

Final Technical Report

Date of Final Report: August 1, 2006

EPA Grant Number: R827351C002

Center Name: NYU-EPA PM Center: Health Risks of PM Components

Center Director: Morton Lippmann

Title: X-ray CT-based Assessment of Variations in Human Airway Geometry: Implications for Evaluation of Particle Deposition and Dose to Different Populations

Investigators: B.S. Cohen¹, E.A. Hoffman²

Institutions: ¹New York University School of Medicine, ²University of Iowa

EPA Project Officer: Stacey Katz/Gail Robarge

Project Period: June 1, 1999–May 31, 2005 (no-cost extension to May 31, 2006)

Period Covered by the Report: June 1, 1999–May 31, 2006

RFA: Airborne Particulate Matter (PM) Centers (1999)

Research Category: Particulate Matter

Objective(s) of the Research Project: To address the paucity of data regarding particulate matter (PM) deposition in the lungs of people with pre-existing pulmonary disease and the normal elderly; subpopulations which may be at special risk, this project investigated the potential for retrieval of morphometric data from three-dimensional images of tracheobronchial airways obtained *in vivo* by x-ray Computerized Tomography (CT). The study also explored the potential for the use of stereolithography (STL) to produce hollow airway casts of normal and abnormal lung airways for the experimental determination of site-specific deposition and for experimental verification of particle deposition models. The ultimate goal was to quantify the impact of the airway variability on PM deposition and dose. The project was a collaboration between the extensive imaging expertise at the University of Iowa and New York University (NYU) PM Center particle deposition expertise.

Summary of Findings:

Progress Years 1-2

A volumetric rendering of the interior surface of a hollow airway cast (used in previous studies at NYU) was generated, producing a surface representation of the airway tree. These three-dimensional images were then converted to a STL file format required for the rapid prototyping of airway casts. This was accomplished by shape-based interpolation to create isotropic voxels and to smooth the surface, after which a volumetric rendering of the resultant segmented luminal space of the airway tree phantom was generated. The stereolithography unit uses a computer-controlled arm connected to a plastic extrusion device to build volumetric structures layer-by-layer. Two heads are present on the machine, one to lay down the plastic compound for the structure of interest and a second head to lay down needed support material for the structure as it is being built, and which can later be separated from the structure. Close concordance was seen between the original hollow airway cast and the STL produced replicate. The casting process was subsequently converted to utilize a water soluble material to build supporting structures.

Thin multi-slice helical CT scanning allows the acquisition of high-resolution volumetric image data sets of the lung in a breath-hold or at multiple phases within a respiratory cycle. From these scans, hollow airway casts that include 5 or 6 bronchial generations can be created. The process was utilized to obtain an image, and then produce a cast, from a living person. The casts can be accurately replicated for use in studies of inhaled particle deposition in replicate casts of both healthy and diseased airways using realistic air flow rates.

Progress Years 3 and 4

Work was performed preparatory to planned *in vivo* studies to compare inhaled particle deposition pattern and efficiency in sheep with the deposition measured in a hollow airway cast prepared from the same animal's three-dimensional image. Our Iowa collaborators continued to work on the development of sheep models for the testing of various measures of pulmonary perfusion, regional ventilation, airway structure and distensibility, diaphragm and rib cage mechanics, etc. We fine-tuned our methods of respiratory gating and succeeded in developing methodology that allows us to gate image acquisition very accurately to an inductance plethysmographic (Respirtrace) signal, and acquire volumetric images of the lung at multiple points within the respiratory cycle over a period of 30 cycles. While it is common to monitor airflow at the mouth and lung volumes, the accuracy required by the above described respiratory-gated image acquisition requires much tighter tolerances than most pulmonary function testing equipment.

Significant advancements in computerized analysis have been made in the areas of lung, lobe and airway segmentation, airway tree matching, and lung feature matching. A set of reproducible feature points are first identified, including airway branching points, for each CT image to establish correspondences across subjects.

The binary airway tree is skeletonized to identify the three-dimensional centerlines of individual branches and to determine the branchpoint locations. Graph algorithms can then be applied to match corresponding branchpoints. A program was developed that visualizes two airway trees side by side and allows a human observer to navigate through the trees in the three-dimensional space and to define matching branchpoints by hand. This is an invaluable tool that provides independent standards. An evaluation using phantom data as well as *in vivo* scans showed excellent agreement (between 85% and 97%) between the automatically obtained matches and matches provided by human experts. These methods will assist development of concordant measures across bronchial branches in different individuals. We also began to establish methodology to perform computational fluid dynamics measures on specific airway geometries imaged by CT so as to predict deposition patterns and to then compare them with direct CT-based measures of deposition.

The Iowa team also examined how spatial resolution varies as a function of position in the field of view. A phantom was made containing 37 copper spheres 1/32 inch (0.8 mm) in diameter that were placed in 3 concentric rings at 50 mm, 100 mm, and 150 mm. The phantom was scanned and reconstructed and a computer simulation was performed to construct a volume similar to that generated by the scanners. Issues of falloff of resolution away from the isocenter remain to be resolved. At NYU we have tried to develop a suitable monodisperse radio-opaque test aerosol.

We have x-ray tested common contrast media to determine the smallest layer that can be distinguished from a unit density background, but results to date are not satisfactory.

Technical Aspects

The positive aspects of this project were the development of a computational capacity to create a 3-D computer model of lung airway dimensions from CT scans of an original cast model on which measurements had been made of airway branch diameter, length, and branching angle. We then demonstrated excellent agreement on measurements made from a silastic reproduction as compared with the original to assure accurate reproduction of these metrics.

We then successfully demonstrated the concordance of lung airway sizes in humans *in vivo*, as measured by CT, with those measured in a hollow lung cast that was produced by stereolithography using the dimensions provided by the CT scans of the same human lung.

The negative aspects were that the sheep studies were not initiated because we have not yet been able to identify appropriate contrast media. Also, our collaborators at the University of Iowa were not yet able to completely correct for the variation of spatial resolution as a function of position in the field of view. Additionally, within the confines of our resources we were not able to extend the study to the production of hollow airway casts of patients with well characterized chronic lung diseases or to model the influence of abnormal airway structures on lung function.

Technical Effectiveness, Economic Feasibility, and Benefits:

Successful techniques were developed for smoothing the data acquired from individual slices to enable the production of three dimensional models of the lung airways from a set of CT scans. Production of such hollow casts is economically viable. The benefits are that reproductions of the airways of patients who receive CT scans for medical purposes, and whose medical history and pulmonary function test are available, can be produced for study of airflow and deposition of particles in accurate, economical and reproducible models. This can provide improved knowledge of how airway particle deposition or airflow varies with morphometry in particular diseases with the possible determination of improved intervention

Supplemental Keywords: NA

Relevant Web Sites: <http://www.med.nyu.edu/environmental/>
<http://es.epa.gov/ncer/science/pm/centers.html>