International Journal of Technical Research and Applications e-ISSN: 2320-8163,
www.ijtra.com Special Issue 22 (July, 2015), PP. 84-93

SIMPLIFIED CHEMIRESISTOR-BASED ELECTRONIC NOSE TECHNOLOGY (SCENT) AS HOME-USED LUNG CANCER SCREENING TOOL

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Abstract **rationale: lung cancer is a formidable disease as only 15% of lung cancer cases are diagnosed at early stage when curative treatment is possible. screening test has been proven to reduce mortality by 20%. my objective was to develop simplified chemiresistor based electronic nose technology (scent) which could detect lung cancer olfactory signals in the breath, so it could be used as home-used lung cancer screening tool.**

Methods: Research work was divided into three phases. In phase 1, data analysis of 17 lung cancer breath analysis results and molecular biology study confirmed alkane could serve as lung cancer breath markers. In phase 2, tetracosane was chosen as matrix because analytes were alkane, and carbon powder was chosen as filler. Chemiresistor sensor was developed by pilot experimenting on different amount of carbon powder, substrates and deposition techniques. Breath-in apparatus was chosen from either vitagen bottle or 500ml bottle. In phase 3, sensors were exposed to water, different vapor concentrations of n-heptane, 2,6,6-trimethyloctane and 3-ethylhexane (which were breath markers) as simulated breath test. SCENT had also been tested on 2 lung cancer patients (stage II and III) and 5 healthy volunteers.

Results: Phase 1 data analysis and molecular biology background research showed that concentration of alkane in cancerous breath was averagely twice that in healthy breath due to elevated oxidative stress in cancerous cells. 100% success rate of fabricating operative chemiresistor sensor was achieved using printed-circuit board, 0.01g tetracosane, 0.01g carbon powder and self-invented layer deposition technique. Vitagen bottle was chosen as breath-in apparatus. Distinct sensor peak outputs ($\Delta R_P/R_b$) were generated by e-nose when exposed to different simulated breath and real clinical tests. Sensor was able to perfectly differentiate lung cancer breath from healthy breath regardless in 300 simulated tests or 7 real tests, and was not sensitive to water vapour.

Conclusion: Infectious and non-infectious respiratory diseases such as asthma and tuberculosis will not be detected from high alkane concentration because their pathogeneses were not related to oxidative stress. Differentiation of lung cancer was done by the magnitude of percentage difference in baseline resistance after exposure to exhaled breath. Chemiresistor sensor was cheap (RM0.50) and could be operated by untrained personnel. Time taken for one test was merely 3 minutes. Insensitivity of sensor towards water meant that water vapor in breath would not affect the result. Clinical trial with larger sample size is currently being performed in University Malaya Medical Centre to further test the sensitivity and specificity of using simplified e-nose to screen for lung cancer and determine the threshold sensor peak output.

Index terms - lung cancer home-screening, simplified chemiresistor, simplified electronic nose, SCENT

I. INTRODUCTION

Lung cancer accounts for 1.3 million deaths annually worldwide [1]. Lung cancer, which is the most common cancer, yet has the lowest survival rates (16.6%) when compared to many other leading cancer sites, such as colon (64.2%), breast (89.2%) and prostate (99.2%) [2,3]. This is because only 15% of lung cancer cases are diagnosed at early stage when curative treatment is possible [2].

Screening helps detect disease in its early stages and enables it to be treated adequately before it obtains a firm hold on community [4]. The currently existing lung cancer screening tool is computed tomography (CT scan) only. In 2010, the National Lung Screening Trial (NLST) in the United States demonstrated a 20% reduction in lung cancer mortality, after screening high risk individuals (heavy smokers) using low dose computed tomography (LDCT). However, major concerns with LDCT screening were: high rate of false positive results which was 96.4% and radiation exposure, which predictably might cause one cancer death per 2500 people screened. Professionals claimed that if LDCT screening was implemented more broadly outside a trial setting, in facilities with less expertise, the outcomes could be different [4]. Cost of CT scan is expensive, usually $300 to $500 [6] or RM 1000 to RM 2000 [7]. Meanwhile, sputum cytology and chest radiograph are

claimed as an ineffective means for the reliable early detection of lung cancer [5,8].

