Bioimaging Defence Functions of the Respiratory Tract

A fresh observation of how particles clear the airway has application in diagnosing and monitoring the patient with respiratory problems.

by Wolfgang G KREYLING and Thorsten WOHLAND

Greeks and Romans reported their use of therapeutic aerosol applications for respiratory problems more than 2,000 years ago. Such applications for diagnosis, however, gained popularity only in the last 30 to 40 years.

Researchers at the GSF-Research Center for Environment and Health, Institute for Inhalation Biology and Focus Network: Aerosols and Health, in Munich, Germany, and the National University of Singapore have developed a method to assess the mucociliary-clearance function of tiny hairs called cilia in mucous membranes. They chose a dog as their animal model because its mucociliary-clearance apparatus compares to that of a human.

According to previous work, the speed of mucus transport from the trachea to the smallest airways in the lungs, or bronchioli, changes by more than 1,000 times. Since a reproducible deposition pattern of test particles is almost impossible to achieve in spontaneously breathing dogs or human subjects, the researchers applied a new technique developed by the Munich team (*Inhalation Toxicology* 11(5):391–422, 1999). They measured the tracheal-mucus-velocity (TMV) profile after spraying test particles onto the surface of the deep end of the trachea and right-main bronchial branch. Evidence shows that tracheal-mucus movement reflects a ciliary wave motion towards the larynx.

To verify this motion's application, the investigators used micro-sized polystyrene particles containing radioactive indium. Using a flexible fibre-optic bronchoscope they sprayed a 50µL particle suspension onto the epithelial surface under direct visual control. They employed a gamma camera to track the movement of the particles, collecting images taken at one-minute intervals. A TMV profile was determined along the trachea from bronchus to larynx.

Figure 2 shows integrated images of the particle pathway along the trachea from the right bronchus to the larynx within one hour of particle application. Hot regions represent anatomical locations at which the particles stayed longer, as demonstrated by accumulation in the larynx before being swallowed. Faint regions indicate rapid particle transport by mucociliary action. Most dogs display a hot spot at the distal end, implying delayed mucociliary

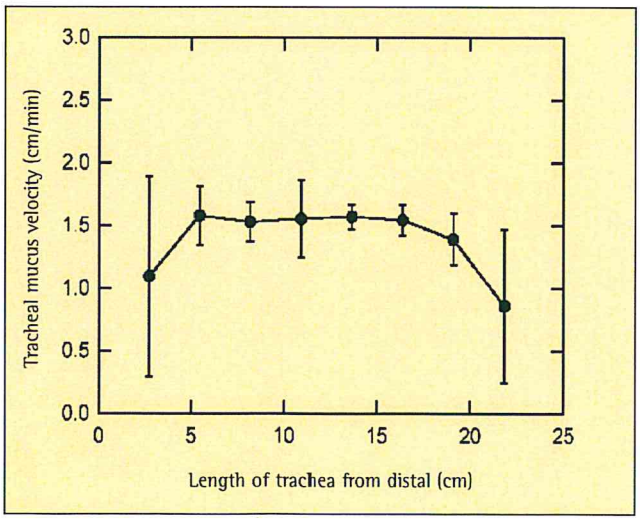

Figure 1: Profile of tracheal-mucus velocity of a dog subject starting from the far end of trachea. Mean value ± SD from three measurements during a six-month period.

