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MECHANICAL HUMAN LUNG FOR INHALATION TOXICITY RESEARCH

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Abstract- *This paper presents a novel application of a multi-stage mechanical human lung (MHL) to undertake in-vitro investigations of the aerodynamic characteristics and toxicity of inhaled atmospheric pollutants. The MHL was designed, and developed in our Biosimulation and Aerosol Research Lab. Its geometry and assembly were based on widely used human lung's morphological dimensions specified in the Ewald R. Weibel's dichotomous lung morphometry. The instrument was validated with the lung deposition data of inhaled particles predicted by the International Commission on Radiological Protection. The toxicity of inhaled atmospheric pollutant particles is typically determined by quantifying the amount of particles deposited inside various regions of the human lung. Researchers frequently use various forms of United States Pharmacopeia approved Andersen Cascade Impactor (ACI) for lung deposition studies. However, the ACI is unable to simulate all lung deposition mechanisms besides inertial impaction, whereas it was documented elsewhere that an MHL can do. Therefore the MHL can be an alternative of the ACI at a fractional cost. It is employable to accomplish inhalation toxicity research as it simulates an adult human lung.*

Keywords: Human Lung, Environmental Pollution, Toxicity, ACI, Vehicle Exhaust

1. INTRODUCTION

A mechanical in-vitro human lung which is built on morphological geometry of various regions of the in-vivo life-size human lung may act as a major research instrument for understanding the deposition of inhaled atmospheric pollutant toxic particles. Aerosol is a collection of solid or liquid particles suspended in a gas. Atmospheric pollutants get inhaled into human lung in the aerosol state. Literature reported that inhaled aerosol particles deposition along the human lungs respiratory tract significantly depends on (1) electro-physiochemical properties of the particles such as size, shape, diffusivity, density, viscosity, electrical charge, and hygroscopicity [1,2]; (2) physiochemical properties of airways' temperature, relative humidity [3]; (3) breathing pattern such as tidal volume, mean flow rate, mean residence time, frequency of inhalation and exhalation. Studying their effects on particle deposition in the various regions of human lung is necessary to quantify the poisonous level. Although, the Andersen Cascade Impactor (ACI) is present days United States Pharmacopeia approved physical model often use in this research to understand particle deposition patterns, besides impaction, it can not simulate four other lung deposition mechanisms as illustrated in Figure 1, they are (a) gravitational settling, (b) diffusion, (c) interception, and (d) electrostatic force [4]. A mechanical human lung (MHL), which closely approximates in-vivo human lung and simulates an environment for all deposition mechanisms to act interactively would unquestionably be a breakthrough.

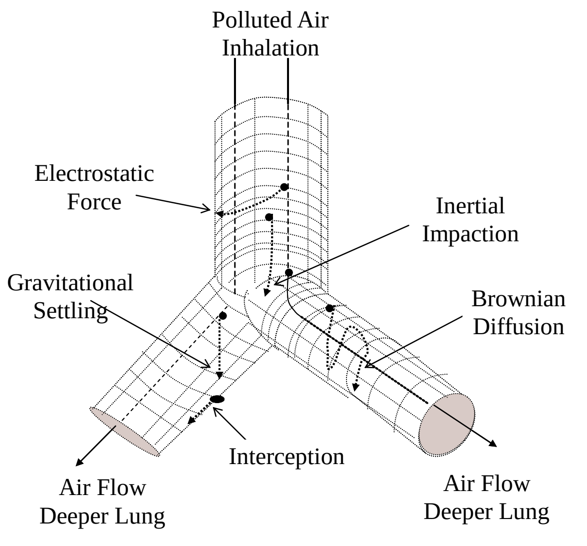

Fig. 1: Illustrations of five electromechanical deposition mechanisms of particles suspended in the inhaled air of human lungs' circular airway [5].

