Göteborg, 2022

Exploring small airways using breath analyses

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i sal Europa vid konferenscentrum Wallenberg, Medicinaregatan 20A, Göteborg. Fredagen den 10 juni 2022, klockan 13:00

Av Emilia Viklund

Fakultetsopponent:
Professor Ellen Tufvesson
Lund Universitet, Sverige

Avhandlingen baseras på följande delarbeten

I. Bake, B, **Viklund, E**, Olin, A-C. Effects of pollen season on central and peripheral nitric oxide production in subjects with pollen asthma. *Respiratory Medicine 2014*; 108: 1277e1283.

II. **Viklund, E,** Kjellberg, S, Schiöler, L, Almstrand, A-C, Gustafsson, P, Olin, A-C. Major surfactant phospholipids, exhaled particles and small airways ventilation inhomogeneity in adult asthma. *In manuscript*

III. **Viklund, E**, Bake, B, Hussain-Alkhateeb, L, Koca Akdeva, H, Larsson, P, Olin, A-C. Current smoking alters phospholipid- and surfactant protein A levels in small airway lining fluid: An explorative study on exhaled breath. *PLoS ONE 2021*; 16(6): e0253825.

IV. **Viklund, E**, Kokelj, S, Larsson, P, Nordén, R, Andersson, M, Beck, O, Westin, J, Olin, A-C. Severe acute respiratory syndrome coronavirus 2 can be detected in exhaled aerosol sampled during a few minutes of breathing or coughing. *Influenza Other Respi Viruses 2022*; 1-9. doi:10.1111/irv.12964.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN

GÖTEBORGS UNIVERSITET

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Exploring small airways using breath analyses

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Abstract

Airway irritants such as allergens, tobacco smoke and viruses may cause damage in the small airways, usually undetected with routine diagnostic methods. Analyses of endogenously produced nitric oxide (NO) and endogenously produced small droplets (i.e. particles) in breath (PEx), have the potential to reflect exposure related changes in the small airways. Furthermore, in PEx, both exposure and effect markers can potentially be analyzed. The overall aim of this thesis was to explore small airway effects of exposure to airway irritants in healthy subjects, in subjects with asthma, in cigarette smokers and in subjects with COVID-19 infection, by examining exhaled breath. We explored methods to model alveolar NO (CANO), the number of PEx as well as content of major surfactant lipids and proteins in PEx. In addition, we explored if COVID-19 infection could be detected in PEx.

Pollen season was not associated with an increase in CANO, although it was markedly increased in some subjects with asthma. Small airways ventilation inhomogeneity in subjects with asthma was associated with slightly increased CANO on group level, and markedly increased in some subjects, with no difference on levels of surface active lipids in PEx but markedly decreased number of PEx. Current compared to never smokers were associated with higher levels of lipids in PEx in subjects with normal lung function. Current smokers were associated with higher levels of surfactant protein A in PEx and number PEx in subjects with impaired lung function. Detection of SARS-CoV-2 RNA was possible in PEx, in some but not all subjects early in disease course of COVID-19. RT-PCR analyses were performed on PEx-samples generated from as little as 20 relaxed breaths, 10 deep breaths and 3 coughs.

These results of breath analyses including endogenously produced particles and alveolar NO highlight the potential of these methods to reveal effects of airway irritants in small airways prior to lung function decline. Furthermore, PEx are shown to contain SARS-CoV-2 RNA in subjects with confirmed COVID-19, highlighting the potential of detecting respiratory virus infection in exhaled breath.

Keywords: Exhaled particles, small airways, alveolar nitric oxide, SARS-CoV-2, birch pollen, smoking, lining fluid

ISBN: 978-91-8009-781-9 (TRYCK) http://hdl.handle.net/2077/70939
ISBN: 978-91-8009-782-6 (PDF)