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Respiratory Odor Recognition and Disease Diagnosis Method of Gastric Cancer Based on the Concept of Combination of Disease and Syndrome

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Gastric cancer is one of the four major malignant tumors, it’s a kind of malignant tumor with a high mortality rate. Patients with gastric cancer often do not get an early diagnosis, and when they are clinically diagnosed with gastric cancer, usually they already miss the best time for treatment, which causes surgery and other treatment methods fail to give full play to their effect. The detection of human respiratory gases based on electronic nose (e-nose) technology is a new emerging rapid non-invasive diagnostic method. By detecting the exhaled gases of human oral cavity and analyzing the volatile gases in the exhaled gases, it analyzes the content and concentration of typical and warning volatile gases of gastric cancer in the exhaled volatile gases, provides early warning of the occurrence of gastric cancer and analyzes and diagnoses the stage of gastric cancer. This paper combines with the current e-nose technology to design an e-nose respiratory gas detection system for gastric cancer detection, aiming to provide a fast and accurate method for early prevention and diagnosis of gastric cancer.

1. Introduction

E-nose (Fend, 2006), namely the odor scanning technology, originated in the 1960s, it combines the gas sensor array (Star, 2006) with certain identification methods for the odor recognition, obtaining results similar to human senses. With the development of gas sensors (Zee, 2001), e-nose technology was first used in food detection in the 1990s (Fenner, 1999). Up to now, after nearly 20 years of research and innovation, especially under the strong promotion of the development of biotechnology, e-nose is no longer simply used to identify gases, but has been widely used for air quality detection (Canhoto, 2004), volatile harmful gas recognition and detection, customs inspection, clinical medicine (Charaklias, 2010) and other aspects of life.
Human respiratory gases (Unterkofler, 2015) can indirectly reflect the condition of the body. Traditional Chinese medicine diagnoses patients through look, listen, question and feel the pulse since ancient times (Wehinger, 2007), it can be said that it is the earliest application of "gas detection" for diagnosis of diseases. With its high-precision gas sensor array (Srivastava, 2003), the e-nose technology can accurately identify the gas content in the oral cavity and then provide more objective and precise calculations through programmed procedures and big data calculations (Liu, 2011), it also has a good applicability in early detection of some diseases, helps to improve the accuracy of clinical diagnosis. Based on the existing e-nose technology, this paper designs an e-nose detection system that can detect gastric cancer more accurately.

2. Detection of gastric cancer

Because China's early screening and prevention measures for diseases are not good enough (Habbema, 1987), the probability of gastric cancer being diagnosed at an early stage (Bergmann, 1990) is very low. Second, China has an overall low-level concept of disease prevention, when Chinese people feel uncomfortable, often they won’t go to the hospital immediately. Moreover, there are many people have stomach diseases, stomach ulcers and other stomach diseases make the gastric cancer hide deeper.

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2.1 Routine gastric cancer diagnosis methods

Methods that are clinically used in the diagnosis of gastric cancer (Liu, 2012) include fiber endoscope, ultrasound imaging, computed tomography (CT) and magnetic resonance imaging (MRI). Specific characteristics of these methods are shown in Figure 1, because gastric cancer patients generally have no special clinical symptoms at early stage, these methods can not accurately diagnose the disease under normal circumstances, and gastric cancer may be diagnosed as some common stomach diseases, therefore, early diagnosis of gastric cancer is very difficult.

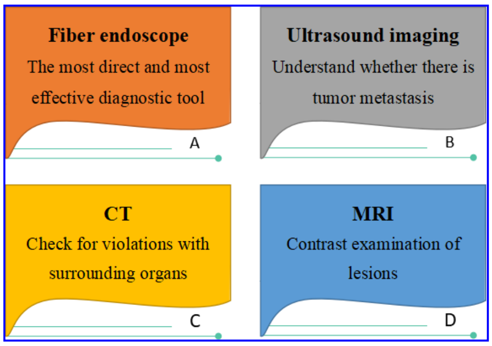

Figure 1: Conventional diagnosis methods of gastric cancer

2.2 Diagnosis method of e-nose respiratory gas detection

Human respiratory gases are mixtures with complex compositions, including nitrogen, carbon dioxide, water and other small molecule inorganic substances, as well as various volatile organic compounds (VOCs) (Baldino et al., 2018), the type and concentration of these compounds are closely related to the metabolic conditions of the human body, and different diseases can cause some gases to deviate from the concentration of these gases in healthy people. Cancer cells often produce special combinations of VOCs, which also gives a way to diagnose cancer by detecting respiratory gases. The known relationship between the abnormality of exhaled gases and the potential problem of a certain part of the body is shown as Table 1.

