

Imaging Based Assessment of Lung Function in a Population Cooking Indoors with Biomass Fuels

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Overview

The work presented in the accompanying manuscript was part of a pilot study, funded by the University of Iowa Environmental Health Research Center (NIH 5P30 ES005605), to explore the impact of biomass fuel use, particularly indoor use, on lung function and health using advanced CT imaging techniques. In addition to pilot data, this project also served to establish international collaborations between the researchers at the University of Iowa (UI) in the United States and at the Periyar Maniammai Institute of Science and Technology (PMIST) in Thanjavur, India. The study was approved by the Indian Council for Medical Research (ICMR) and by the Human Subjects IRB at the University of Iowa.

Subject engagement and geographical location

As a pilot study, this work was limited in the number of subjects and study locations, but it provided a greater insight into the community at large, including valuable information on fuel types, detailed analysis of combustion and bioaerosol particles generated in the indoor cooking environment, the associated neighborhood community environment, and individual subjects'

quality of life, and lung function metrics. All subject recruitment and field work for this project were carried out in the Thanjavur district in the state of Tamil Nadu, in India (Figure E1). To maximize data collection from biomass homes, and due to the scarcity of adequate controls within in the same communities (to avoid other potential confounders), we had an unbalanced cohort size, with over 80% of subjects belonging to the biomass group. All subjects reported no history of pulmonary or cardiovascular disease, however, detailed medical records in the geographical region are uncommon, and rural community members may ignore health conditions unless it significantly affects their quality of life. Therefore, some underlying conditions may be undiagnosed. Environmental factors cannot be completely decoupled from such conditions, and an epidemiological study is needed to better characterize the prevalence of respiratory diseases in these communities.

Field work and data acquisition

A team of US investigators (ASKP, EMS, APC, EAH) traveled to Thanjavur, India in 2019 for field work associated with data collection. The Indian efforts were coordinated by investigators and students at PMIST, through their well-established community relations. Two study locations (inset, Figure 1) were identified, one in the immediate vicinity of the Indian institution (peri-urban), and second, a village approximately 20 miles from the urban area. Both teams visited site locations and interacted with the potential subjects to provide detailed overviews of the scientific background, study aims and protocols, and expected outcomes, in the local language, Tamil. All subjects underwent a urine pregnancy test prior to recruitment for the CT imaging component of the study. Thirty-four homes were initially recruited for the study. Exposure data from two homes were excluded due to equipment malfunctions.

Characterization of the cooking environment

Experts in environmental research from the US team (EMS, APC) conducted visual kitchen assessment in each home, detailing information on stove location and height, fuel type, ventilation and window locations, average kitchen area, presence of domestic animals, and building material of the stove, walls, and roof. A typical example from a brick-walled home is shown in Figure E2, depicting the stove, biomass fuel, and windows providing cross-ventilation. Participants also completed a survey on their cooking and personal exposure history, and a brief medical questionnaire. The air quality of the cooking environment was quantified by the following data collection steps: 1) Vacuuming sediment mass collected over a 7-day period from clean rubber-backed rugs placed in the kitchens. 2) Daily PM_{2.5} concentrations measured using gravimetric analysis using a filter from a personal sampler with a size-selective inlet (UPAS, Access Sensor Technologies, Ft. Collins, USA); 3) 24-hour fluctuations in PM_{2.5} measurements using a direct reading instrument (PATs+, Berkeley Air, Berkeley, USA); 4) Black carbon concentrations using a filter absorption coefficient derived from the UPAS filters; and 5) Endotoxin concentrations analyzed at UI and derived from an electrostatic dust collector, over both a 24-hour and 7-day period. Rug mass from two homes was excluded due to accidental interference. Black carbon measurements were not performed in three homes due to high particle load, above the sensitivity thresholds of the filter. Our team performed further biochemical and microbiological analyses on cooking environment samples to further quantify particulate chemical and bacterial composition, *in-vitro* assays to test particulate cytotoxicity, effects on antimicrobial activity, and alterations to cell wall permeability and conductance. A detailed overview of these analyses and results has been

previously published (23). In brief, the cooking environment of biomass homes had significantly higher concentrations of PM_{2.5}, black carbon, and endotoxin.

In addition, we quantified the ambient levels of airborne fungal pathogens. β -(1,3)-D-glucan concentration were determined using the GlucateLL® assay of air samples collected EDC filter membranes. The assay is based upon a modification of the Limulus Amebocyte Lysate (LAL) pathway. The reagent does not react to other polysaccharides, including β -glucans with different glycosidic linkages, and is a well-established β -(1,3)-D-glucan measurement method (53–55). Samples were analyzed with appropriate negative and blank-control samples to obtain the final β -(1,3)-D-glucan concentrations in the sample. Samples were typically collected over an approximate 24-hr window, and the concentrations were scaled by the exact duration of exposure and extrapolated to a 7-day (168 hours) adjusted estimate for uniform comparison.

