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Regional Aerosol Deposition in Human Upper Airways

Annual Progress Report
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Abstract

During the report period significant progress on the quantitative understanding of regional upper airway deposition of airborne particle has been realized. Replicate models of the human upper airways obtained from post-mortem casting of the nasal, oral, pharyngeal, laryngeal and upper tracheal regions and in vivo magnetic resonance imaging (MRI) of the same regions of adults and children have been employed to determine the overall and local deposition characteristics of aerosols in the ultrafine (1-100 nm diameter) and fine (0.8-12 um diameter) region. Studies have been carried out for both nasal and oral breathing during inspiratory and expiratory flow at constant flow rates representative of rest and states of exercise.

The results of these investigation indicate that particles in the size range of "unattached" radon progeny (1-3 nm) are deposited in both the nasal and oral passages with high efficiency (60-80%) for both inspiration and expiration, with the nasal deposition being somewhat greater (5-10%) than oral deposition. The effect of flow rate on upper airway deposition for both pathways is not great; data analysis indicates that the deposition for all flow rates from 4-50 liters/minute can be grouped by plotting deposition vs $Q^{-1/8}$, where Q is flow rate, a far weaker dependency than observed for inertial deposition. Diffusional transport is the primary mechanism of deposition, and size dependence can be accounted for by plotting deposition percent vs D^n where D is particle diffusion coefficient and n ranges from 0.5-0.66.

Deposition studies of fine particles are more strongly dependent on flow rate and airway dimension, behaving similarly to idealized impactors in the particle size range 0.8-12 um. Typical "impactor" curves are observed in every case which are flow dependent even when deposition efficiency is plotted against a pseudo-stokes number.

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Construction of Replicate Models for Human Upper Airways

During the report period significant progress in the construction of replicate upper airway models has been achieved in accordance with the research proposal. In the initial phase of the study, two adult replicate models were employed, both obtained post-mortem by casting with silicone rubber compound (RTV). One model extended from nasal entrance to mid-trachea and included an oral passage alternative. Studies of this model were carried out in the initial phase of the project and are reported in publications appended to this report. The other model consisted of a half-nasal passage extending only from nasal entrance to naso pharynx, also obtained post-mortem from a different normal adult.

With the wider use of magnetic resonance imaging (MRI), it became possible to obtain in vivo coronal sections of the nasal and oral passages, including naso- and oropharynx from which replicates can be constructed. The method for converting sectional scans into replicate models had to be considered first. Two methods of construction were considered, free hand passage cutting of "sandwich" elements or machine cutting employing interpolated surface coordinates using a three dimensional milling machine. While the latter permits exact copies to be constructed, the software to convert perimeters of successive MRI slices into machining directions was not at hand, and it was decided that this would entail extensive development, inconsistent with the project goal accomplishment. Therefore, we adopted the free hand method. Each slice had successive perimeters outlined on its two faces and the passage was cut to match the outlines front and back. The next slice element had the same element on its front and the next perimeter on its back; thus the element junctions represented the section perimeter and transition was cut through the slice elements of clear acrylic plastic of thickness equal to the image separation. After initial cutting, several elements were placed together in correct orientation and abrupt changes were smoothed.

Adult models contained from 25-40 element slices depending on the image separation. This sandwich replicate is useful in that after aerosol exposure, the elements can be separated and the local deposition can be measured by any of several methods, depending on the physicochemical or isotopic nature of the aerosol. Furthermore, local changes in airway dimension can be made by inserting appropriate sections of the replicate model to represent physiological changes while keeping the remainder fixed.

Two adult models, based on successive scans of the same normal individuals have been completed and used for deposition studies. The first scan consisted of 3mm sections and the second of 5mm sections. The second scan also included an oral passage breathing

oronasally at rest; thus the behavior of particles through the nasal or oral passage could be investigated with this model.

Three MRI scans of normal children were obtained from the MRI facility at Johns Hopkins Hospital, ages 1 1/2, 2 1/2, and 4 years. Models based on these scans have just been completed at this writing and have been used in initial overall deposition studies in collaboration with the U.K. National Radiation Protection Board (NRPB). Additionally, an "ersatz" six year old model has been constructed from the adult scans by scaling down all dimensions by a factor related the ratio of minimum areas in the nasal valve between the adult subject and the average minimum area of six year old children measured in Copenhagen, Denmark (1). This "scaled down" six year old model is intended to be compared with an actual six year old model (yet to be obtained) in order to test the hypothesis that the upper airway passages of small children and infants can be considered as a "scaled down" adult passages with respect to radon progeny and other environmental aerosols.

For the remainder of this current period and in the next period, studies of overall and local deposition of such aerosols will continue in all of the models described above, in accordance with the research program goals. The construction of these models is an important accomplishment toward the project completion, and it does not appear that any difficulties will prevent the full realization of the project goals.

Overall Deposition Studies - Adult Models

In the initial phases of this research program, overall deposition of particles in the size range 5-200nm was measured in the nasal and oral passages of the adult models described above. These initial studies were carried out in collaboration with John Strong and Anthony James at NRPB and with Yung-Sung Cheng and Hsu-Chi Yeh at the Lovelace Inhalation Toxicology Research Institute (ITRI) in Albuquerque, NM and are report in summary on the previous progress report. These studies showed that particle diffusion was the dominant deposition mechanism and that overall deposition was strongly particle size dependent, ranging from less than 5% for the nasal passage upper airways (>100 nm) to greater than 70% at 5 nm. Over large ranges of flow rate overall deposition percent changed little, the trend being increasing deposition at decreasing flow rate. Surprisingly, oral passage deposition of these ultrafine aerosols was almost equal to nasal passage deposition, and the deposition percent for constant flow inspiration was equal to that for expiration.

