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Regional Aerosol Deposition in Human Upper Airways

**Annual Progress Report
for Period March 1, 1991 - February 29, 1992**

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Abstract

During the current report period experimental studies of upper respiratory deposition of radon progeny aerosols and stimulant aerosols were carried out in replicate casts of nasal and oral passages of adults and children. Additionally, preliminary studies of nasal passage deposition of unattached Po^{218} particles was carried out in four human subjects.

Data on nasal inspiratory deposition in replicate models of adults and infants from three collaborating laboratories were compared and a best-fit curve of deposition efficiency for both attached and unattached particles was obtained, showing excellent inter-laboratory agreement. This curve demonstrates that nasal inspiratory deposition of radon progeny is weakly dependent upon flow rate over physiologically realistic ranges of flow, does not show a significant age effect, and is relatively independent of nasal passage dimensions for a given age range.

Improved replicate models of the human adult oral passage extending to the mid-trachea were constructed for medium and higher flow mouth breathing states; these models were used to assess the deposition of unattached Po^{218} particles during oronasal breathing in the oral passage and demonstrated lower deposition efficiency than the nasal passage. Measurements of both Po^{218} particle and attached fraction particle size deposition were performed in a replicate nasal passage of a four week old infant.

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Replicate Model Construction

During the project report period two adult oral passage models extending from the oral entrance to the upper trachea have been constructed. These represent light and moderate exercise states of oral breathing and were made as one piece cast passages of clear polyester resin. The negative forms were fashioned from wax impressions employing a representative post mortem pharynx-larynx-upper trachea section and an anterior oral passage mold made in vivo with dental alginate material. A silicone form for this wax negative was produced to permit multiple copies of the wax negative. These oral passage models have been employed in Po^{218} unattached particle studies reported below.

Pharynx-larynx-upper trachea airway models have been obtained for infants and small children ranging from newborn to 6 years. These models are to be used with nasal models for infants and small children already constructed and with oral passage replicate airways for children which are planned to be obtained.

The construction of an adult nasal replicate which includes a surrogate liquid layer and is heated to body temperature requires an accurate one piece cast obtained from in vivo MRI Sections. A negative wax airway template is being constructed to facilitate such a nasal model, meeting the dimensional specifications of Model A.

Studies of Unattached Radon Progeny Aerosols in Replicate Models

Collaborative studies of Po^{218} aerosols with diameter averaging 0.70 nm in several upper airway replicate model have been carried out with John Strong at The Harwell Laboratory, UK. Three adult human oral passage models have been employed to obtain overall aerosol deposition data at constant flow rates ranging from 5-30 l min^{-1} . A comparison of data obtained for these studies with nasal deposition of similar size particles at similar flow rate demonstrates that for the wider mouth configurations described above, aerosol deposition is reduced to values from 45-60%, compared to values of 80-95% for the nose. Similar to the nasal studies, the dependence upon flow rate is weak, suggesting that the airway configuration is a much more important factor than the breathing rate as regards percent deposition during inspiration.

Studies of aerosol deposition have also been performed in replicate nasal passages representative of newborn and young children ($1\frac{1}{2}$ and $4\frac{1}{2}$ year old). These model nasal airways yielded deposition efficiencies nearly identical to values for adults with the same dependence upon flow rate. It is increasingly evident that the child nasal passage removes unattached radon progeny aerosol with approximately the same efficiency as the adult. The studies of adult and child nasal passage deposition carried out at three collaborating laboratories up to the beginning of the current report period have been plotted in Figure 1. A best fit curve and confidence limits are shown and it is anticipated that this curve will be used in radon progeny dosimetric models to define nasal removal of both unattached and attached aerosols.

Fig. 1

Studies of Unattached Radon Progeny Aerosol Deposition in Human Subjects

As proposed in the renewal application, it is the intent in the next project period to carry out a selected number of studies of aerosol deposition in adult human subjects to compare with the replicate model studies. During the present report period, a preliminary study of nasal deposition in four adult human subjects was carried out employing Po^{218} unattached aerosols. The nasal deposition studies were performed at constant flow rates similar to those employed with the replicate adult nasal airways. In these experiments the aerosol was drawn passively into the nasal passage and withdrawn from the mouth through a filter to collect any aerosol not deposited. The oral passage was assumed to have a removal capacity approximately equal to that of the larynx and upper trachea, so that the penetration of aerosol onto the filter represents that fraction which is accessible to the bronchial airways.

One of the factors which was hypothesized to be different in the in vivo situation (discussed above) was the diffusion of water vapor into the inspired dry air. Two features of this water vapor transport might change diffusive aerosol transport to the nasal airway surfaces. The first is the possible hygroscopic growth of the nanometer size particles which would result in a reduced diffusion coefficient and a lower deposition percent. The other is the possible phoretic motion of particles as a result of the transport of vapor away from the airway surface, also tending to reduce deposition.