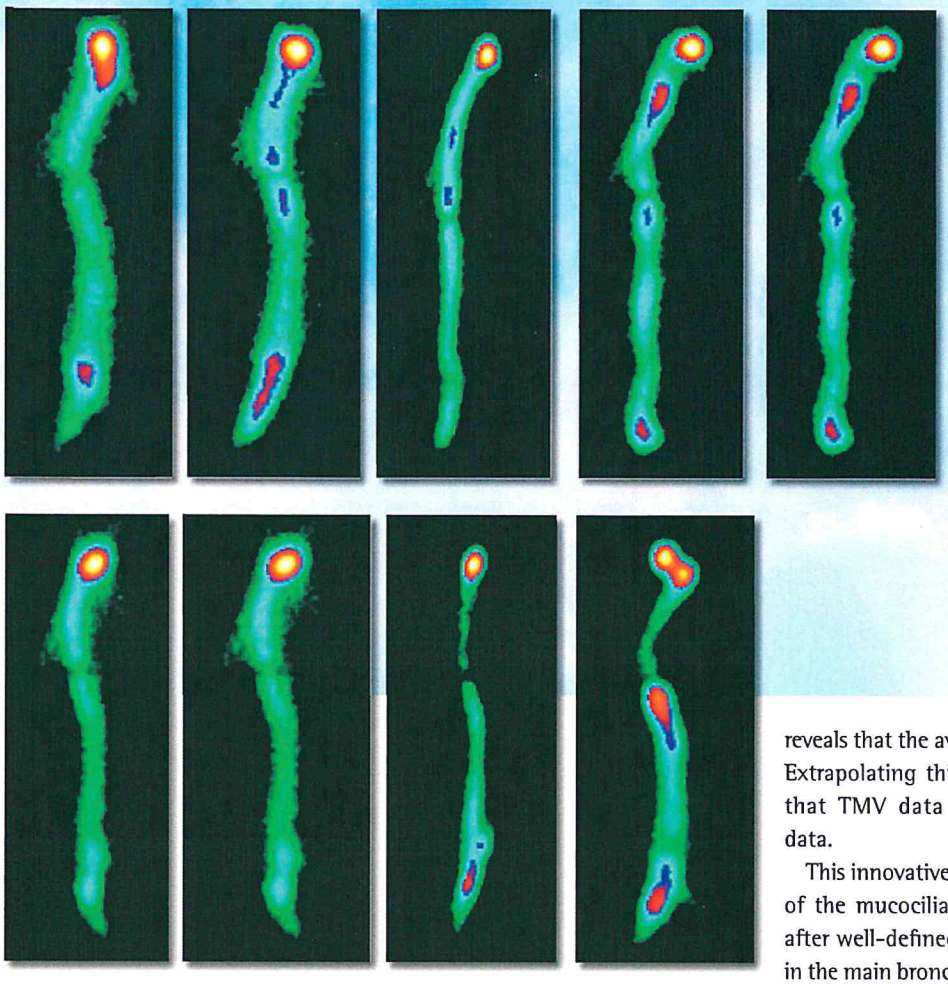

Figure 2: Integrated images of nine dogs during the hour following particle application from the right side of each dog's upper chest and neck. The dog rests in a custom-made box that positions the animal comfortably in front of the gamma camera. Particles in the right upper bronchus correspond to the lower end of the frame.

Each image shows the particle pathway along the trachea from the right bronchus to the larynx. Hot regions represent locations at which the particles remained longer as demonstrated by the larynx's accumulating particles before they were swallowed. Faint regions indicate rapid particle transport by mucociliary action. The black spot in the upper third of each image results from gamma-ray absorption of the plate of the body box in front of the dog's thorax with a projection thickness of 12cm between the neck of the dog and the gamma camera.

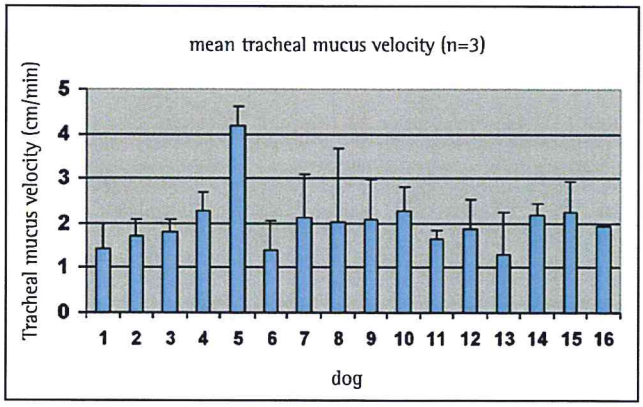

Figure 3: Mean tracheal mucus velocity of three measurements of 16 beagle dogs within a period of six months.

transport from the location of deposition, perhaps caused by absorption of the 50µL aqueous liquid. Most dogs show delayed particle transport in the upper trachea, as indicated by high-radioactivity regions. The TMV profile, seen in Figures 1 and 3, reveals that the average ranges from 1–3cm per minute. Extrapolating this data to a human subject suggests that TMV data are fingerprint-like representative data.

This innovative method allows precise measurements of the mucociliary clearance function in the trachea after well-defined deposition of uniform test particles in the main bronchus, allowing quantitative insight into a critical function of the respiratory tract that maintains the sterility of the conducting airways.

This approach's value lies in its diagnostic accuracy resulting from the precise deposition of the test particles at the lower end of the trachea and the subsequent clear scan along the airway. Currently, no such diagnostic tool exists in hospitals that treat lung problems. Its risk is low with the relatively low radio-dose.

Even though introduction of the test particles is slightly invasive, a patient undergoing inspection with a bronchoscope – flexible fibre-optic instrument with a small light on the end for inspection of the epithelial surface of the bronchi – does not face any additional risk.

Therefore, the methodology can be used to describe changes in patients who suffer from disease of the conducting airway epithelium. In addition, this test may be applicable to personnel exposed to occupational hazardous aerosols and to smokers.

Wolfgang Kreyling is a researcher with GSF-Research Center for Environment and Health, Institute for Inhalation Biology and Focus Network: Aerosols and Health, Munich, Germany. For more information contact him at kreyling@gsf.de or Thorsten Wohland at chmwt@nus.edu.sg