A STUDY ON BREATH ANALYSIS FOR STOMACH CANCER PREDICTION USING MACHINE LEARNING TECHNIQUES

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***Abstract*— Early disease detection is now a crucial concern in medical research because of the current, rapid population growth. Cancer-related deaths are becoming exponentially more likely due to the increasing population rise. A dependable, efficient, and quick response are provided by an automatic disease detection system, which also lowers the chance of fatalities while assisting medical staff in disease identification. A relatively new area of research with great clinical potential is breath analysis. The study of volatile organic compounds (VOCs) is a fascinating area of study that has the potential to produce new biomarkers for earlier stomach cancer detection. Numerous research teams investigated the use of machine learning and deep learning techniques in the fields of biomedicine and bioinformatics to categories stomach cancer patients into high- or low-risk groups. This efficient review aims to encapsulate the published literature concerning stomach cancer- associated exhaled breath VOCs and their machine learning algorithms.**

***Keywords*— Volatile Organic Components, Stomach, gas chromatography, mass spectrometry, Machine Learning algorithm.**

I. INTRODUCTION

Stomach cancer is the fourth most frequent cancer-causing human in the world. Roughly 5.0% of stomach cancer patients are diagnosed before the age of 40. Stomach cancer turns to develop slowly over years. Stomach cancer is a disease in which cancer cells create in the lining of the stomach. For a person affected by stomach cancer, the presence of the specific volatile metabolites has been exposed for them, which are useful as markers and allows the early diagnosis of the cancer, which facilitates the adaptation of treatments for the prevention, diagnosis, and cure of the patient. By using gas chromatography, it is possible to realize a qualitative and quantitative analysis of the composition of breathing in healthy people or with cancer, which allows identifying biomarkers, so it could be a diagnostic method for such diseases, with the advantages to discriminative rapidly, safety way with a non-invasive method for the early detection of the disease, which can be applied for screening tests to be carried out on population at risk [1].

The earlier detection of cancer is still a life-threatening contrivance in the era since there are only invasive methods available. A solid body of research literature shows that the chance of survival in people with different types of cancer is increased with earlier detection. Today, most diagnostic tools are unable to detect cancers at the very early stages of disease progression. Moreover, some of those tools are invasive and may present clinical risks for the patient. Therefore, the demand for alternative methods for cancer diagnosis has increased in recent years [2].

Breath analysis has recently emerged as a promising tool to diagnose numerous types of cancer and was shown to have especially high sensitivity and specificity for cancers. The human breath contains a complex mixture of almost 3000 different VOCs that enter the exhaled air via the alveolar-capillary membrane of the respiratory tract. These can be identified through gas chromatography and mass spectrometry, which is a highly sensitive but costly and time-consuming technique because it requires both specialized equipment and a trained person [3].

A subset of artificial intelligence known as machine learning uses a number of statistical, probabilistic, and optimization techniques to help computers learn from previous experiences and recognize subtle patterns in vast, noisy, or complex data sets. Cancer detection and diagnosis commonly make use of machine learning [4]. Machine learning has more recently been used for cancer prognosis and prediction. Research on stomach cancer has long used machine learning. For almost 20 years, decision trees and artificial neural networks (ANNs) have been employed in the detection and diagnosis of cancer. A dangerous condition, cancer is one of the major causes of mortality in the globe. Early stomach cancer detection will increase the effectiveness of treatment and lower the mortality rates from the disease [5].

II. RELATED WORK

Stomach Cancer is the anomalous growth of cells in the lining of the stomach. The stomach is a portion of the digestive system which is a muscular sac discovered in the upper middle of the abdomen, beneath the ribs. Cancer tackle when a cell in the stomach progress to transpose in its DNA. A DNA of a cell directs a cell what to do. The changes inform the cell to grow rapidly and continue to live which make healthy cell die. The Aggregated cells configure the Tumor which can conquer and demolish healthy cells, which spreads to other portions of the body. Helicobacter pylori infection is the known risk factor for the stomach cancer. Helicobacter pylori induced chronic inflammation may be closely related to the altered metabolic pathways of stomach cancer cells [6]. Stomach cancer can be determined with categories that are rated on a numbered scale, with higher numbers indicating

the raised severity. The categories can be grouped into stomach cancer stages from 0 to 4 shown in Figure 1.