Human breath contains more than 200 volatile organic compounds (VOCs) and their varying compositions in breath can indicate diseases [9]. Nitric oxide serves as marker for asthma [10] while acetone in exhaled breath indicates diabetes[11]. For lung cancer, researchers demonstrated success using trained dogs in the breath diagnosis of both early and late stage lung cancers with sensitivities and specificities approaching 99%, providing promise for future lung cancer breath tests [12].

Electronic noses include three major parts: a sample delivery system, a detection system, a computing system [13,14] and all of them can be simplified.

Electronic nose sensor can be divided into several types: colorimetric, catalytic field-effect sensors, conducting (polymer/metal oxides) sensors, etc. Conducting polymer are probably the most suitable e-nose sensor types available due low operation temperature which is at room temperature, low power consumption, good sensitivity to a wide range of gas or volatile analytes, and inexpensive operating costs. However, its problem is highly sensitive to water vapor, which may affect results when detecting volatile organic compounds in human breath as human breath is composed mostly of water vapor, with all other analytes existing only as minor substituents [14]. Thus, conducting polymer sensor materials is changed to monomeric organic molecules of moderate length which is used as matrix, mixed with carbon black or carbon particles. They show the ability to discriminate and classify both similar and different types of analytes, even at low concentration in air with saturated water vapor. Furthermore, the sensors share the advantages of conducting polymer sensor materials [15,16].

Upon exposure to an analyte, the analyte diffuses into the monomer composite (matrix) and the matrix swells, which causes the dispersed conductive carbon particles to move further apart from each other. As a result, the resistance of the chemiresistive film of sensor increases. The resistance change is directly proportional to concentration of analytes [17].

Other problems with current e-nose technology are despite the numerous E-nose selections commercially available in the market, most researchers are still fabricating their own E-nose prototypes, because of the high price of commercial E-noses and the limitations of their methods. For example, E-noses vary in price from US $ 10,000 to US $ 33,300 [18]. Besides, each piece of equipment must be trained to distinguish odors. This causes a problem of standardizing the practice between different research centers [19].

The purpose of this study was to design a simplified chemiresistor-based electronic nose technology (SCENT) to detect lung cancer breath markers in the form of volatile organic compounds for lung cancer screening. The criteria of SCENT were sensitive, specific, cheap, non-invasive, generate results rapidly, simple in design and untrained personnel can operate and interpret the end result easily. This study was divided into three phase: targeting lung cancer breath markers, developing SCENT, and testing the SCENT.

II. METHODOLOGY

Phase 1: Selection of Lung Cancer Breath Markers of Interest (Research-oriented)

Informatics approach, background research and molecular biology background research were used to choose the best single type of breath marker for lung cancer.

Informatics Approach

Study Materials: Breath analysis results on 752 lung cancer patients, 31 cancerous cell lines, 957 healthy controls and 7 healthy bronchial cell lines from 17 journals [20,21,22,23, 24,25,26,27,28, 29,30,31,32,33,34,35,36]

Methods: Dataset of potential breath markers comprising 109 volatile organic compounds (VOCs) was built from 17 lung cancer and healthy breath analysis reports using Microsoft Excel 2007. All the volatile organic compounds markers reported were classified into classes (hydrocarbon, aldehydes, carbinol, alcohol, ester, ether, nitrile, amines). Chemicals which could be exogenous origin[36] were excluded before being examined under selection criteria.

Selection Criteria:

- Markers must be found in more than two reports
- Marker's class should contain more than 15 compounds
- Marker's concentration must elevate in lung cancer breath
- High contrast between lung cancer breath and healthy breath VOCs markers concentration

(See result of informatics approach in section RESULTS AND DISCUSSION)

Background Research

Lung cancer exhaled breath had been studied in several gas chromatography-mass spectrometry (GC-MS) and the results showed elevated level of alkane and monomethylated alkane (C_4-C_{20}). In one study, 9 alkane compounds exhibited sufficient sensitivity (89.6%) and specificity (82.9%) to discriminate lung cancer patients and healthy people [24]. 22 volatile organic compounds comprising mostly alkanes, monomethylated alkanes and benzene derivatives could distinguish lung cancer patients from normal people [31].

