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A Miniature Sorbent-Coated Capillary Device for Efficient Breath Volatile Organic Compound Capture and Analysis

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Short Report

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Abstract

Non-invasive breath analysis holds immense potential for early-stage cancer detection due to its ease of sample collection and the presence of disease-specific volatile organic compound (VOC) markers. Existing methods often face limitations in portability, sample-to-analysis speed, or capture efficiency. Here, we present a novel miniaturized device utilizing a sorbent-coated capillary for rapid and efficient capture of diverse VOCs directly from exhaled breath. Utilizing a liquid polymer-based sorbent, the device successfully captured VOCs from real breath samples, demonstrating its potential for broader VOC detection and disease-specific analysis.

Introduction

With advancements in measurement techniques, the human breath has emerged as a rich source of information about our health. Thousands of volatile organic compounds (VOCs) have been identified within breath samples, some of which exhibit a remarkable correlation with specific disease states. For example, breath signatures have been linked to asthma (Namjou et al., 2006), diabetes (Deng et al., 2004; Wang et al., 2010), breast cancer (Phillips et al., 2006, 2010), colorectal cancer (Altomare et al., 2013), esophagogastric cancer (Kumar et al., 2013), and lung cancer (Poli et al., 2010; Mazzone et al., 2012). Recent comprehensive analysis has even identified and catalogued nearly 1800 VOCs present in healthy human breath (de Lacy Costello et al., 2014). This exciting field underscores the potential of non-invasive breath analysis for early-stage disease detection and personalized medicine.

However, as Horvath et al. highlighted in their summary of the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations for breath analysis, successful translation of this potential into clinical practice requires robust technologies that address key challenges (Hovarth et al., 2017). Existing methods often suffer from limitations such as bulky instrumentation, complex sample preparation steps, or limited capture efficiency for diverse VOCs. To address these limitations, we present a novel miniaturized device utilizing readily available sorbent materials to capture and analyse a broad range of VOCs directly from exhaled breath (Fig. 1, 2 panel A, B). This approach holds promise for overcoming current hurdles and advancing the field of breathomics-based diagnostics.

The overall purpose of this work is to develop a new and easy breath sampling technique to collect and detect lung cancer biomarkers. The technique achieves specificity and sensitivity suitable for screening high-risk lung cancer patients. The specific aims are:

a) To Screen for lung cancer biomarkers using exhaled breath condensate.

b) To develop a new sampling technique for breath analysis.

c) To enable early-stage lung cancer screening.

FIGURE 1

Materials and Methods

This short communication describes the development and application of a novel breath sampling device for capturing volatile organic compounds (VOCs). Our device utilizes a simple yet effective design (≈ 5 cm^3). Exhaled breath flows directly through a coated glass capillary containing a high-affinity sorbent material.

GC-MS instrument: The GC-MS system consisted of a HP 6890-Plus gas chromatograph and a mass selective detector model 5973 (Palo Alto, CA USA) equipped with a programmed temperature vaporiser (PTV). The software used for data processing, Enhanced Chemstation G1701BA version B.01.00, was supplied by Hewlett Packard Company (Atlanta USA). The column used was a fused silica capillary column, CP-Sil8CB, (25 m, 0.32mm, df: 0.25 mm) from Chrompack (Netherlands). Helium and methane gas were obtained from ScanGas (Stockholm, Sweden).

Results

Coated Capillaries

Glass (quartz) capillaries were used in our study (inner diameter = 3 mm, length = 100 mm). The glass capillary was activated with acidic and basic solutions before the immobilisation of the liquid polymer (phenyl methyl silicone or polyethylene 35 glycol). For the activation of the capillary surface, i.e. producing reactive silanol groups, the capillary was filled with hydrochloric acid (0.1 M) and left for 60 minutes at room temperature. The capillary was rinsed with Milli-Q water and left to dry. The capillary was then filled with sodium hydroxide (1.0 M) for 60 minutes at room temperature to activate the silanol groups (hydroxyl groups, OH). After an additional Milli-Q rinse, the capillary was left to dry. The polymer (phenyl methyl silicone (OV 17 from Sigma-Aldrich) or PEG-400 (Sigma-Aldrich)) used for coating was dissolved in acetone or dichloromethane to a concentration of ~ 2.0mg/ml to facilitate the coating procedure. The activated capillary was filled with polymer solution and was left for 4 hours at room temperature allowing evaporation of acetone and dichloromethane. The capillary was left at 40°C overnight. The following day, the capillary was heat-treated by progressively increasing the temperatures from 40°C up to 250°C, where it was left for 2 hours. Figure 2 (panel C and D) shows SEM micrographs of uncoated and coated capillary surface. The polymeric coating could be observed.