- Stage 0: This is the initial stage of cancer, known as Carcinoma in situ. In this stage, cancer will not spread into other cells.

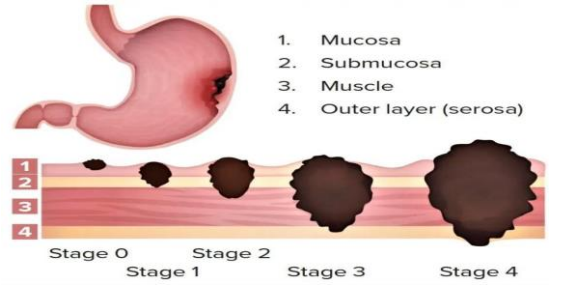

Figure 1. Clinical staging of gastric cancer

- Stage I: This stage can be split into two stages:
  - Stage IA: Cancer spreads into one or two lymph nodes near the stomach, but not to other tissues.
  - Stage IB: Cancer develops into the main muscle layer but does not spread near to the lymph nodes or tissues. The cancer spreads to the subserosa layer of the stomach
- Stage II: These stages can be split into two stages:
  - Stage IIA: Cancer spreads beneath top cell layers. It gets spread into three to six lymph nodes and main muscle layers.
  - Stage IIB: Cancer Spreads to the layers of the stomach wall but not grown onto other nearby organs.
- Stage III: These stages can be split into three stages:
  - Stage IIIA: Cancer spreads into many muscle layers and grown completely through every layer of the stomach wall including the outer covering of the stomach.
  - Stage IIIB: Cancer spreads onto the stomach wall and to the nearby organs or structures.
  - Stage IIIC: Cancer spreads to all the layers of the stomach and spreads to the nearby organs but not to the distant sites.
- Stage IV: It is the last stage of stomach cancer. In this stage cancer has spread to other parts of the body [7].

III. Exhaled Breath Analysis

An emerging non-invasive method for detecting disease depend on the difference of VOCs from breath has observed a huge improvement in cancer diagnosis [8]. The exhaled breath contains many components mainly VOCs which help to identify the cancer with the help of various analysis with a better clinical prognosis and survival rate (fig 3).

Breath analysis holds a distinguished status in this context, as it is non-invasive and some breath constituents have already been linked to particular disease processes, including cancer [9].

Human breath is mainly composed of nitrogen, carbon dioxide, oxygen, water vapor and inert gases. In addition, thousands of VOCs are exhaled at very low concentrations (estimated as parts per trillion or parts per billion by volume of the exhaled breath). Part of these substances are of endogenous origin and could be characteristic for metabolic processes in the human body (including cancer), while several hundred others are exogenic, that is, passing through the human body [10].

A. Volatile Organic Components (VOC)

Volatile Organic Components are fabricated and discharged via the metabolism of cancer cells or by the body immune system. Cancer related VOCs can be identified which increase the chance of better survival. Cancer biomarkers are classified into two categories, general cancer biomarker and biomarker for specific cancer type [11].

B. VOC Classification

The classification of VOCs can be done based on two ways i.e., on the basis of boiling points and that of source.

Types	**Boiling Points(°C)**
VVOC	<0 to 100
VOC	<250
SVOC	240 to 400

- On the basis of boiling points

Volatile organic compounds can be classified based their boiling points such as Very Volatile Organic Compounds (VVOC), Volatile Organic Compound (VOC) and Semi Volatile Organic Compounds (SVOC). Table1 shows the classification of VOCs based on boiling point

TABLE 1. VOC CLASSIFICATION BASED ON BOILING POINT

- Bases of Source

The VOCs based on sources includes Natural VOCs and Human-made or Anthropogenic VOC. Table 2 shows the VOCs based on source,

TABLE 2. VOC CLASSIFICATION BASED ON SOURCE

Type	**Description**
Natural VOCs	Obtained by gaseous emission by conifers and deciduous trees, flower perfume and from human respiration
Human-made or Antropogenic VOC	Emitted by the production of hydrocarbon like industrial combustion, solventevaporation, painting, etc.