Molecular Biology Background Research

Molecular biology studies strongly suggest that the endogenous alkanes produced as a result of lipid peroxidation originate from the methyl end of the fatty acid administered.

Scission of an alkane fragment extends from the methyl end of the fatty acid to the double bond during the process of peroxidation of polyunsaturated fatty acids. So, alkane is produced [37,38] For example, ethane is produced from n-3 acid and propane from n-4 acid. Besides, scientists view breath alkanes as index of lipid peroxidation [39].

Studies show that lipid peroxidation is elevated in lung cancer patients due to oxidative stress, by indication of higher (malondialdehyde) MDA level [40,41]. Reactive oxygen species (ROS) radicals which initiates lipid peroxidation by radical-chain reaction elevates as studies shown hydrogen peroxide radicals and glutathione levels elevated in lung tumour tissue [42,43,44].

In essence, breath alkanes increases as oxidative stress is elevated in lung cancerous cells. **Alkanes** can serve as markers for detection of lung cancer as its concentration in cancerous breath is higher than healthy breath.

Phase 2: Design of SCENT

Selection of Sensor Materials (Research-Oriented)

As targeted marker which was alkane compounds was well-defined, selective sensing technique which used **tetracosane,** $H(CH_2)_{24}H$ as monomer matrix or binder was chosen. **Carbon** powder was the filler of chemiresistive film.

Fabrication of Sensor

Wide array of trial experiments was conducted by combining two substrates with different mass ratio of sensor materials and four sensor materials deposition techniques. Success rate of fabricating sensor which showed baseline resistance was calculated to find out the best combination of substrate, amount of sensor materials and deposition technique.

(a) Substrate Design

Study Materials: Single-sided printed circuit board, copper wires, soldering iron and solder

Methods: Two types of substrate (Substrate I and II) (fig. 1) for deposition of sensor materials were designed. Substrate I was a single-sided printed circuit board with mounted copper wires as electrodes. Sensor materials would be deposited in between mounted copper wires. Substrate II was a single-sided printed circuit board with interdigitated built-in copper sheets which serve as electrodes. Sensor materials would be deposited between two copper sheets. Connecting wires were soldered to electrodes.

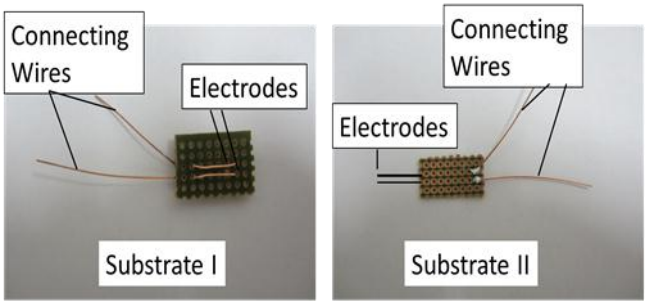


Figure 1 shows Substrate I and Substrate II

Figure 1 shows substrate I (left) and substrate II (right). Substrate I was a single-sided printed circuit board with copper wires as electrodes. Substrate II was a single-sided printed circuit board and its copper sheets as electrodes. Connecting wires were soldered to the electrodes.

(b) Sensor Materials Deposition Technique

Technique 1 (Drop Casting Technique) [45]:

Study Materials: Tetracosane, Carbon powder, bis(2-ethylhexyl) phthalate, Cyclohexene

Methods: 0.06g tetracosane, carbon powder and 0.02g bis(2-ethylhexyl) phthalate were mixed with 2ml cyclohexene liquid. Then, 0.5ml solution was dropped between two electrodes of printed circuit board using a syringe. The substrate was heated at 85 °C for 2 hours. The connecting wires were connected to digital multimeter to measure the sensor film's baseline resistance. 400 pilot experiments were carried out using 0.01g, 0.02g, 0.03g, 0.04g, 0.06g, 0.09g and 0.12g carbon powder.

Technique 2 (Dip coating Technique) [46]:

Study Materials: Tetracosane, Carbon powder, bis(2-ethylhexyl) phthalate, Cyclohexene

Methods: 3.00g tetracosane, carbon powder and 1.00g bis(2-ethylhexyl) phthalate were mixed with 100ml cyclohexene liquid in a beaker. The substrate was dipped into the solution for 20 minutes. Substrate was then heated at 85 °C for 2 hours. The connecting wires were connected to digital multimeter to measure the sensor film's baseline resistance. 400 pilot experiments were carried out using 0.50g, 0.75g, 1.00g, 1.50g, 2.00g, 3.00g and 6.00g carbon powder.