Breath Collection

Breath samples were collected from four participants with lung cancer, who refrained from eating for 4 hours prior to the test. Each patient performed tidal breathing of unfiltered room air, inhaling through their nose and exhaling through their mouth into the breath collection device for several minutes. Care was taken to ensure absence of plants, perfumes and other sources of VOCs in the breath collection rooms, so that the VOCs in the collection devices could be considered mainly originating from patient's

exhaled breath. The breath sample was stored at room temperature in a plastic tube until analysis by GC-MS.

The capillaries were inserted into a GC injector chamber for analysis. Analytes were thermally desorbed by programmed heating (50°C-250°C), separated on a GC column, and identified through mass spectrometry. Figure 3 shows the MS-spectra obtained from two lung cancer patients.

Discussion

The device successfully captured and concentrated distinct VOCs from breath samples, demonstrating its efficacy for non-invasive biomarker detection. We could identify acetaldehyde (a known breath biomarker), decane, pentane, and octane from the breath of patients with lung cancer. Figure 3 presents GCMS spectra from the breath analysis of two patients and clearly shows the presence of ions corresponding to acetaldehyde (m/z 44), pentane (m/z 48), acetone (m/z 57), butanal (m/z 71), octane (m/z 114) and decane (m/z 142) among others. Importantly, the effective capture of such diverse VOCs highlights the device's potential for identifying complex and unique VOC signatures potentially associated with specific diseases, including cancer. The identification of these specific VOCs aligns well with previous studies focussed on identifying lung cancer biomarkers, confirming the clinical relevance of our preliminary findings (Poli et al., 2010; Mazzone et al., 2012). Future studies will focus on validating these findings in larger patient cohorts and assessing the device’s quantitative capabilities. The VOC capture capability is broad, and the possibility to incorporate sorbents such as sol-gel, MIP and others can increase the number and variation of captured VOCs, holding significant promise for improved breathomics analysis and personalized medicine.

Conclusion

This short communication demonstrates the successful development and initial results of a miniaturized device for capturing an array of diverse VOCs directly from exhaled breath. The identification of several distinct compounds from breath, including known biomarkers for respiratory illnesses, highlights the device's potential for broader VOC detection and disease-specific analysis. Given its ease of handling, rapid performance, and cost-effectiveness, this method holds significant promise for future applications. Further research will focus on optimizing the device's sensitivity and selectivity for a wider range of VOCs and conducting clinical studies to validate its potential for cancer screening and personalized medicine applications.

Declarations

Human Ethics Declaration:

Breath sampling was performed by licensed physicians at Gävle Hospital in accordance with the institution's clinical guidelines and the Declaration of Helsinki. Procedures complied with local regulations for non-interventional clinical sample collection.

Ethics Approval:

Human breath sampling was performed by licensed physicians at Gävle Hospital in accordance with the hospital's clinical governance and ethical oversight procedures. The activity fell within routine clinical practice and did not require additional research ethics approval.

Consent to Participate:

All participants provided informed consent prior to breath sampling and analysis.

Conflict of Interest:

The authors declare no conflict of interest.

Funding Declaration

This study received no external funding.

Author Contribution

M.A conceived the study, designed the device, and generated the results. M.A and A.A. wrote and reviewed the manuscript.

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Data Availability

We generated the included results (SEM images and spectra). The uncropped images has been provided in supplementary materials now attached.

