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Exhaled breath particles – a biomarker for detection of lung disease?

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The chemical analysis of exhaled breath is a convenient and non-invasive method for the examination of the lung that provides information on pulmonary status directly from the airways and alveoli. The exspired air contains small particles generated in the deep lung. Due to lack of systematic data correlating the particle emission flux with respiratory variables it is unclear to which extent the chemical analysis of the particulates could be used for detection and monitoring of airway disease. Therefore we carried out a clinical study to determine the relevant parameters for number and mass flux of the exhaled particles.

An experimental set-up was designed to record the particle concentration, the size distribution and the air flow with high time resolution. The particle concentration was measured by a condensation nuclei counter (TSI 3760), the size distribution was analysed using a laser spectrometer (PMT Lasair II-110) sizing particles in six channels in the range between 0.1 µm and 5 µm. The airflow is recorded simultaneously using a flow sensor. Precautions were taken to prevent water vapour condensation in the measuring system: the flow sensors and the CNC were placed inside a box thermostated to 37 °C. The sample air of the particle sizer was sufficiently diluted.

For 14 healthy volunteers (aged 21 – 55 years) and four patients with moderate-to-severe COPD the properties of the exhaled aerosol were recorded for different tidal volumes.

For all healthy subjects, the number of particle emitted per breath, N, rose exponentially with increasing ventilation ratio, defined as ratio of tidal volume, V_T, to vital capacity, VC,

$$N = A \cdot \exp\left(\beta \frac{V_T}{VC}\right)$$

with β in the range of 6 – 10. A high interday and intraday reproducibility was found for the number of the exhaled particles. However, there was a large inter-individual variability in N covering about two orders of magnitudes (factor A in the range of 0.8 to 103 for healthy subjects).

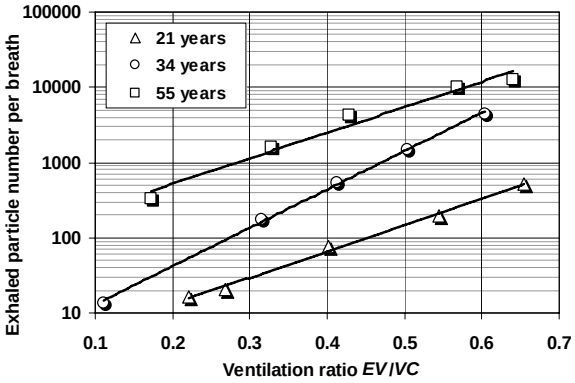

Figure 1. Exhaled particle number for healthy subjects of different age

The number of exhaled particles is determined by the particle generation rate in the lung and the rate of redeposition in the airways during exhalation, mainly due to diffusive and gravitational deposition. For all subjects the particle size was predominantly in the submicron range, with count median diameter at 0.4 µm. Larger particles are deposited by gravitational settling.

The tidal volume turned out to be the most important variable determining the exhaled particle flux of the individual subject. The exponential behaviour of the particle emission flux as function of the ventilation ratio suggests that reopening of collapsed terminal airways linked with a sudden break-up of the surfactant film is the main mechanism for aerosol generation in the lung. Further studies have to be carried out to identify other relevant determinants for the number of exhaled particles and eventually to explain the large inter-subject variability. This is necessary to evaluate the usefulness of exhaled breath particle analysis as a biomarker for detection of lung disease.