Technique 3 (Self-invented technique):

Study Materials: Tetracosane, Carbon powder, bis(2-ethylhexyl) phthalate

Methods: 0.01g of tetracosane, carbon powder with 0.02g of bis(2-ethylhexyl) phthalate was mixed in a beaker. The mixture clump was placed between two electrodes of substrate within the area of 10mm × 5mm. Then, the substrate was heated at 110 °C for 30 seconds. The connecting wires were connected to digital multimeter to measure the sensor film's baseline resistance. 200 pilot experiments were carried out using 0.01g and 0.02g carbon powder.

Technique 4 (Layer Deposition Technique):

Study Materials: Tetracosane, Carbon powder

Methods: 0.01g tetracosane was placed between the copper strips of substrate within the area of 10mm × 5mm. Next, the substrate was heated at 110 °C for 30 seconds. Then, carbon powder was spread atop the tetracosane film on the substrate using spatula. The substrate was heated again at 110 °C for 30 seconds. The connecting wires were connected to digital multimeter to measure the sensor film's baseline resistance. 200 pilot experiments were carried out using 0.01g and 0.02g carbon powder.

III. *Design of Breath-in Apparatus*

Study Materials: Plastic bottle (500ml), empty vitagen bottle and sensor

Methods: Two breath-in apparatuses were designed. Apparatus I (fig. 2) was built by adhering sensor to a plastic bottle. Apparatus II (fig. 3) was built by adhering sensor at the base of vitagen bottle and a straw fixed at the mouthpiece of bottle.

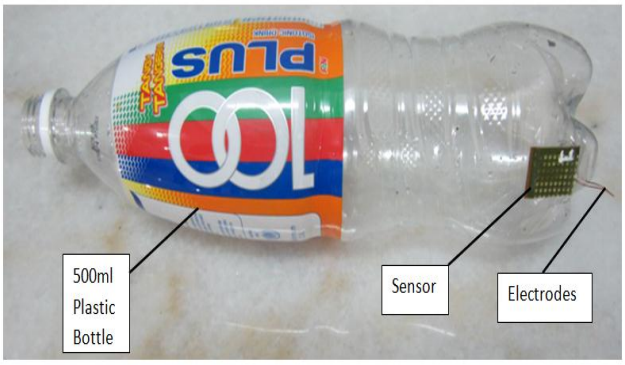


Figure 2 shows a 500ml plastic bottle with sensor inserted at the base (top)

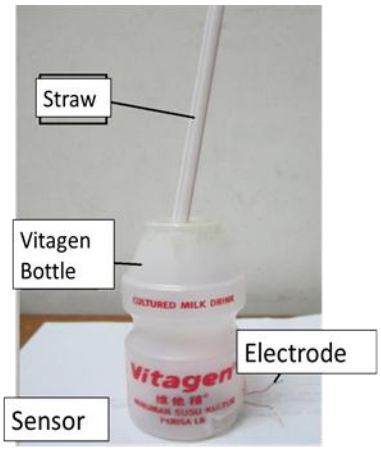


Figure 3 shows vitagen bottle with sensor adhered to the base inside (bottom).

Best breath-in apparatus was selected based on the sensor response when simulated lung cancer and healthy breath were injected into the bottle.

Phase 3: Performance of SCENT

Data Collection and Interpretation Technique

Digital multimeter was connected to copper wires which were soldered to electrodes of chemiresistor. Resistance value shown by multimeter before sensor exposes to analytes is baseline resistance. After exposing to breath, the resistance value shown in multimeter will be recorded every 10 seconds. Recorded sensor response will be interpreted using formulae (Equation 1 and 2):

$$\textbf{Sensor typical response} = \Delta R/R_b \quad (1)$$

where R_b is the baseline resistance of sensor in the absence of analyte and ΔR is the baseline-corrected steady-state resistance change of sensor upon exposure of the sensor to analyte;

$$\textbf{Sensor peak output} = \Delta R_p/R_b \quad (2)$$

where ΔR_p is the change in value between peak resistance and baseline resistance R_b.