Table 1: Relationship between abnormal gas concentrations in the oral cavity and potential diseases

Abnormal gas	Possible Indication of Disease
Acetone	Diabetes
Ammonia	Kidney disease
Pentane and Carbon Disulfide	Schizophrenia
Dimethyl Sulfide	Liver Disease
Benzene, Hepone and Cyclohexane	Tuberculosis

Cancer cells often produce special combinations of VOCs, and e-nose technology can realize early non-invasive and rapid detection of gastric cancer, and provide reliable reference information for the diagnosis of gastric cancer. Through the detection and analysis of a large amount of data, we obtained the differences of VOCs in the exhaled gases of healthy people and gastric cancer patients through the sensor array. The specific differences are shown in Table 2 below.

Table 2: Differences in VOC content in exhaled gases between healthy people and gastric cancer patients

Chemical Name	Gastric Cancer Patient	Healthy People
Hexanal	+	-
Nonyl	+	-
5-ethyl-5-methyl-decane	+	-

+ represents the presence of such substance, - represents the absence of such substance.

Hexanal, 5-ethyl-5-methyl-decane, and nonane are detected in exhaled gases from cancer patients only, and they can be used as VOC markers for patients with gastric cancer. In addition, the relative contents of ethanol, acetone, and hexanol in exhaled gases of patients with gastric cancer are also significantly higher than those of healthy people. Combined with the existing literatures, the content of alkanes in respiratory gases that is higher than the normal value indicates that there occurs oxidative stress (OS) in vivo, if the aldehydes are also higher than the normal values at the same time, it indicates the occurrence of cancer. Therefore, these VOCs of ethanol and acetone can be used as VOC warning substances for patients with gastric cancer. Compared with the conventional method which cannot obtain the exact results without the biopsy laboratory test even if used in combination, the VOC gas test method based on the respiratory gases is more efficient and convenient.

3. E-nose odor recognition system

3.1 Basic principle of e-nose

The basic principle of e-nose is to simulate the human olfactory organ, which is mainly divided into three steps. The corresponding e-nose system is also composed of a gas sensor array that collects gases, a signal processing system that processes signals, and a pattern recognition system that makes judgments, as shown in the following figure 2.

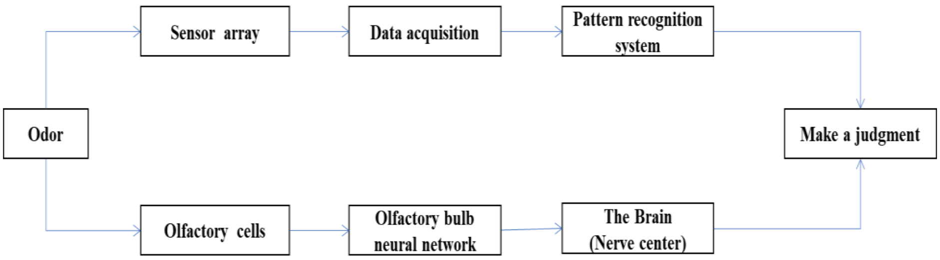

Figure 2: Constitution of e-nose and human olfaction

The e-nose respiratory detection system consists of an array of multiple gas sensors, and the sensitivity of each sensor is different, so the response of the gas sensor array to complex gases is the superposition of the response of each sensor to the various gas components of complex gases, which makes it possible to truly reflect the content and concentration of each gas in the gases. The following figure 3 is the basic principle diagram of the e-nose odor recognition system. The e-nose respiratory detection system can analyze and process complex gases by the gas sensor array. When the gases to be tested enter the gas sensor array and react with it, the obtained analog electric signals are transmitted to the signal processing system for preprocessing, finally, the signal processing results are analyzed by the pattern recognition system and the final results are obtained.

