Agnė Krilavičiūtė
Dr. sc. hum

Potential use of analysis of volatile organic compounds in exhaled breath for cancer screening

Fach/Einrichtung: DKFZ (Deutsches Krebsforschungszentrum)
Doktorvater: Prof. Dr. med. Hermann Brenner

Cancer is a leading cause of death worldwide. Early detection is essential to improve successful treatment and reduce cancer mortality, and cancer screening in the asymptomatic general population might be a particularly promising approach to achieve this goal. However, direct screening of the asymptomatic population may be suboptimal due to potential harms arising from the invasiveness of the screening methods, high resource utilization and cost. There is a need for reliable non-invasive screening tools that can preselect high-risk populations for further invasive screening and that could achieve high levels of adherence at virtually no risk in population-based screening.

The aim of this dissertation is to provide further insight into exhaled breath analysis for cancer detection and to explore the potential of non-invasive breath testing for cancer screening.

First, a systematic literature review was performed to summarize the current state of exhaled breath analysis for cancer detection. Overall, 73 studies were identified that focused on detecting cancers through exhaled breath, including common malignancies, such as lung, breast and colorectal cancer (CRC), as well as more rare malignant diseases (e.g., malignant mesothelioma). Very good diagnostic performance of breath tests was demonstrated for all cancer types, but overoptimistic results could have been reported as one out of four studies did not employ any validation procedures. Furthermore, substantial differences were revealed in breath collection, storage and analysis methods between the studies. Further studies on exhaled breath analysis for cancer detection, particularly, the validation of already reported results, together with exploring factors that may have an influence on breath analysis results, are needed.

Second, potentially important covariates that can influence breath test results were investigated using data obtained by gas chromatography-mass spectrometry (the gold standard for analytical methods) analysis. Breath samples from more than 1,400 healthy individuals were used to explore whether socio-demographic (e.g., sex, nationality), lifestyle factors (e.g., smoking prevalence, diet) and various medical conditions (e.g., diabetes), can influence breath analysis results. Fourteen volatile organic compounds which were present in the breath samples in the majority of the patients were analyzed, and statistically significant differences were demonstrated for sex and nationality, as well as between people consuming certain food products (e.g., coffee, fermented milk and onion leaves) at different frequencies. These results suggest, that differences in socio-demographic and lifestyle factors can be measured in exhaled breath and they might influence the results of breath testing for cancer detection as prevalence of such factors varies between populations.

Finally, using available data on breath tests diagnostic performance for CRC and gastric cancer (GC) detection, the potential of breath testing for cancer screening was examined. For that, the prevalence of preclinical CRC and GC (the target for the screening) was estimated and these data were used to derive positive predictive values (PPVs) of breath tests in various populations worldwide. My results suggest that restricting the screening to high-risk populations preselected by breath testing can substantially improve screening programs. For example, the number needed to screen to detect one GC in populations positive for breath testing is approximately 10-fold lower than that in populations without prescreening. Prescreening by breath testing might improve overall screening effectiveness through reducing the number of unnecessary invasive procedures and lowering overall cost, as well as improving participation rate that currently is not satisfactory. However, more data on breath testing for CRC and GC detection derived from diverse populations are needed to determine the full potential of breath testing in cancer screening.

In summary, breath analysis as a non-invasive, harmless and potentially cheap method holds great potential for cancer screening. Existing evidence on diagnostic performance for cancer detection suggests that breath testing can be a powerful tool to enhance cancer screening programs. While breath testing might not be suited to determine the final cancer diagnosis, the use of breath testing for the preselection of high-risk groups for further screening by more invasive methods could substantially improve effectiveness and cost-effectiveness of screening programs.