Simulated Breath Test

Study Material: n-Heptanes, 2,6,6-trimethyloctane, 3-ethylhexane

Methods: Simulated breath of lung cancer and normal breath was prepared by diluting heptanes vapor in static dilution bottle (2L) until it reached desired concentration. The heptanes vapor concentration in simulated lung cancer breath was 15.0×10^{-12}M while 9×10^{-12}M in healthy breath. Then, simulated breath was injected into the breath-in apparatus with syringe to imitate subjects breathing into the apparatus. The sensor was connected to multimeter to measure its resistance before and during gas injection. The procedures were repeated with 2,6,6-trimethyloctane and 3-ethylhexane to replace heptane.

100 sensors were tested on each type of alkane vapour (50 sensors tested on simulated healthy breath, other 50 on simulated cancerous breath).

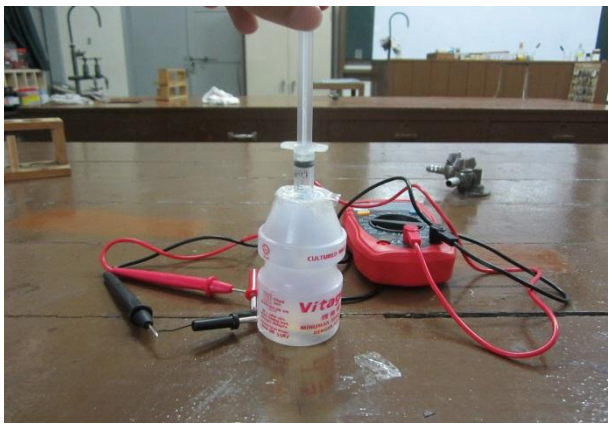


Figure 4 shows simulated breath prepared by diluting in static dilution bottle was injected into the breath-in apparatus which contained sensor by syringe.

Water Test

Study Materials: Water

Methods: Three drops of water were dropped onto the sensor. The sensor was connected to multimeter to measure its resistance before and after water dropping. 500 sensors were tested.

Real Breath Test

Study Group: 2 lung cancer patients and 5 healthy non-smoker volunteers. All of the subjects had been confirmed with or without disease with CT scan.

Table 1 shows demography of subjects participated in real breath test study

Subjects	Age	Gender	Stage of Lung Cancer	Cigarettes smoked per day
Patient 1	48	M	II	4
Patient 2	56	M	III	3
Volunteer 1	38	F	-	0
Volunteer 2	25	M	-	0
Volunteer 3	54	F	-	0
Volunteer 4	44	M	-	0
Volunteer 5	45	M	-	0

Methods: Subjects exhaled into the breath-in apparatus containing sensor for 6 minutes. The sensor was connected to multimeter and resistance values shown were recorded each 10 seconds interval. The tests were conducted by the subjects themselves under supervision to investigate if untrained personnel could conduct the test by following instructions.

IV. RESULTS AND DISCUSSION

From informatics approach, alkane compounds were found to be the best markers as they met all the criteria and overall, 26 in 29 alkane compounds (90%) were elevated in lung cancer breath compared to healthy breath. Concentration of alkanes in cancerous breath was averagely twice that in healthy breath. Background research and molecular biology background research were carried out because many breath analysis results didn't measure and compare the concentration of breath analytes.

Elevated alkane concentration would not be detected in long-term degenerative respiratory diseases such as asthma, bronchitis, emphysema, bacterial infection such as tuberculosis and hereditary pulmonary disorders such as cystic fibrosis and primary ciliary dyskinesia because their pathogeneses are not related to oxidative stress.

Tetracosane was chosen as matrix as it had remarkably high solubility and affinity towards alkane compounds due to structural similarities [47]. It had also been used as sensor materials in 3 electronic nose studies regarding alkane detection [15,48,49]. Carbon was selected as filler as it was transducing ingredient which conducts electricity and shows resistance. It is cheap and environmental-friendly. It has been used as fillers in several carbon-black electronic nose studies [17, 50,51,52,53].