1.1 Significance of Mechanical Lung in Environmental Research

Air pollution is one of the most important factors affecting the quality of life and the health of the increasingly urban population of industrial societies. Due to an increasing awareness of the potential hazardousness of air pollutants, numerous studies have addressed traffic-related particulate matter and pollutants. By contrast, only few studies used the advanced technology of mobile exposure analysis. Furthermore, there is not enough data gathered to evaluate the amount of toxic pollutant particles that are inhaled by the humans whose daily activities characterize them as city dwellers, commuters, street vendors, bus and truck operators in the densely populated cities such as Dhaka, Bangladesh. Therefore, an in-vitro study is necessary to understand such toxicity. This paper is proposing to use Mechanical Human Lung (MHL), a surrogate lung model that closely approximates the flow characteristics, surface area, and inhaled aerosol particle deposition mechanisms of the in-vivo human lung.

1.2 Atmospheric Pollution and Inhalation Toxicity

Toxicity of the inhaled pollutant particles depends on their physical and chemical properties. These fine and ultrafine particles are able to move easily from the nasal passageway to the brain [6]. Such particles are very transportable in human's biological systems that they enter bloodstream directly from lung, thereby gaining easy access to secondary target organs such as the lever, the heart and possibly the brain [7]. The major toxic air contaminant substances in these particles are inorganic lead, mercury compounds, arsenic, dioctylphthalate, phenol, cadmium, dibutylphthalate dioxins, dibenzofurans etc. These synthetic chemicals and phytoestrogens are proven endocrine disruptors that act on the endocrine systems of humans and animals by mimicking, blocking and interfering in some manner with the natural instructions of hormones to cells [8]. The endocrine system is made up of glands, hormones, and receptors found in numerous places in the human body.

Automobile exhaust is the chief source of polycyclic aromatic hydrocarbons in the form of fine particles which are emitted by vehicles either as a result of evaporation or incomplete combustion of fuel. The result in emission of a heavy load of toxic pollutants such as, Benzene, Xylene, Toluene, Anthracene, Fluoranthene, Pyrene, and Benzo-pyrene [9].

The relationship between exposure to traffic induced particles, respiratory health, and cardiac diseases is a well-established fact documented in numerous literature and environmental regulatory agency reports. Petrol and diesel engine exhausts contain millions of fine (diameter $< 10\ \mu m$), and ultrafine particles (diameter < 100 nm). City dwellers, commuters, street vendors, bus and truck operators in densely populated cities are exposed to those particles everyday and ultimately inhale particles (1245-1601 $\mu g/m^3$ at commercial places, and 445 $\mu g/m^3$ at residential places), which are far above the United States pathogenic level (50 $\mu g/m^3$) or World Health Organization's tolerable level (60-90 $\mu g/m^3$).

1.3 Acute Atmospheric Environmental Pollution in Densely Cities of Bangladesh

Outreproducing other members of one's population is the very basis of natural selection and is the driving force in the evolutionary process, however, against unthinkable discussing over population must be discarded in order to avoid millions of people prematurely dying of hunger and disease and to maintain an environmental balance [10]. Many countries throughout the world have the problem of overpopulated cities but none more than those countries that are still developing themselves. This problematic nature of increasing overpopulation in the cities of developing countries is the biggest environmental pollution problem needing to be addressed in the 21st century, and will continually need to be addressed in the future, as overpopulation is increasing at an alarming rate.

One country suffering such problems is Bangladesh, and its hugely overpopulated capital city of Dhaka. It is a country of disaster prone, and is a victim of repeated natural disasters such as cyclones, floods, droughts and earthquakes. It is these horrific natural climatic conditions that make it hard for farming and so on but also forces a lot of people into the cities like Dhaka. The effects of expanding urbanization on the environment are also evident. When the number of petrol, diesel, and compressed natural gas (CNG) vehicles in a certain area gets too big the environments own power of regeneration decreases and the pollution accumulates.

Being one of the highest populated cities (per square mile area) in the world, Dhaka has acute problem of air pollution due to vehicle exhausts. Air quality standards and severity of pollution in Dhaka city were studied by several investigators. The prime reasons that were reported include: high number of aged and two-stroke engine vehicles, absence of catalytic converters, high leaded petrol (gasoline), impure diesel with high sulfur content, and overall inefficient traffic management [11,12].

