On-line breath analysis of volatile organic compounds as a method for colorectal cancer detection

Francisco Zambrana1, Ana Herrero2, Guillermo Vidal-Mínguez2, Gonzalo Balador2, Ernesto Criado1, Carmen Sánchez-Avila1, Isabel Marquina3, Maria Senero1, César Gómez-Raposo1, Miriam López-Gómez1, Maria Merino1, Cristina Aguayo1, Mario Alvarez-Gallego1, Damián García-Orló1, José C. Erdoeslín1, Carmen Comas1, Noemi Manzurrién1, Jaime Feliu1, Enrique Casado1

1. Oncology Department, Hospital Universitario Infanta Sofia, Madrid, Spain, 2. European Society of Differential Mobility Analysis (SEADM), Valladolid, Spain, 3. Surgery Department, Hospital Universitario La Paz, Madrid, Spain

Abstract

Background: Analysis of breath volatile organic compounds (VOCs) in breath is an emerging approach for cancer diagnosis, but it is less known about its potential use as biomarker for colorectal cancer (CRC). We investigated whether combination of VOCs could distinguish CRC patients from healthy volunteers.

Methods: In a pilot study, we prospectively analyzed breath exhalations of 38 CRC patient and 43 healthy controls allicollectedenized for average mass. The samples were analyzed and analyzed using a Secondary Electrospray Ionization (SESI) coupled with a Time-of-Flight Mass Spectrometer (SESI-TOF-MS). After a minimum of 30 min fasting, volunteers deeply breathed in through the mouth and sampled at the same time: a normal breath and a deep breath. In each sample, it was necessary to have at least one VOC with a minimum mass of 30 Da and a maximum mass of 431 Da. The background contamination is reduced by an average factor of ten. Potential contaminants from the patient or the environment that could interfere with the result were analyzed.

Results: 259 VOCs, with masses ranging from 30 to 431 Da have been identified in the exhaled breath. The obtained data was compared with the Metlin Database to identify the candidate VOCs, a set of 9 biomarkers were detected: 6 from healthy volunteers was obtained, showing an average recognition rate of 81.94%, a specificity of 76.85%.

Conclusions

- Although these results are quite promising, we have discovered that some of these variables present a confounding evolution which may be produced by contaminants in the environment. Therefore these results should be taken with caution.

References


1. - 255 VOCs, with masses ranging from 30 to 431 Da have been identified in the exhaled breath.

- Using a classification technique based on the ROC curve for each VOC, a set of 9 biomarkers discriminating the presence of CRC from healthy volunteers was obtained, showing an average recognition rate of 81.94%, a sensitivity of 87.04% and specificity of 76.85%.

2. - CRC is one of the most common cancers in the Western world, with high incidence and mortality. Slow progression from adenoma to carcinoma and high patient survival in case of early detection makes CRC an ideal candidate for screening. Screening programs for CRC are being developed throughout the world, mainly due to the CRC participation rates under 60% in the average-risk population using the recommended tests (gFOBT or endoscopic techniques).

There are some evidence supporting a different pattern of VOCs in breath in cancer patients, due to the different metabolism of cancer cells producing different VOCs.

- Although these results are quite promising, we have discovered that some of these variables present a confounding evolution which may be produced by contaminants in the environment. Therefore these results should be taken with caution.

3. - Despite these, overall sensitivity and specificity results are encouraging to pursue investigating the potential use of breath analysis for detecting CRC.

We are recruiting in a new pilot study including breath cleaning procedures, random distribution of patients and a sporonic analysis incorporated into the postprocessing algorithms, to better control for confounding variables.

Conclusions

SEADM-based analysis shows high sensitivity for the discovery of candidate biomarkers in breath and allows online analysis without a pre-concentration step.

We couldn’t find in breath obvious differences in the pattern of VOCs between CRC patients and healthy controls. Species coming from the inhaled air and those related to the long term diet seem to be the main confounding variable to control.

Despite these, overall sensitivity and specificity results are encouraging to pursue investigating the potential use of breath analysis for detecting CRC.

We are recruiting in a new pilot study including breath cleaning procedures, random distribution of patients and sporonic analysis incorporated into the postprocessing algorithms, to better control for confounding variables.

Objectives

- To determine whether a combination of VOCs could distinguish CRC patients from healthy volunteers. It was our purpose to provide a framework for a new pilot study in this area.

References