Selective sensing technique was chosen over cross-sensing array technique. Selective sensing employs a highly selective receptor/detector that is designed to specifically bind to or detect an analyte of interest. This approach was suitable for this study as target analyte was well-defined, which is alkane. (alkane in this study) This technique allowed chemiresistor sensor to distinguish healthy and cancerous breath without pattern recognition algorithms. Analog-to-digital converter card, data logging software and laptop could be simplified to digital multimeter to measure the resistance of sensor. This made untrained personnel able to operate the SCENT system and interpret the end result easily.

Table 2 shows the result of 800 pilot experiments on two substrates and four deposition techniques. Substrate II (printed circuit board) combined with layer depositing technique and 0.01g carbon powder had achieved 100% success rate of fabricating chemiresistor sensor which showed baseline resistance. Besides, its baseline resistance fell between 100 Ω and 600 Ω, making it easy to be measured with common digital multimeter.

Table 2 shows the success rate of fabricating chemiresistor which could operate by showing baseline resistance. 50 out of 50 chemiresistor (not shown in table) made by substrate II, technique 4 and 0.01g carbon powder could produce baseline resistance.

	Technique 1	Technique 2	Technique 3	Technique 4
Substrate I	12/200	7/200	5/100	36/100
Substrate II	19/200	11/200	13/100	86/100

Substrate I could not work because sensor materials deposited was unable to contact with mounted electrodes, resulting in open circuit. Besides, the distance between electrodes was 4mm, which was too large, might cause chemiresistive film's resistance become too big until it was immeasurable by multimeter. Substrate II with built-in electrodes in printed circuit board solved these problems. Its laminated copper sheets electrodes ensured its contact with chemiresistive film while distance between two adjacent electrodes was <1mm, ensuring the chemiresistive film's resistance was low enough to be within the measurable range of multimeter. Substrate II was simpler in design.

Layer depositing technique (Method 4) deposited 0.01g tetracosane by melting it on the substrate and lay 0.01g carbon powder atop it so carbon powder will mix with the tetracosane liquid, producing chemiresistive film. The advantages were requiring no usage of organic solvent for deposition and low production cost. It was more environmental-friendly and only required 3 minutes to produce a sensor.

Vitagen bottle was chosen over 500ml plastic bottle as breath-in apparatus because sensor at the base of bottle could not detect low concentration of analytes (10^{-12} M) in bottle's voluminous space. Vitagen bottle was much smaller in size so it could concentrate the analytes for detection. It was cheap and disposable too.

Simplified chemiresistor-based electronic nose technology (SCENT) (fig. 5) comprised digital multimeter, a sensor (fig.6) and a breath-in apparatus. The breath-in apparatus consists of straw and vitagen bottle. Sensor is adhered to the base of vitagen bottle.

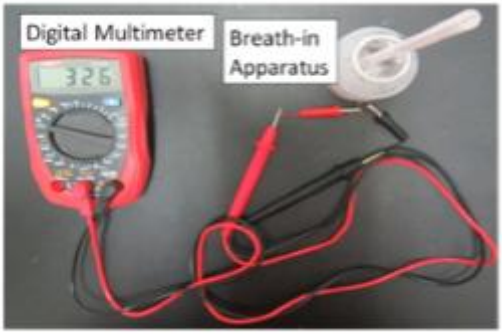


Figure 5 shows simplified chemiresistor-based electronic nose technology (SCENT).

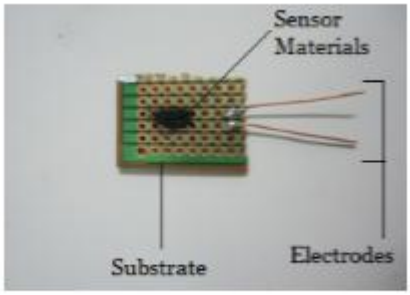


Figure 6 shows a fabricated sensor.

Figure 7 shows the sensor peak outputs when 300 sensors were exposed to simulated healthy as well as lung cancer breath. It showed that sensor generated higher sensor peak outputs (between 0.11% and 0.21%). when exposed to simulated lung cancer breath than that to simulated healthy breath (between 0.00% and 0.10%). In addition, Figure 8 demonstrates that sensors showed no response towards water, denoting near 100% of humidity in breath would not induce sensor's response. Out of 500 sensors, only 8 sensors which believed were faulty (1.6%) showed response to water. The current limitations of research were characteristic of sensor such as limit of detection, detecting power of sensor under humidity environment and exposure to other alkane compounds as well as interfering volatile organic compounds had not been studied.