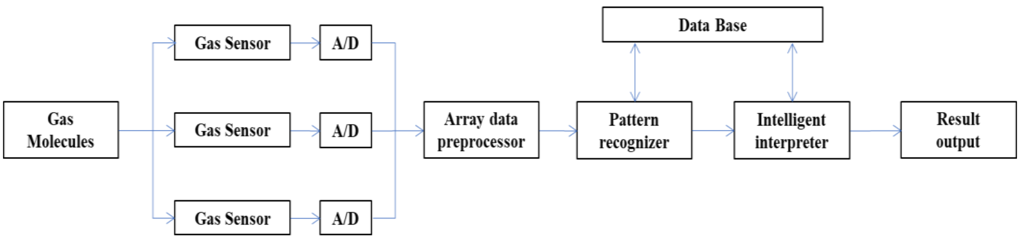

Figure 3: Principle and structure of e-nose

3.2 Gas sensor

In the e-nose detection system, the gas sensor array outputs standard electrical signals in response to the gases, so the selection of gas sensor is a key to the overall system recognition capability. The classification of gas sensors is shown in figure 4 below. Among them, the metal oxide semiconductor sensor array has been widely used due to its good stability (Mohd et al., 2018), long life, wide application range and low cost.

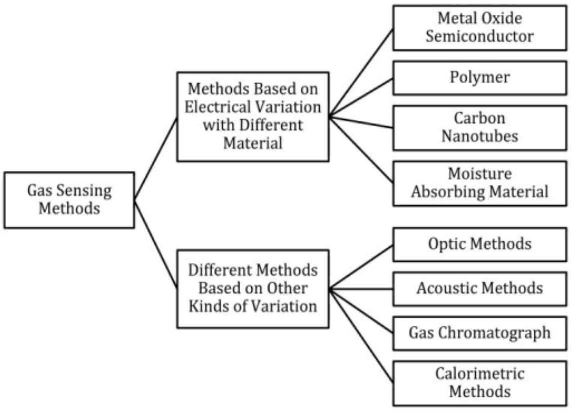

Figure 4: Gas sensing methods

3.3 Wavelet transforms

In the e-nose respiratory detection system, the parameters of the gas obtained through the high-sensitivity gas sensor array are still high-dimensional data after smoothing and filtering, and the computer processing is difficult. Therefore, the wavelet transform feature extraction method is used to identify the initial variables by using a few variables, so as to reduce the dimension.

The idea of wavelet transform is to stretching and panning a basic wavelet to form a set of wavelet basis so as to decompose or reconstruct the event signals. The wavelet function $\psi(\mathrm{t})$ is a square integrable function that satisfies the formula (1).

$$\int_{-\infty}^{\infty} \left|\psi\ (\omega)\right|^{2} \left|\omega\right|^{-1} \mathrm{d}\omega \prec \infty \tag{1}$$

A set of wavelet basis formed during the wavelet transform can be used to scale the basic wavelet, so as to obtain a fitting of the analysis signal. The transformation relationship between this set of wavelet functions $\psi_{\mathrm{a}}(t)$ and the basic wavelet function is shown in formula 2.

$$\psi_{a}(t) = \frac{1}{\sqrt{|a|}} \psi(\frac{t-\tau}{a}) \tag{2}$$

The change of parameter a will affect the spectral structure of the wavelet, and the parameter τ will paly a translational role.

4. Study on recognition and disease diagnosis of respiratory gases in patients with gastric cancer

4.1 Exhaled gas sample collection

A total of 50 respiratory samples from 50 gastric cancer patients and 50 healthy people were collected in the experiment. In order to qualitatively determine whether there is correlation between gastric cancer VOC markers and warning substances with gastric cancer patients, the selected 50 gastric cancer patients include diagnosed early-stage gastric cancer patients, and patients at all stages of the treatment period, and they are not limited in gender. The inclusion criteria and discharge criteria for patients with gastric cancer are shown in Figure 5.

