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Study of exhaled air composition during recovery after respiratory disease by mass spectrometric analysis

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Abstract. This article considers the possibility of monitoring recovery after respiratory diseases by mass spectrometric methods. Two groups of test subjects took part in the study: 18 individuals who had had a respiratory viral infection and 31 healthy volunteers in good physical condition. A noninvasive mass spectrometric method of controlling the gas composition of exhaled air was used in the study. The results of the experiment demonstrate the effectiveness of the technique: the differences detected in the mass spectra of healthy people and subjects who had a respiratory viral infection allow the technique to be used to search for pathology markers.

Keywords: mass spectrometry, gas composition analysis, exhaled air, acute respiratory viral infection, principal component method

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Исследование состава выдыхаемого воздуха в период восстановления после респираторного заболевания методом масс-спектрометрического анализа

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Аннотация. В статье рассматривается возможность мониторинга восстановления после перенесенных респираторных заболеваний методами масс-спектрометрии. В исследовании приняли участие две группы испытуемых: 18 человек, переболевших респираторной вирусной инфекцией, и 31 здоровый доброволец в хорошей физической форме. В исследовании использовалась неинвазивная масс-спектрометрическая методика контроля газового состава выдыхаемого воздуха. Результаты эксперимента показывают эффективность методики: выявленные различия в масс-спектрах здоровых людей и испытуемых, перенесших респираторную вирусную инфекцию, позволяют использовать методику для поиска маркеров патологий.

Ключевые слова: масс-спектрометрия, анализ газового состава, выдыхаемый воздух, острая респираторная вирусная инфекция, метод главных компонент

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Introduction

Human health and work capacity of individuals are largely determined by metabolic processes in various organs and tissues, the products of which are distributed in various biological media of the body (in cells, blood, exhaled air, urine, etc.) and are indicators of the functional state of the physiological systems of the body. Analysis of the molecular composition of biological media is a possible technology for assessing the degree of deviation of diagnostically significant components from the norm, used for diagnosis, disease prognosis and monitoring the effectiveness of treatment. Human exhaled air contains a wide range of low- and high-molecular weight compounds that change their composition in the presence of pathology. Each person has their own individual "imprint" of the composition of exhaled air, which can be detected by highly sensitive mass spectrometric methods of analysis.

The use of mass spectrometric methods of controlling the gas composition of exhaled air in the diagnosis of diseases will provide a high accuracy of research and rapid analysis results, which is an important criterion in periods of high workload of medical institutions, such as in a pandemic. The method is non-invasive (in contrast to methods requiring the collection of biological material [1]), which also increases the speed and reduces the complexity of sampling, and the lack of the need for special preliminary preparation significantly reduces the likelihood of error in the finished analysis.

The purpose of the work is to implement in practice the new approach proposed earlier [2] to medical and biological research of the functional state of a human by physiologically significant components of exhaled air with the use of mass spectrometric methods of analysis. This will make it possible to determine the presence of respiratory viral infections and, in the future, to identify physiological criteria for the return of workers to work while monitoring the dynamics of recovery after a viral illness.

Materials and Methods

The composition of exhaled air samples was analyzed on a small-size quadrupole mass spectrometer MS7-200 with direct sample introduction at atmospheric pressure, developed at IAP RAS [2–6].

The analyzed gas at atmospheric pressure is fed into the ionization chamber of the electron impact ion source through a capillary inlet. The resulting ions are injected into a quadrupole mass analyzer. The resulting mass-spectrometric signals are processed using specialized software and compared to spectra in a library of standard mass spectra, then individual spectrum components are identified and their concentrations determined. A heated capillary injection system allows sample flow within a distance of up to 5 meters from the mass spectrometer. The sample flow rate is 2 μl/sec.

Sampling was performed using sampling devices: specially prepared medical syringes with a volume of 20 ml. Predominantly two-component syringes without rubber pistons were chosen. Each sampling device was pre-purified for 3 days. Before sampling, mass-spectrometric checking of the composition of the sampling devices filled with atmospheric air for the absence of background impurities was carried out. The described technique of preparation of sampling devices allows obtaining an accurate undistorted mass-spectrum of the gas composition of the studied sample.

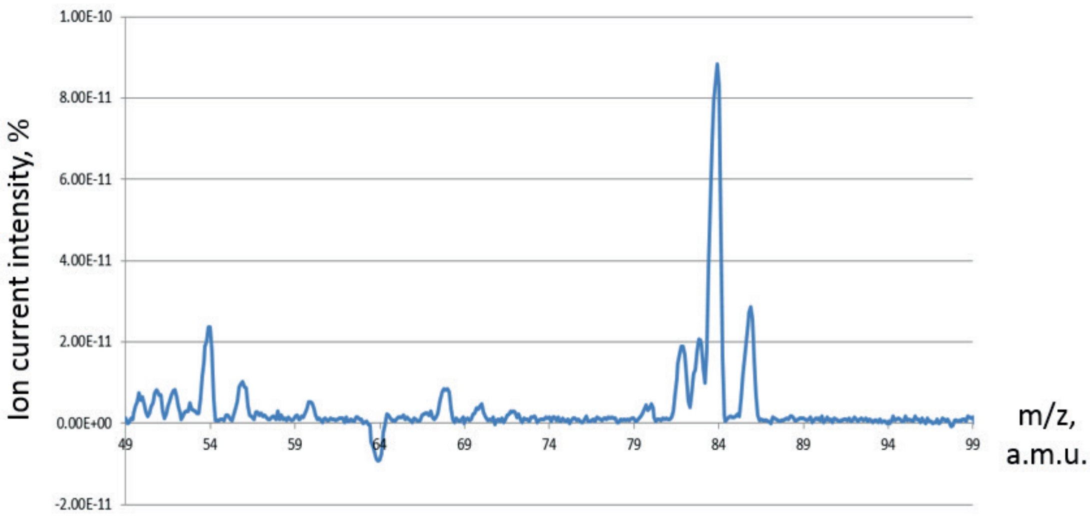

Fig. 1. Mass spectrum of an air sample in the room where exhaled air was collected