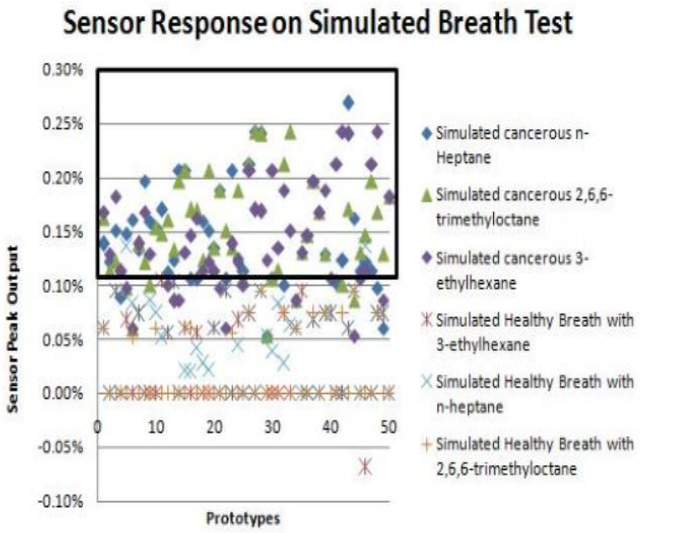
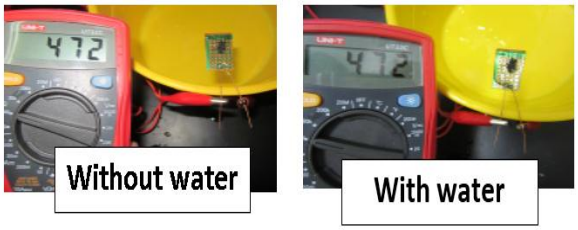


Figure 7 shows sensor peak output of SCENT when it was exposed to simulated lung cancer and healthy breath. Lung cancer breath induced greater resistance change when compared to healthy breath, as framed by the rectangular box.



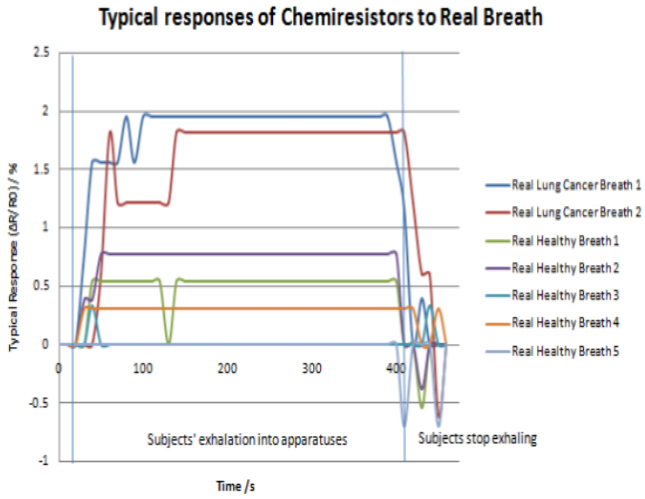


Figure 6 shows the sensor did not experience resistance change even though water drops were dropped on top of sensor materials.

Figure 9 demonstrates the power of SCENT to perfectly distinguish lung cancer patients from healthy people. However, the threshold sensor output values could not be determined because it ranged from 0.77% to 1.24%.

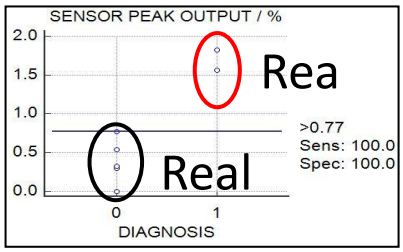


Figure 7 shows that the sensor peak output of SCENT towards lung cancer breath is higher than that towards healthy breath.

