

Breath for breast cancer: Volatile aldehydes for diagnosis

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Breath analysis for cancer

Breath is beginning to take on increasing importance in the clinical world as its potential for diagnosing various diseases is unfolding, especially cancers. There have been a number of studies describing how particular volatile compounds that are exhaled by patients can predict the presence of lung cancer. However, cancers in other parts of the body that are disconnected from the lungs can also produce signal metabolites that end up in the breath, such as colorectal, prostate, and head and neck cancers.

In China, Yixiang Duan and colleagues from Sichuan University have been taking a closer look at breast cancer and the possibility of breath for diagnosis. While this is not a new approach for breast cancer, the reports from other research groups have differed in their diagnostic potential.

Duan decided to concentrate on straight-chain aldehydes, which have been earmarked as lung cancer biomarkers. These compounds are produced in the body by lipid peroxidation and are relatively insoluble in blood, so pass quickly into breath and are excreted within minutes of their formation. In preliminary studies, the levels of hexanal, heptanal, octanal and nonanal in exhaled breath differed between breast cancer patients and healthy controls, so these four were selected for a more detailed examination.

They decided to use direct GC/MS to analyse the breath samples with no preconcentration, a technique that has not been applied previously to the analysis of aldehydes for detecting breast cancer.

Aldehydes analysed by direct GC/MS

Exhaled breath contains about 200 different volatile organic compounds, so the efficiency of the GC column in separating the four aldehydes is highly important. A popular nonpolar commercial column coated with 5% phenyl methylpolysiloxane did not perform well, the aldehydes not being detected by GC/MS at all. A longer column with a weakly polar coating of 6% cyanopropyl-phenyl-94% dimethylpolysiloxane performed much better, separating the aldehydes clearly from the other metabolites within 24 minutes.

Breath from patients with breast cancer and benign breast tumours was compared with that from healthy people. They blew through a cardboard mouthpiece into a sample device comprising an inert plastic syringe with a one-way valve piston which trapped the last portion of the breath without contamination from breath from the mouth or bronchial tubes.

The trapped breath was transferred to a Tedlar bag for storage before being sampled with a glass syringe and injected onto the GC/MS system. The aldehydes were confirmed from their retention times and mass spectra and measured by integrating three ions each from the extracted ion chromatograms.

Accurate cancer diagnosis

The levels of each of the aldehydes clearly separated the three groups of people, ranging from 3.74-6.53, 10.78-19.77 and 22.52-47.27 ppbv for healthy, benign tumour and breast cancer patients. However, rather than relying on one individual compound, the researchers devised a model based on all four intended to predict the presence of breast cancer.

This model distinguished breast cancer patients from healthy controls with a sensitivity of 72.7% and a specificity of 92.7%. This accuracy is of the same order as those of conventional methods of diagnosing breast cancer but the non-invasive sample collections, the ease of breath collection and the relatively rapid GC/MS procedure make it an attractive option.

The direct nature of the analysis, omitting preconcentration of the volatiles in the breath samples, meant that only 30 volatiles in total were detected, the majority being of low abundance. However, the target compounds were measurable and allowed the breast cancer patients to be identified.

It is still early days due to the low number of patients tested: 22 with breast cancer, 17 with benign breast tumours and 24 controls. A wider study that also encapsulates further volatiles, possibly more aldehydes, will strengthen the diagnostic capability of the method.

Related Links

(*) [Clinica Chimica Acta 2014, 436, 59-67](#): "Investigation of potential breath biomarkers for the early diagnosis of breast cancer using gas chromatography–mass spectrometry"

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Investigation of potential breath biomarkers for the early diagnosis of breast cancer using gas chromatography–mass spectrometry

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Highlights

- We identified and assessed exhaled straight aldehydes as potential BC biomarkers.
- Exhaled hexanal, heptanal, octanal, and nonanal levels were higher in BC.
- Breath biomarkers for BC early diagnosis were successfully verified.
- These aldehydes might be BC biomarkers and their joint use had superior result.

Abstract

Background

Breast cancer (BC) remains the most commonly diagnosed malignancy in women. We investigated 4 straight aldehydes in the exhaled breath as potential early BC diagnostic biomarkers.

Methods

End-tailed breath were collected by Bio-VOC® sampler and assayed by gas chromatography–mass spectrometry. Kruskal–Wallis one-way analysis of variance test and binary logistic regression were used for data analysis. The diagnostic accuracies were evaluated by receiver operating characteristic curves. A predictive model/equation was generated using the 4 biomarkers and validated by leave-one-out cross-validation.

Results

All four potential biomarkers demonstrated significant differences in concentrations between BC and healthy controls (HC) ($p < 0.05$). The areas under the curves (AUCs) in HC vs BC_{I-II} model using hexanal, heptanal, octanal, and nonanal were 0.816, 0.809, 0.731, and 0.830, respectively. The AUC for their combined use was 0.934 (sensitivity 91.7%, specificity 95.8%) in the early diagnosis of BC. The predictive model/equation exhibited good sensitivity (72.7%) and specificity (91.7%) in distinguishing between HC and BC (cross-validation: sensitivity 68.2% and specificity 91.7%).

Conclusions

The diagnostic values of 4 exhaled straight aldehydes as early diagnostic biomarkers for BC were successfully verified and the diagnostic accuracy improved in their combined use.

Keywords

- Breast cancer;
- Early diagnosis;
- Noninvasive diagnosis;
- Biomarkers;
- Breath analysis

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