Decoding of the mass-spectrum of the analyzed sample allows determining the qualitative composition of the components in the exhaled sample and revealing markers of pathological conditions. The composition of the spectrum can be influenced not only by the subject's health condition, but also by the presence of impurities contained in the atmosphere; therefore, the gas composition of the atmosphere was analyzed before starting the experiment. The resulting mass spectrum obtained during the measurement is the difference of mass spectra of the atmosphere and the sample is shown in Fig. 1.

In mass surveys of public health during a pandemic coronavirus infection, there is usually no prior information about the type of causative agent of the patient. When diagnosing the health status of patients by exhaled air analysis, it is advisable to record the entire spectrum of exhaled gases (disease markers) and then compare it with data from one of the control groups with a known disease.

Table 1

Comparison table of two subjects from the group of healthy subjects and the group that had had a respiratory viral infection

m/z	I_{ion}(health)	I_{ion}(pathology)
53	1.70E-11	2.17E-12
55	–3.98E-13	6.14E-12
56	8.10E-12	1.07E-11
57	3.16E-13	9.58E-12
58	3.95E-11	2.20E-11
60	1.39E-11	5.11E-12
67	2.63E-11	3.62E-12
68	1.52E-11	-7.01E-13

Experimental studies

49 samples were examined in order to evaluate and demonstrate the performance of the diagnostic system in terms of the ability to obtain mass spectra of the functional state of the subjects and their visual representation.

To work out the methods of experimental study of the effect of viral infection on the subject's mass spectrum, studies of healthy subjects and subjects who had had a viral infection were performed. The samples were taken in the state of physical rest. To create a reference group of healthy subjects, 31 young men aged from 18 to 21 years and the second group of subjects, 18 people with symptoms of respiratory infections from 20 to 50 were recruited and samples were taken during the recovery period after the disease. The subjects were offered a special exhalation technique: deep inhalation, breath-holding for 10 seconds, slow exhalation into the sampling device, involving the lower parts of the lungs. This measurement procedure made it possible to determine the concentration of exhaled air components and form an individual print of each subject.

Results and Discussion

As a result of the experiment, a preliminary methodology for diagnosing respiratory viral infections was developed, and mass spectra of two groups of subjects were obtained.

Based on the results of the experiment, Table 1 with the masses of substances responsible for the presence or absence of disease was compiled.

The composition of exhaled air of a healthy person contains three main components: isoprene (masses 53, 67, 68), acetone (58), acetic acid (60) [2]. The mass spectra obtained as a result of measurements had significant peculiarities. In the group with symptoms of respiratory viral infection, a significant decrease in the concentration of acetic acid and isoprene was recorded, and some additional components were detected.

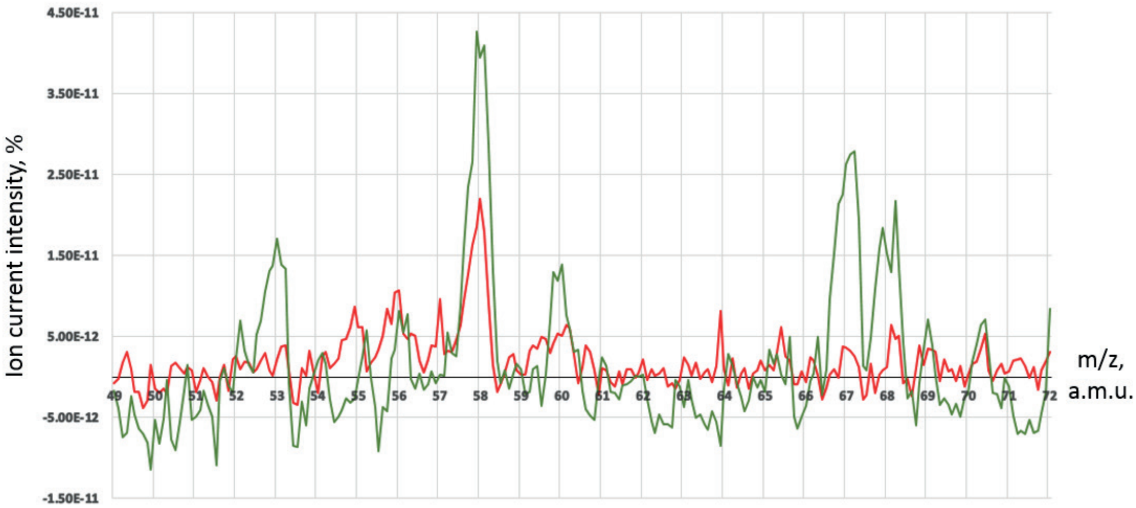

Fig. 2. Two mass spectra are illustrated: of a healthy subject (green line) and of a subject with respiratory viral infection symptoms (red line)

Conclusion

Thus, the possibility of monitoring recovery from respiratory viral infections using the developed noninvasive high-sensitivity mass spectrometric technique has been shown. Further research in this area is necessary to improve the technique and expand the range of possibilities, such as diagnosis of viral infections in the acute phase.

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