The motor vehicle statistics prepared by the Bangladesh Road Transport Authority showed that currently there are approximately 500,000 registered vehicles are on the streets of Dhaka with an annual growth rate of 8.6% [13]. Nevertheless, there are huge numbers of unregistered vehicles on the streets as well. These vehicles However, the toxicity of these particles can only be determined by quantifying the amount of particles deposited inside various regions of the human lung. The in-vitro MHL can be employed to accomplish such quantification objectives since it simulates an adult human lung.

2. MATERIALS AND METHODS

A wealth of semi-continuous data including particle size distributions, mass of $PM_{2.5}$ and PM_{10} (particulate matter less than 2.5 and 10 micrometers, respectively) major species, and gaseous pollutants would be required to collect. Major instruments will include Scanning Mobility Particle Sizer Spectrometer (SMPS), Aerodynamic Particle Sizer (APS), Engine Exhaust

Particle Sizer (EEPS) spectrometer, Condensation Particle Counters (CPC), Mechanical Human Lung, and Convertible Small Truck.

2.1 The MHL Design Methodology

According to the United States Environmental Protection Agency's "Guidelines on Speciated Particulate Monitoring" human respiratory tract is an aerodynamic classifying system for inhaled particles [14].

A sampling device can be used as a substitute for the human lung as a particle collector, and it can effectively simulate the mechanisms of electromechanical deposition of the inhaled particles including inertial impaction, gravitational settling, interception, diffusion, and electrostatic force as depicted in Figure 1. Others have shown that a physical lung model simulated by a multi-layer granular bead filter provides a good approximation of the deposition detected in the in-vivo experimental data [15].

In order to study the regional deposition of aerosol particles, it was necessary to design a multi-stage model to simulate various regions of the lung anatomy. The description of the MHL design and performance have been demonstrated in our previous work [16]. The MHL uses a United States Pharmacopeia induction throat, and several packed beds (Stages) of glass beads in the shape of a wedding cake (Figure 2). Since the MHL was constructed to mimic flow parameters (Reynolds number), surface area and dimensions of the lung airways, it could simulate all five mechanisms of deposition of inhaled aerosol particles as illustrated in Figure 1.

Based on the human lungs' physiological characteristics [17], and engineering principles the MHL was designed and developed in our Biosimulation and Aerosol Research Lab. Then the model was employed to investigate the inhaled aerosols particle deposition generated by a commercially available aerosol generators; and validated the deposition results with empirical lung deposition model proposed by the International Commission on Radiological Protection (ICRP) deposition model [18], and Andersen Cascade Impactor (ACI) [19].

The experimental data of the MHL agreed with the reported aerosol particle deposition measurements using the United State Pharmacopeia approved ACI, which is often used for inhaled aerosol deposition studies. The ACI is multistage particle collection system from flowing aerosols by mimicking environment of inertial impaction. The MHL mimics an environment of all five deposition mechanisms by employing engineering theories an principles [16]. The potential application of this instrument in determining inhaled load of particles for a city dweller, a commuter, a street vendor or a vehicle operator while working during their daily activities will be addressed in the next paragraph.