Figure 10 shows difference of SCENT sensor typical responses towards cancerous and healthy breath; in which healthy breath generated lower magnitude of sensor's resistance change. Sensor responded quickly by just a few seconds to detect lung cancer. Comparing simulated and real breath results, it was demonstrated that sensor peak outputs in real breath test were higher than that in simulated breath test because there were more alkane compounds in exhaled breath.

After the subjects stopped exhaling, the resistance of chemiresistors fell back to baseline resistance and underwent fluctuations of average ±0.31%. The mean sensor peak responses towards real healthy breath was 0.62% whereas its standard error 0.1378%. Addition of fluctuation error and twice the standard error gave a total error of ±0.5756%. Mean sensor peak responses towards real lung cancer breath was 1.7%, which was significant as the mean value was far beyond the range of total error. In other words, it was not generated by random or due to fluctuation.

V. Conclusion

This research achieved two things: simplification of electronic nose and detection of lung cancer using simplified electronic nose.

Phase one had demonstrated that lung cancer breath contains a higher level of light-chained monomethylated alkanes due to elevated oxidative stress. This means that other long-term degenerative respiratory diseases, bacterial infection and hereditary pulmonary disorders will not affect the result. Alkanes could be an accurate indicator for lung cancer.

In phase two and three, more than 1000 trials had proven that simplified chemiresistor could function like normal electronic nose, which generate different electrical signal against different concentration of analytes. Chemiresistive film of SCENT which had high affinity for alkane compounds would experience greater resistance change when exposed to lung cancer breath. There was distinct difference between sensor responses towards lung cancer breath and healthy breath.

Simplified Chemiresistor-based Electronic Nose Technology (SCENT) comprised vitagen bottle as sampling system, printed circuit board, tetracosane and carbon powder as sensor set and digital multimeter as analog-to-digital signals apparatus. Computational data processing was replaced using simple calculation of sensor peak output**:**

Sensor Peak Output = $\Delta R_p/R_b$

where ΔR_p was the change in value between peak resistance (greatest resistance of chemiresistive film upon exposure to breath) and baseline resistance R_b. Each test consumed one sensor.

During the fabrication process, new deposition technique was invented. SCENT tool does not require trained personnel for operation and result interpretation and is disposable. The

entire system costs about RM 60.00, which is 2500 times cheaper than current electronic nose system ($5000).

Under trials involving small number of participants (n=7), SCENT is able to perfectly differentiate 2 lung cancer patients (stage II and stage III) and 5 healthy volunteers. Although further research with larger sample size is required, SCENT has demonstrated its potential to revolutionize lung cancer screening. It costs RM 0.50 for each test which is 200 times cheaper than one computed tomography (CT scan) [6,7]. Each test takes less than 10 minutes to generate result, which is 6 times faster than CT scan [54]. Besides, subjects can receive end result immediately, unlike CT scanning, people need a few hours or days to receive screening result.

However, only seven human subjects were included in this study, which was statistically too small to determine the SCENT's threshold value to screen for lung cancer. Sample size between 30 and 500 were therefore required for further clinical research of SCENT sensitivity and specificity as well as threshold sensor peak output value which separate lung cancer patients group from healthy group.

By changing sensor materials, SCENT can perform test in other field such as disease diagnosing, food processing and monitoring as well as environmental pollutants detection. It addresses the major electronic nose problem which is each piece of equipment must be trained to distinguish odour, resulting in problem of standardizing the practice between different centers or factories.

VI. Acknowledgment

I would like to thank Dr. Kim Shyong Siow and Dr. Azrul Azlan from Institute of Microengineering and Nanoelectronics (IMEN) of University Kebangsaan Malaysia for guiding me and mentoring me on planning methodology, searching information, bolstering my spirit to continue my research though I met many difficulties when fabricating sensors.

I would like to thank Dr. Hoi Siew Kit from National University of Singapore (NUS) for giving insightful remarks on improving the overall performances of SCENT and research work. I also appreciated help from Mr. Leaw Ah See for letting me access to school chemistry lab to fabricate sensors and develop SCENT. I would thank Prof. Liam Chong Kin as well as Dr. Tan profusely for willingly helping me conduct SCENT lung cancer screening trials in University Malaya Medical Centre and guiding me on criteria taken in real breath test. At last, I would thank my parents and teachers for giving financial support, helping me search aid from professionals and give advice on improvements of my paper.

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