The gas collection time was selected in the morning. All subjects performed gas collection under fasting conditions, and the ambient temperature and humidity of the gas collection were kept constant, creating a relatively pure environment as much as possible, so that the VOCs in the collected gases were all from the respiratory gases of the subjects.

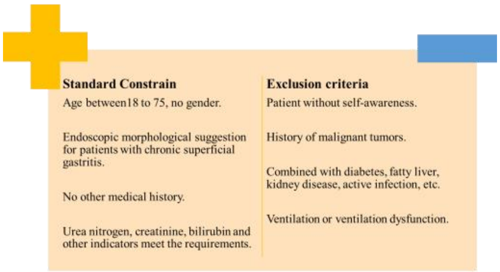

Figure 5: Patient inclusion criteria and discharge criteria

4.2 Gas sample processing

The collected gases were adsorbed through a Tenax-TA sampling tube and then subjected to thermal analysis. After analysis, 100 samples were subjected to gas chromatography analysis. The content of various VOCs in the detection gas was obtained by gas chromatography. First, the gas detection results of gastric cancer patients and healthy people were separately weighted and averaged, and then summarized after qualitatively analyzed by mass spectrum database and roughly and quantitatively analyzed by relative peak areas.

4.3 Analysis of test results

The gas chromatogram comparison results of exhaled gases of gastric cancer patients and healthy people after sorting and analysis are shown in the following figure 6.

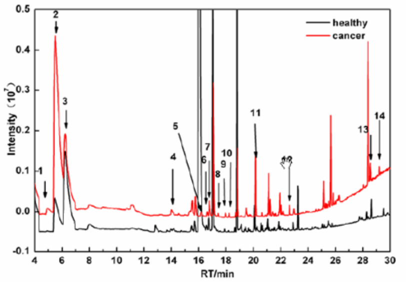

Figure 6: Gas chromatogram of gastric cancer patients and healthy people

The figure shows that there are large differences in 14 kinds of VOCs in the exhaled gases of cancer patients and the exhaled gas components of healthy people, in which, the hexanal, 5-ethyl-5-methyl- decane and nonane are only contained in the exhaled gases of patients with gastric cancer, and the corresponding relative peak area in the gas chromatogram is larger. In addition, the relative contents of ethanol, acetone, and hexanol in the exhaled gas of gastric cancer patients are also significantly higher than those of healthy people. Therefore, the detection of specific VOCs can be used to diagnose gastric cancer, and in addition to VOC markers in gastric cancer patients, there are some warning substances that can provide reference for the diagnosis of gastric cancer.

4.4 E-nose respiratory gas detection system

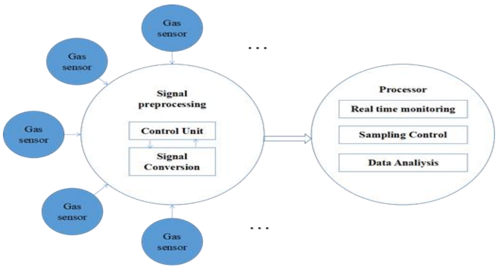

Figure 7: Composition of e-nose respiratory gas detection system

Based on the above experiments, we obtained the characteristic gases of several gastric cancer patients. The e-nose respiratory detection system was designed according to the characteristic gases, it consisted of two parts of hardware system and software system, as shown in figure 7. The system can detect VOC markers and warning substances of gastric cancer patients, find the markers and send out warning information during the detection. When markers are not detected, it analyzes the warning substances, if the concentration of the warning substances is higher than the normal, the system also issues an alert message.

5. Conclusion

Based on the existing e-nose system, combined with the problems existing in the routine diagnosis of gastric cancer, an e-nose respiratory gas detection system was designed in this paper to assist the diagnosis of gastric cancer. The specific research results are as follows:

(1) This paper introduced the routine diagnosis methods of gastric cancer, and cancer diagnosis methods based on the e-nose technology, it also made a brief introduction to current e-nose odor recognition systems.

(2) By comparing with the respiratory gases of healthy people, the VOC markers and warning substances of respiratory gases in patients with gastric cancer were qualitatively verified, which also laid a theoretical foundation for the detection of gastric cancer by e-nose respiratory gas detection system.

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