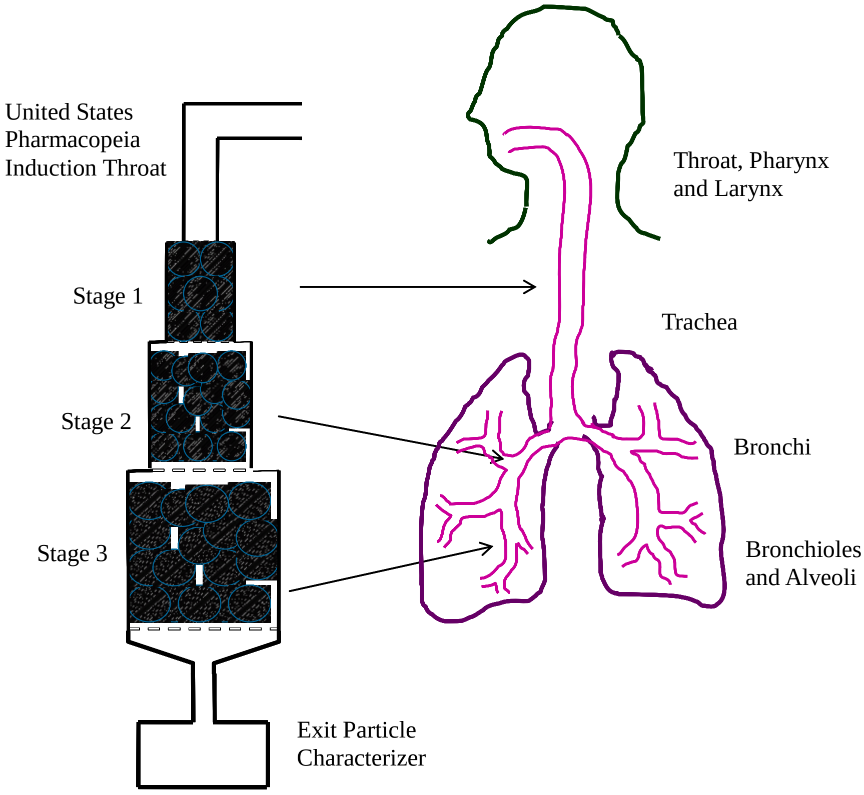

Fig. 2. Multi-stage Surrogate Mechanical Lung Simulates Various Regions of an Adult Human Lung [16].

2.2 Study Design

Monitoring can be carried out using convertible vehicles in open positions, and stationed at various highly air polluted points in the city of Dhaka. Figure 3 depicts the simplified schematic diagram of real-time particulate monitoring system. The MHL experimental setup will be installed on that convertible utility van or pickup truck. Driving conditions and time for sampling should be standardized to represent typical urban behaviors for the different seasons of the year. The routes can be chosen in different settings: traffic zone, motor way, and other urban settings including shopping areas. Depending on traffic conditions, these can be analyzed and categorized differently.

Upon completion of data collection, it needs to be averaged from replicates in order to provide estimates of exposure for a distinct situation. Also, timing of the analysis routes (which may include pre-defined intermediate waypoints or randomized routes) should be monitored by electronic watches which are synchronized against the different monitoring devices and GPS-systems. Also, wind speed should be measured once on each route, using anemometers. The data can also be compared to meteorologic and emission outdoor air parameters.

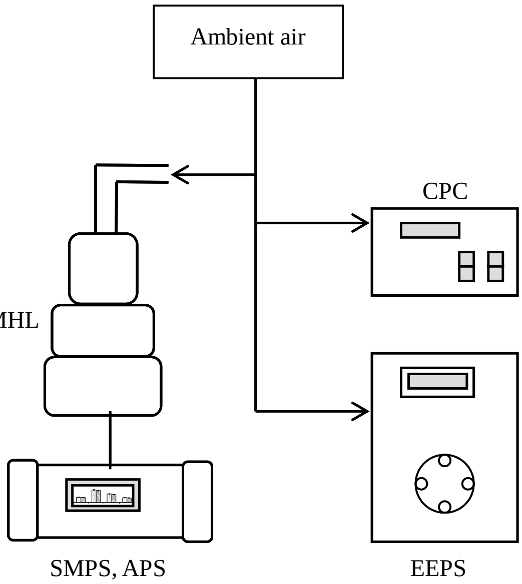

Fig. 3: The simplified schematic diagram of the real-time particulate monitoring system. SMPS: Scanning Mobility Particle Sizer Spectrometer, APS: Aerodynamic Particle Sizer, EEPS: Engine Exhaust Particle Sizer spectrometer, CPC: Condensation Particle Counters, MHL: Mechanical Human Lung.

3. DISCUSSION

The advantages of the MHL model in studying human pulmonary systems studies and simulations are many. Among them, most importantly it will eliminate safety issues and variability that are inherent with the use of human subjects. Also it can be employed as a mimic of the human lung for in-vitro studies on determination of regional lung deposition and toxicity from CNG, petrol, and diesel exhaust particles, and inhalation of workplace atmospheric pollutant dust. Additionally, the benefits of a real-time in-situ measuring instrument are a) instantaneous readout on the quantity of inhaled pollution particles, b) total concentration profile measurement, c) contamination sources identification, and d) continuous air-intake monitoring. Therefore this instrument can find a novel application in determining toxicity of air pollution in densely populated cities in Bangladesh.

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