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Figures

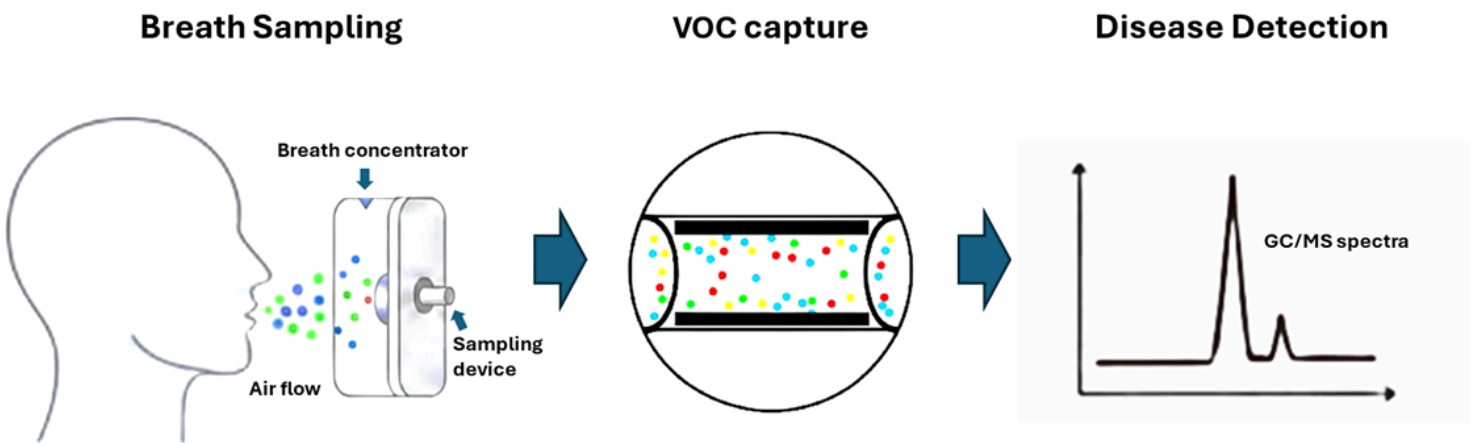


Figure 1

Graphical Abstract: Illustrated workflow of the miniature VOC capture device for non-invasive disease detection, showing breath collection, VOC capture, and analysis.