C. Sampling Techniques

Air sample collection is an important technique for the analysis of cancer. Collection of samples can be taken using two sampling methods,

- Grab Sampling: This is a technique in which collection of samples will be taken for a short period of time usually less than 5 min when the composition of gas present in air does not change over time grab sampling can be done.
- Integrated Sampling: This is technique in which collection of samples will be taken over a large time period. This sampling is a full shift sampling which is performed over 8 hours or to 10-12 hours shift [12].

TABLE 3. PROPERTIES OF SUMMA CANISTERS AND TELDAR BAGS

Properties	**Summa Canisters**	**Teldar bags**
Analysis of holding time	1-30 days	1-3 days
Surface Inertness	Excellent	Good
Volume of sample	400 ml to liters	ppm
Advantage	Long holding time	cheap

D. Sampling Medias

Sampling is processing of collecting exhaled breath air samples in a medium. The air sampling media is of two types, Canisters and Bags.

Canisters: For air sampling, containers are used for sample collection. The containers are made up by stainless steel and have cylindrical or spherical shape. Valves are used for the regulation of air samples. Flow controllers are used for the collection of desired samples. Valves are closed after the collection of samples. In the container, a nearly 1-6 litre sample has gathered. 6L containers are employed for the ambient air sample. One litre container is used for soil vapours. [13].

- Summa Canister: Summa canisters are created using a method that combines electropolishing with chemical deactivation to create a surface that is chemically inert and has a brilliant, shiny, and smooth finish. Stainless steel is used to build Summa canisters. It collects certain gases, including CO2, CO, N2, and O2. Stability of gases and analytes in it for 30 days. Wide size range is 400 ml to 6l. They can be used for grab and integrated sampling [14].

Bags: Air sampling bags are used to gather samples for soil gas, stationary source and landfill gas samples

- Teldar Bags: It is a polyvinyl fluoride film formed in 1960's and helpful due to various applications [15]. Nalofan is formed by polyterephthalic ester and Teflon is formed by propylene copolymer and fluorinated ethylene. It has mechanical properties, flexible, tough over 200 °F. It shows good chemical inertness, good resistance and low permeability. Tedlar bags requires pump for sampling. They can be used for the collection of various samples like hydrocarbons, solvents, atmospheric and biogenic gases and chlorinated solvents etc. Naphthalene that has low vapour pressure cannot be collected in these bags due to their low recovery in short time period. Hydrogen and Helium has low molecular weight so they can also be diffused from them and bags show the low storage stability. Stability of analytes and gases is 1-3 days in it. Tedlar bags are easy for handling and transportation and are less expensive [16].

Table 3 shows various properties of summa canisters and teldar bags.

E. Method of Analysis

For the analysis of VOCs the following methods are used

- Gas chromatography-mass spectrometry:

  In this technique, a fused silica column is used and temperature of detector and injector is 260 °C. The capillary columns have diameter of 0.25-0.53 mm and non-polar compounds can also be separated by this technique. In mass spectrometry, linear quadrupole or ion trap mass spectrometer is used for the separation of volatile compounds. They have capability of scanning from 35 to 300 amu in every one second by using the 70 volts. Ions are generated and moves in parallel way under the production of generated field and their m/z values are calculated. Only 0.1-0.2 % ions are detected through the detector [17].
- Mass spectrometry:

  When high voltage is applied on the gas molecules then the ionization takes place in which the gas molecules changes into ions or fragments. These ions are entrapped and flow in a beam. This ion beam is subjected to the magnetic field and deflected from their path. The degree of deflection shows the charge to mass ratio of the fragments. This technique requires the sample in small size (microliters). Hydrocarbons, ozone, carbon monoxide, carbon dioxide, nitrogen oxide, nitrogen dioxide and sulphur dioxide are detected by this technique [18].
- Voltammetric:

