchial Airways of Adults and Children. *Aerosol Science and Technology.* Vol. 35, Iss. 3.

Taubin, G. (2000). Geometric signal processing on polygonal meshes, State of the Art Report (STAR), *Eurographics*.

Tawhai, M., Hunter, P., Tschirren, J., Reinhardt, J., McLennan, G., Hoffman, E. (2004). CT-based geometry analysis and finite element models of the human and ovine bronchial tree. *Journal of Applied Physiology.* 97(6): pp. 2310-2321.

Viceconti, M., Zannoni, C., Pierotti, L. (1998). TRI2SOLID: an application of reverse engineering methods to the creation of CAD models of bone segments. *Comput. Methods Programs Biomed*. 56: pp. 211–220.

Wang, Q., Squires, K.D., Chen, M., McLaughlin, J.B. (1994). On the Role of the Lift Force in Turbulence Simulations of Particle Deposition. *Int. J. Multiphase Flow*. Vol. 23: pp. 749-763.

Wang, S., Passias,P., Li,G.,et al. (2008). Measurement of vertebral kinematics using noninvasive image matching method-validation and application. Spine33: E355–E361.

Wilquem, F., Degrez, G., (1997). Numerical modelling of steady inspiratory airflow through a three-generation model of the human central airways. *J. Biomech. Eng*. 119 59–65.

Wood, N. B. (1981). The Mass Transfer of Particles and Acid Vapour to Cooled Surfaces. *J. Institute of Energy*. 76: pp. 76-93.

Wright, N. G., Gaskell, P. H. (1995). An Efficient Multigrid Approach to Solving Highly Recirculating Flows. *Computers and Fluids*. 24: pp. 63-79.

Yang, J. Y., Yang, S. C., Chen, Y. N., Hsu, C. A. (1998). Implicit weighted ENO schemes for the three-dimensional incompressible Navier-Stokes equations. *Journal of Computational Physics.* 146: pp. 464{487.

Zhang, Z., Finlay,W. H. (2005). Experimental measurements of particle deposition in three proximal lung bifurcations models with an idealized mouth-throat. *J. Aerosol Med.*18: pp. 460–475.

Zhang, Z., Kleinstreuer, C., (2001). Effect of particle inlet distributions on deposition in a triple bifurcation lung airway model. *Journal of Aerosol Medicine*. Vol. 14(1): pp. 13-29.

Zhang, Z., Kleinstreuer, C., Kim, C.S., (2001). Flow structure and particle transport in a triple bifurcation airway. *ASME Journal of Fluids Engineering.* Vol.123: pp. 320-330.

Zhang, Z., Kleinstreuer, C., (2002). Transient airflow structures and particle transport in a sequentially branching airway model. *Phys. Fluids*. 14: pp. 862–880,.

Zhang, Z., Kleinstreuer, C., Kim, C. S. (2002). Micro-particle transport and deposition in a human oral airway model. *Aerosol Science*. 33: pp. 1635–1652.

Zhang, Z., Kleinstreuer, C., (2004). Computational Analysis of Two-Phase Air-Particle Flow in a Human Airway Model. *5th International Conference on Multiphase Flow, ICMF'04*.

Zunic, Z., Matjaz, H., Leopold, S., Jure, R. (2006). *European Conference on Computational Fluid Dynamics.*