Despite these two hypothesized mechanisms of deposition reduction, it was found that the nasal deposition efficiency for the Po^{218} aerosols was actually

slightly increased; the measured values of deposition for particles in the models was 80-95% whereas for the four subjects, the measured deposition percent in inspiratory flow ranged from 94-98%. This finding, although preliminary in terms of sample size, suggest that the high nasal percent deposition observed in the models does not overstate the ability of the nasal airways to remove unattached progeny aerosols, but, if anything, slightly underestimates the nasal efficiency. More studies of this nature are needed to confirm these initial observations in adults.

Studies of Attached Radon Progeny Aerosols in Replicate Models

During the current report period studies of aerosol deposition in models of the nasal passage of infants and children with particles in the 4-200 nm size range have been performed. These have been carried out with surrogate silver metal aerosol produced by evaporation-condensation, classified by electrical mobility selection, and measured prior to and after the replicate model by a previously described condensation nucleus counter (CNC). While these studies are still in progress, the results obtained to date suggest that the deposition efficiency curves for these models differ only slightly from those for adult nasal passage models and show the same trends with flow rate and particle diffusivity. These studies, when completed, will provide deposition efficiency information for infants and children for selected ages from 4 weeks to 6 years over the entire size range of unattached and attached radon progeny aerosols.

Studies of Aerosol Particles in the 0.8-12 μm Size Range

During the present report period, investigations of the deposition of inertial size particles have been carried out with adult and child nasal passage replicate models. These were performed in order to compare the behavior of large particle (0.8-12 μm) whose major mechanism of deposition is inertial impaction with small particles (attached and unattached radon progeny) whose major mechanism of deposition is diffusion. Additionally, there are a number of energy related processes which result in potential or actual human exposure to such large particles, and particularly in the case of children, no data exists which can be employed for dosimetric models of such aerosols.

Two methods have been employed to determine the size dependent nasal deposition efficiency in these replicate model. The first employs particle counting of the aerosol before and after the models by the method of size dependent time-of-flight aerosol analysis. The other method involves a radiotracer tagged monodisperse aerosol. This second method has the added advantage of being able to measure the local deposition of aerosols in a replicate model or in a human subject.

Most of the studies carried out during this period have employed the aerosols counting method with the use of an aerodynamic time-of-flight particle spectrometer (TSI Model 3300 APS). Studies performed with particles at constant flow rate (from 3 to 50 l min^{-1}) through one adult and one infant nasal model showed typical signoid shaped efficiency curves for each model when deposition

efficiency curves for each model when deposition efficiency was plotted against an inertial parameter $d_A^2 Q$ where d_A is particle aerodynamic diameter and Q is flow rate. The two curves were similar in shape but displaced along the inertial parameter axis, the infant curve showing greater efficiency for a given flow. However, when efficiency was compared not at flow rate but at similar states of rest or exercise breathing, the curves gave similar efficiencies.

These results are in general agreement with idealized impactors in that, contrary to the radon progeny results, the efficiency is a strong function of the flow rate and is also strongly dependent upon the dimensional characteristics of the prime deposition site. Because the studies were not performed with radiolabelled particles a comparison of local deposition could not be made. One study of overall deposition was performed in the adult nasal Model A with radiolabelled aerosol which yielded efficiency characteristic only slightly different from the counting method. Further studies of local deposition in the replicate nose and mouth models of adults and children are planned.

Collaboration with Other Laboratories

During the report period, studies involving collaboration with three other laboratories were performed; these were the ITRI laboratory in Albuquerque, NM, the Harwell Laboratory, UK, and the Radon Research Laboratory at Clarkson University, Potsdam, NY. These collaborations have yielded much useful information which has been reported in this and previous reports and it is anticipated that these collaborative arrangements will continue in the coming years. An indication of the continuing collaborative relationship with the ITRI

laboratory is the recent appointment of the project P.I. (D.L. Swift) as an Adjunct Scientist at the ITRI Laboratory. This appointment recognizes the continuing participation in collaborative studies and simply formalizes a working relationship which has existed for several years.

Presentation of Research at Scientific Meetings

During the period March 1, 1991 - February 29, 1992 the P.I. has presented results of studies supported by this grant as a Plenary Speaker at the U.K. Aerosol Society (March 25-27), at the American Industrial Hygiene Conference (May 20-24), at a specially conference and faction, Chemical Signals in Vertebrates (June 18-20), at the Seventh International Symposium on Inhaled Particles (September 16-20), and at the annual conference of the American Association for Aerosol Research (October 7-11). Additionally, presentation and discussion of research findings and plans was held at the D.O.E. Radon Research Contractors Meeting (August 25-27).

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