  A potential difference is produced between the reference electrode and sensing electrode. The gas molecules carried the current and linked between these electrodes. The gas molecules have charges or ionic and migrate towards the sensing electrode. Then current is flowed between the electrodes or through the system [19].
- Electron impact ionization:

  It is also called the electron ionization and it is oldest method. This method involves passing a 70eV, Rhenium or Tungsten electron beam through the material. These electrons produce a molecular ion or positive ion colloid with the sample molecules, called the fragment ion and detected by the means of photomultiplier tubes. This method is important due to determining of volatile organic

compounds, fragmentation structural information and well understood. The major draw backs of this method are that the molecular ion peak may be present or absent in VOCs and sample must be stable and thermally volatile CO, CO2, Methane etc. are detected by this method [19]

- Thermal conductivity:

A wire is heated as current flows across it. The heated wire is being traversed by a carrier gas stream, and the rate of present is equal to the heat generated. At this procedure, the wire temperature and resistant will be constant. If volatile organic compounds will be added in the carrier gas stream, then the amount of heat will be change and as a result the resistance and temperature will also change [20].

F. Sensors

Sensors can be used to identify the presence of VOCs from the exhaled breath samples. There are four types of direct reading instruments that are used for the analysis or detection of VOCs:

- PID (Photoionization detector): For the Ionization of VOCs UV radiations are used. For Ionizing the molecule of VOC UV lamps emits the energy, but many are not ionized molecule, they are chlorinated molecules. PID is more sensitive than FID because of the order of magnitude. PID response is of the form Total Volatile Organic Compound (TVOC). It is easy to use so the sample will be destroyed. The main drawback of PID is that it is highly variable responses and contamination present [21].
- PAS (Photo-acoustic sensors): In this detector, the infrared radiation is absorbed by a Volatile Organic Compounds and the changes in pressure of organic compounds are detected and the acoustic signal is observed by Microphones and output temperature. his is acquired by the variety of acoustic recurrence with power of infrared radiation. PAS reaction is reliant upon the infrared radiation and passage of fumes of methane and water with reaction [22].
- FID (Flame-ionization detector): In this type of detector, ions are produced by burning the volatile organic compound with a hydrogen flame. Ions are produced by this combustion and are attracted towards the combined electrode. Due to the production of ions, an electric current is generated. The number of carbon atoms and the structure of the VOCs affect the signal strength. It is the most widely used reagent and detects a large number of volatile organic compounds. It is a stable detector. The advantages of FID are insensitive to carbon dioxide, carbon monoxide, and water. It is very expensive due to hydrogen as a fuel, is rugged and gives linear response at a wide range.
- Gas Sensor: Different kinds of sensors have been produced for breathed out breath VOC
- Artificial Neural Network: A computer technique known as an artificial neural network (ANN) is severely hampered by interconnected processing units known as neurons that classify data as feedback to environmental stimulation. It is completed in two

investigation. VOC sensors are generally less expensive, versatile, programmable, and simple to utilize. They can get information continuously, with high sensitivities. In this way, numerous sensor-based VOC identification procedures have immense potential in clinical mark of- care use. VOC sensors are regularly cheap, versatile, programmable, simple to utilize, and can acquire information progressively with high sensitivities [23].

The following are the sensors which are some other sensors used to identify the presence and analysis of VOCs in the exhaled breath,

- Metal oxide chemoresistive sensors
- Nanomaterial-based chemoresistive sensors
- Colorimetric sensors
- Carbon Nano Tube Sensors
- Electrochemical Sensors
- Hot-wire Sensors and so on [24]