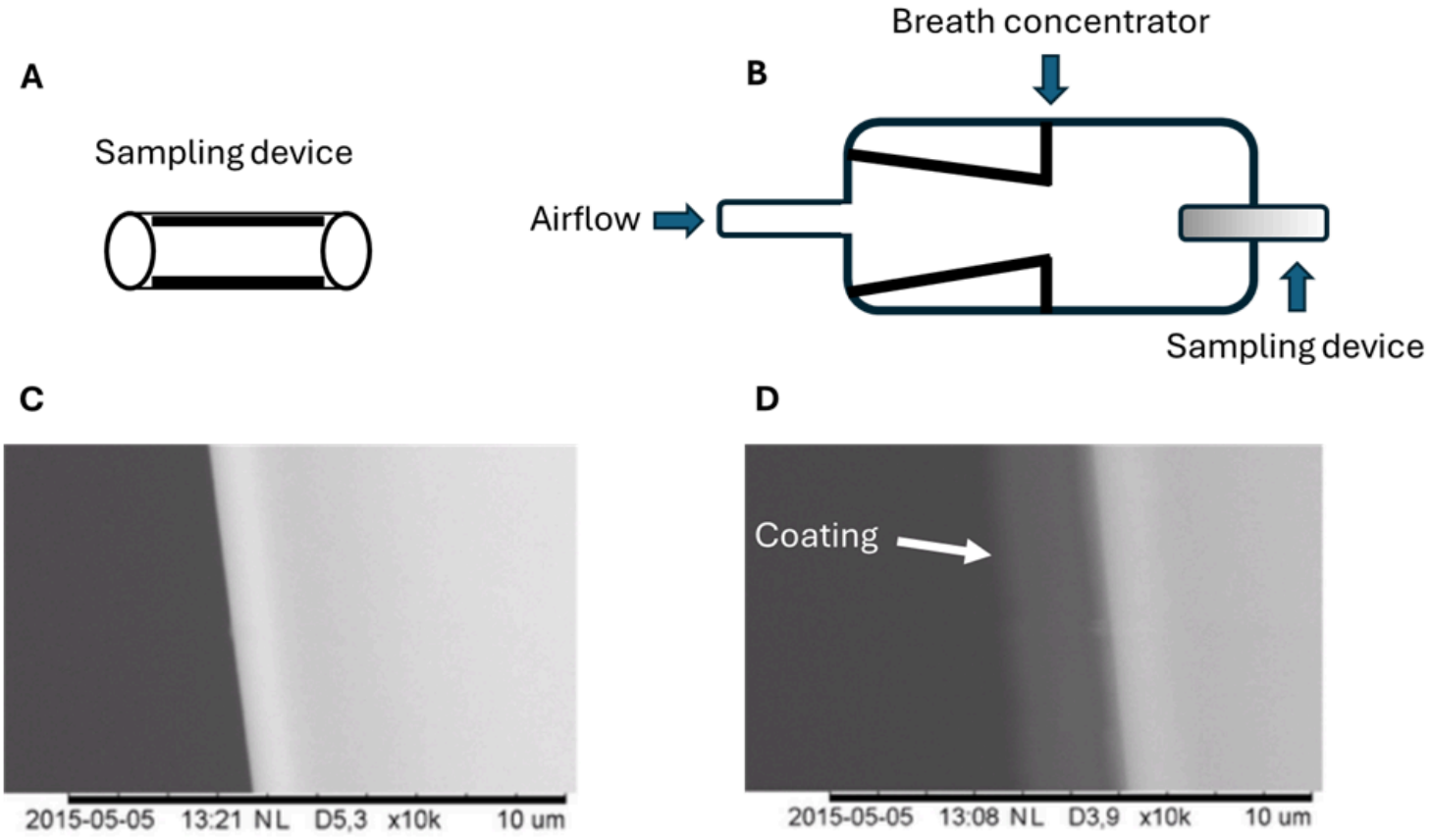


Figure 2

Sampling device consisting of a capillary containing a polymeric coating (A). Example of the sampling device as part of a breath concentrator to capture VOCs from larger volumes of breath (B). SEM micrographs of uncoated (C) and coated (D) capillary surface. The polymeric coating can be observed as a diffuse layer on top of the white capillary.

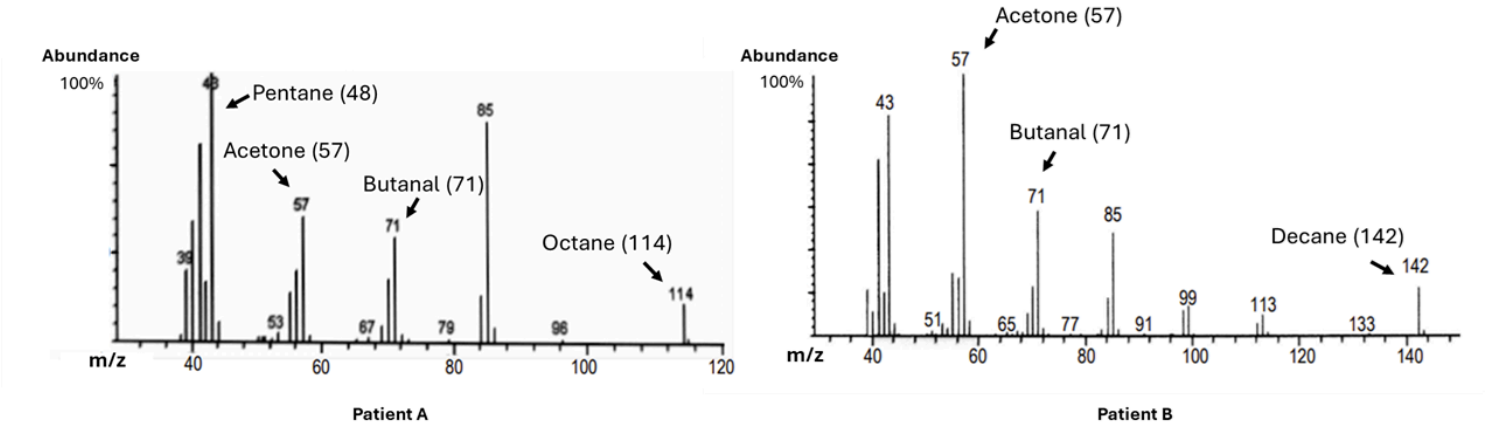


Figure 3

GC/MS spectra of the analysis from two lung cancer patient breath samples. Names of identified compounds are indicated along with m/z.

Supplementary Files

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- SupplinfoCommunicationmicrochimicaacta.docx