Physiological Assessment

A subset of 25 subjects were recruited for physiological assessment. All subjects underwent a standardized pulmonary function test at a nearby hospital. Spirometry was performed before and after administration of 200 μ g of Salbutamol, under the supervision of a trained technician at a partnering hospital.

CT imaging protocols and quality control

The imaging parameters outlined in the SPIROMICS protocol (16) were used in this study. The scanner specific settings for GE scanner models were applied to the GE Optima 128 slice scanner used in the study. Scan settings, Table E1, were modulated for patient size based on BMI estimates from measured height and weight. A CT density phantom (The Phantom Laboratory,

Salem, NY, USA) was transported to India for calibration purposes (16). At study onset, the phantom was used to verify dose estimates for the specified scan parameters and for validation of HU values. Calibrations were performed on the same week as subject data acquisition. All imaging was performed by a trained CT technician, under the supervision of a resident Radiologist (SN). CT imaging experts from the US (EAH, ASKP) provided additional review of the acquisition protocols and inspiration maneuvers to total lung capacity (TLC) and residual volume (RV) for the CT technologist and observed all studies. Image datasets were deidentified at the imaging site and transferred via CDs (one for each subject) to secure servers at the UI for image processing.

Image processing

Standard densitometric analysis was performed on the TLC and RV datasets to label individual voxels as emphysematous (below -950HU on TLC images), air-trapped (below -856HU on RV images), or normal, as in the parametric response map (PRM) approach. While the PRM uses image registration, voxel labels are based on static density thresholds at the specified lung volumes. In contrast, to assign voxel labels, the disease probability measure (DPM) approach generates a probability map based on estimates of regional lung volume change from image registration, and the resident lung volume at RV. We hypothesized that in the presence of diffuse inflammation, as may be expected from high inhalation exposures, the DPM approach would be less susceptible to the inflammation associated lung density shifts compared to the PRM reliance on density thresholds. The image registration approach also provides regional estimates of the Jacobian, which is a measure of regional lung expansion, and Anisotropic Diffusion Index (ADI), a measure of the non-uniformity of regional lung expansion. Whole lung measures (mean and coefficient of variation) of the Jacobian and ADI metrics provide insight into alterations in patterns

of ventilation distribution and tissue compliance. The Total Airway Count ratio (*TACratio*), i.e. ratio of countable airway branches at TLC and RV, provides additional information on airway morphometry and dynamic compression, resulting from tissue compliance and branch stiffness. All CT analyses described above were carried out by VIDA Diagnostics Inc. (Coralville, IA) using their proprietary Apollo 2.0 image analysis software.

Additional CT metrics related to texture classification were performed by an in-house developed software package, the Pulmonary Analysis Software Suite (PASS). A modified version of 3D Adaptive Multiple Feature Method (AMFM) (28) was applied on the CT volume acquired at TLC. This CT analysis technique calculates a set of 27 volumetric features, including statistical, fractal, and histogram features, on $7.5 \times 7.5 \times 7.5$ mm lung tissue sub-volumes (we refer to here as patches), and applies a Bayesian classifier to label such patches as emphysematous, ground glass, ground glass-reticular, honeycombing, bronchovascular, or normal. This technique has previously been applied for parenchymal characterization in smokers (28), and in patients with interstitial lung disease (29, 56).

Summary

This pilot study successfully provided a well-quantified assessment of the cooking environment's indoor air quality and characterized pulmonary function and regional lung mechanics via multi-volume CT imaging. There is a need for a larger scale approach to expand this study to explore the impact of biomass fuels and the relative contributions of indoor and occupational exposures. We believe that this preliminary data can drive new hypotheses on the acute insults to the lung suffered from biomass cooking smoke, and the potential mechanisms of pathogenesis and progression of chronic lung disease in these at-risk communities.

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Figure E1. Red boxes indicate study locations (Thanjavur) and the location of the state capital (Chennai). Subject recruitment was carried out in Vallam and Budalur villages, seen in the inset. Indian investigators are based in the village of Vallam.



Figure E2. Example of an indoor cooking stove from a subject home in Thanjavur. Stoves are typically located at floor height, or slightly elevated on bricks. When present, windows provide occasional passive ventilation. Particulate matter can persist in ambient air after cooking and this was identified by our real-time $PM_{2.5}$ devices. Particulate matter deposits on walls and floors and can later be resuspended into the air, increasing the probability of its inhalation.

Table E1. CT Scan parameters

kVp	120
mAs – Inspiration (TLC)	
Small (BMI < 20)	145
Medium (20 ≤ BMI < 30)	180
Large (30 ≤ BMI)	270
mAs – Expiration (RV)	
Small (BMI < 30)	100
Medium/large (30 ≤ BMI)	145
Thickness (mm)	0.625
Rotation time (s)	0.5
Detector configuration	64 × 0.625
Pitch	0.984
Interval (mm)	0.5