The aerosols for these studies consisted of either Nacl or Ag produced by evaporation and condensation and classified to produce nearly monodisperse aerosols of desired diameter. Aerosol concentration entering and leaving the models was measured by condensation nucleus counting (CNC), thus only overall deposition

was measured. In the current studies of unattached radon progeny, the aerosols were produced directly from radon decay (Rn^{222} or Rn^{220}) which led to particle sizes from 0.75 - 2 nm, characteristic of the unattached fraction. As before, aerosols were collected "upstream" and "downstream" of the model but the aerosol concentration was determined by isotope counting rather than by CNC. In each instance, the radon gas was initially filtered, followed by a holdup chamber permitting a period of time to allow for formation and growth of the aerosol particles. The size of aerosol passing through the model was determined by a parallel flow diffusion battery.

These studies gave results consistent with previous measurements, in that the overall deposition of the particles was greater than for 5 nm particles, although not as large a difference as was initially predicted by extrapolation of the data from previous studies, which predicted nasal passage deposition of 90-95% for 1.0 nm particles. The deposition values for different models in this size reqime was between 70-85% with a weak dependence (as before) upon flow rate, increasing with decreasing flow rate.

Deposition studies for particle sizes from 0.8-12 um were also carried out with the adult model during the present period. In these experiments, polydisperse corn oil aerosols were produced by nebulization and passed through the models at flow rates ranging from 10-80 liters/min. Aerosol samples "upstream" and "downstream" were collected isokinetically and analyzed with a TSI APS 3300 analyzer. The overall deposition percentage as a function of particle size was plotted against a pseudo-stokes number d^2Q, where d is particle diameter and Q is flow rate. According to impactor theory, a single curve should be obtained over a range of flows producing the same kind of flow in the deposition region. In these experiments, curves similar to those for cascade impactor stages were obtained, but these <u>did</u> demonstrate flows dependance. Higher flow rates produced efficiency curves which demonstrated higher percent deposition at the same value of d^2Q. Presently, a mathematical model of Reynolds number dependence is being sought which will fit the data obtained to a single efficiency curve for each model over the range of flow rates. Additionally, a model dimension which predicts the deposition curve for different models is also being investigated.

Similar overall deposition studies are being undertaken with the replicate models for the children; however, these studies are just beginning because the replicates have only recently been completed. The initial studies of overall deposition with unattached radon progeny aerosols show deposition percent less than that for adults, although the difference are not large. These results seem consistent with the fact that the path length for the child's nasal or oral airway is somewhat less than that for an adult, resulting in a lower diffusional loss. No studies of the deposition percent of attached aerosol (100 nm diameter) or fine aerosol (0.8-12 um diameter) have been performed with the child

upper airway models, but initial studies are expected to be completed within the remainder of the current research period.

Local Deposition Studies

Two methods for determining the location of deposition in the nose or mouth passages of adult or child replicate models are being employed. These techniques are in the initial phase of development, but both appear to have the capability of yielding good quality spatial information about nasal passage or oral passage deposition. This is important not only to determine what dimension or region is critical to deposition (changes in this dimension markedly alter deposition percent), but to determine the ultimate fate of aerosol deposition in the upper airways, whether retained for significant periods or rapidly cleared by tissue absorption, mucociliary clearance, or swallowing.

One method, already described, is measurement of deposition upon each element of the sandwich replicates, either chemically or radiologically. The other method is the measurement of radioactive aerosol deposition by gamma camera, a technique used extensively in nuclear medicine employing collimated detector arrayed over a large area (1 ft^2). This requires that a large quantity of activity be deposited in the cast because of the low efficiency of the collimation to improve resolution.

Initial studies of both adult and child replicates have been performed using the sandwich element technique with Ra^{220} progeny at ITRI and the gamma camera detection of surrogate particles at The Royal Free Hospital, London, England in collaboration with NRPB. In the latter case, the particles were produced by a technique known as "technegas" containing the isotope Tc^{99m} in which the particle size has a MMAD of 125 nm (2). The full analyses of these initial studies has not been completed, but the initial indication is that both methods will yield important spatial information about deposition site and fate of deposited aerosol. It is hoped to develop a simple method for producing 1.0 nm particles containing TC^{99m} which can be conveniently imaged with a gamma scintillation camera.

Proposed Studies for the Following Year

During the next research period, we propose to carry out additional studies of overall and local deposition of aerosols in the three size ranges discussed above in replicate models. An additional adult model, including the state of nasal congestion and decongestion will be constructed in order to determine its effect on aerosol deposition. A model of the nasal passage of the newborn will be constructed to give additional age related information of overall and local deposition. The technique described above will be employed with the present replicates and

new models to fill in missing pieces of information concerning overall and local deposition.

Additionally, studies of local and overall deposition specifically in the laryngeal region will be carried out. An adult larynx region has already been constructed from MRI images in the "sandwich" model fashion but deposition studies in this isolated region have not been performed. The larynx in children may be an important region for removal of aerosols, but models constructed to date have not included this region. We intend to obtain such information as with the nose and mouth regions for several representative ages in children to include this region in our description of upper airway aerosol behavior.

Bibilography

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2. Strong, J.C. and Agnew, J.E. The particle size distribution of technegas and its influence on regional lung deposition. Nuclear Medicine Communications, 10, 425-430, 1989.