G. Data Analysis Classifier Methods

- Principal Component Analysis: It is a multivariate data method used for data classification. This is a linear supervised method which is able to extract the most relevant information and project information into low- dimensional plane with the help of scores plot [25].
- Partial least square Discriminant Analysis: Partial least squares. A flexible approach called discriminant analysis (PLS-DA) can be used for discriminative variable selection, predictive and descriptive modelling, and both for cancer prediction.
- Support Vector Machine: The most common technique used for prediction, regression, and classification is SVM. By providing a boundary known as a hyperplane that divides the dataset into two sections, it classifies the incoming data set. SVM's data-driven methodology and viability without a fictitious system that generates accurate classification is its advantageous feature. especially when the sample size is small. When the datasets are biomarkers, SVMs are frequently employed for classification in order to forecast and identify cancer, neurological, and cardiovascular disorders [26].
- Neuro-Fuzzy Algorithm: The use of neuro-fuzzy algorithms in medical diagnosis is important. Simple physical exams and diagnostic tests such upper endoscopy, MRI, blood tests, ECGs, and so on are the first steps in the diagnostic process [27]. The diagnostic system typically uses AI techniques including neural networks, fuzzy logic, genetic algorithms, and support vector machines [28].

ways, namely by testing and learning [29]. Learning is a tool for categorising fresh input. In the testing phase, it takes a network-provided input signal and computes it to produce an output. ANN methods are helpful in a variety of healthcare settings, including cancer

diagnosis and treatment [30]. Table 4 shows survey of stomach cancer from various articles.

TABLE 4. SURVEY OF STOMACH CANCER PREDICTION

S.N O	TITLE	JOURNA L	OVERVIEW OF THE PAPER	METHODS USED
1.	Digging deeper into volatile organic compounds associated with cancer	Biology Methods and Protocols	An updated picture of cancer-related VOCs based on recent findings in the field focusing on cancer odor databases.	Biological matrices, Analytical methods
2.	Ex vivo emission of volatile organic compounds from stomach cancer and non-cancerous tissue	Journal of Breath Research	Identify chemical patterns associated with a cancerous state and can be considered as a complementary source of information on volatile biomarker found in breath	Gas chromatography with mass spectrometric detection (GC- MS) coupled with head-space needle trap extraction (HS- NTE)
3.	Pilot Study: Detection of stomach cancer from exhaled air analysed with an electronic nose in chinese patients	Advances in Science	Investigate the ability of an electronic nose to distinguish malignant stomach histology from healthy controls in exhaled breath.	Statistical analysis
4.	Stomach cancer detection through exhaled breath using biomarkers	Chemical Engineering Transactions	This study describes a methodology for the stomach cancer detection through biomarkers in colombia	PCA (Principal Component Analysis), Statistic Analysis of biomarkers
5.	Non-invasive detection of stomach cancer	International Society of Oncology And Biomarkers (ISOBM)	Review the advances in stomach cancer detection by protein and nucleic acid tumor markers, circulating tumor cells, and tumor- associated autoantibodies in peripheral blood.	Emerging fluid biomarkers for stomach cancer diagnosis, Exhaled Breath Analysis
6.	Artificial neural network for prediction of lymph node metastases in stomach cancer: A phase II diagnostic study	Society of Surgical Oncology.	The aim of this study was to evaluate Artificial Neural Networks (ANN) for predicting In patients with stomach cancer	Artificial neural network (ANN) has been used for the prediction
7.	Profile of exhaled breath volatile organic compounds to diagnose pancreatic cancer	British Journal of surgery	To evaluate differences in exhaled breath VOCs of patients with pancreatic cancers	Analysis was performed using gas chromatography – mass spectrometry.
8.	A flexible stomach gas sensor based on functionalized optical fiber	IEEE sensor journal	The aim of the paper is to develop new sensor for the diagnosis of pylori infection and also aim to improve the accuracy.	Developed a new sensor called a conjoined dual fiber optical sensor. This sensor will predict the cancer related VOCs.

IV. CONCLUSION

Breath analysis for cancer screening is a rapidly developing field. The VOCs are analyzed through various techniques such as GC-MS, GC–IMS and SPME. These methods increase the probability of survival for a person with cancer since the cancer can be detected at an earlier stage.

Gas sensor method is available for the detection of VOCs in the exhaled breath, VOC identification is breath test. This method increases the probability of survival for a person with

cancer since the cancer can be detected at an earlier stage. The use machine learning algorithms and healthcare is highlighted. This review highlights the breath analysis and investigation of various ML approaches used to treat stomach cancer.

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