|| Volume 6 || Issue 7 || July 2021 || ISSN (Online) 2456-0774
INTERNATIONAL JOURNAL OF ADVANCE SCIENTIFIC RESEARCH
AND ENGINEERING TRENDS

CARBON NANOTUBES AND GRAPHENE BASED SENSORS FOR THE DETECTION OF LUNG CANCER RELATED VOLATILE ORGANIC COMPOUNDS

Muhammad Hassan Raza[1], Abdul Wahab[2], Iqra Zulfiqar[3], Muhammad Hamza[4], Muhammad Mudassar Rasheed[5] Muhammad Shahzeb Khan[6*] Muhammad Asif[7*]

[1]*Department of Biotechnology, COMSATS University Islamabad, Abbottabad Campus-Pakistan*
[2]*School of Agricultural Sciences and Veterinary Medicine University of Padua Italy*
[3]*Center For Applied Molecular Biology University of Punjab Lahore-Pakistan*
[4]*Department Molecular pathology and genomics Forman Christian college University, Lahore-Pakistan*
[5]*Institute of Industrial Biotechnology Government College University Lahore-Pakistan*
[6]*Department of Chemistry, International Islamic University Islamabad Pakistan*
[6]*Department of Environmental Science, COMSATS University Islamabad, Abbottabad Campus, Pakistan*
Corresponding Author: 03047092647asif@gmail.com

Abstract: Cellular breakdown in the lungs is an exceptionally deadly infection and causes the demise of 1.76 million individuals consistently which is higher than different sorts of cancers. A lung cancer diagnosis is a serious concern for everyone because mostly lung cancer is diagnosed at a later stage that is not curable. Recently, work is being done on the detection of non-invasive breath biomarker to diagnose lung cancer. Carbon based sensors displayed high affectability and selectivity towards the lung cancer related volatile organic compounds that are exhaled out by lung cancer patients. Carbon based sensors are quick, delicate, specific, and give at spot results. Our review focuses on the detection of lung cancer related volatile organic compounds through Carbon nanotubes and graphene-based sensors.

Keywords: *Carbon Nanotubes, Graphene Based Sensors, Detection of Lung Cancer*

I INTRODUCTION

Lung cancer is a very fatal disease and causes death of 1.76 million people every year that is very higher than the other types of the cancer [1]. Lung cancer diagnosis is a serious concern for all the researchers because most of the patients are not curable due to later stage diagnosis [2-4]. There are several conventional techniques that are under practice to diagnose lung cancer but these are painful and expensive that's why patients did not go for regular lung cancer test and it can't be diagnosed early [5]. Researchers are working to develop modern diagnostic techniques through which a patient can be diagnosed lung cancer at an early stage. Modern researches show that lung cancer patients exhaled out various volatile organic compounds with breath. These VOCs belong to various classes of organic compounds [6-10]. The scientists are working to develop such novel sensors which will be able to detect lung cancer related VOCs with high selectivity and sensitivity [11]. Recently, Carbon based sensors exhibited very high sensitivity and selectivity towards the VOCs. Carbon based sensors are rapid, sensitive, selective and give at spot results [12-14]**.** Carbon Nanostructures have a key role in the field of nanotechnology. These have large surface area and hollow structure due to which they give a signal when a molecule attaches at their surface. Among different types of Carbon, carbon nanotubes (CNTs) and graphene are good sensing materials for various types of analytes especially VOCs due to their unique optical and electronic properties [15-17].

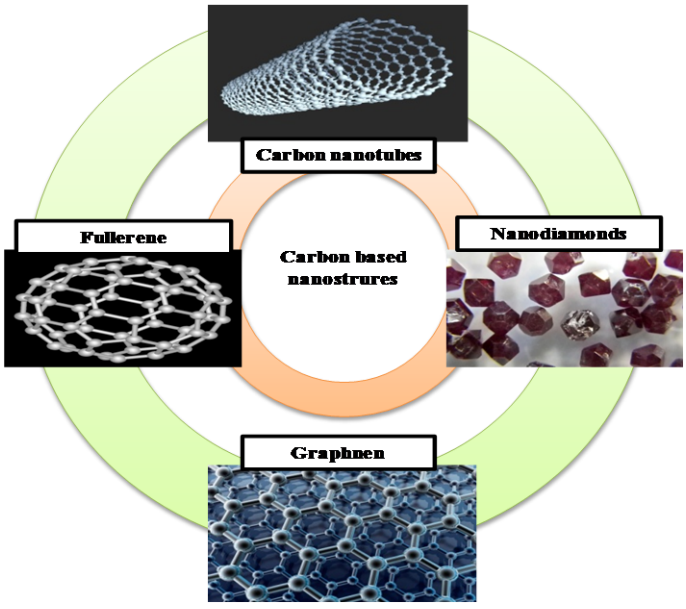

Figure 1. Carbon-based structures

Lung cancer is the major cause of cancer deaths in humans. In most cases, the indication of Lung cancer in the body of patient disclose through early symptoms. Treatment of Lung cancer depends on the stage and overall health condition of patient. There are three possible treatments for Lung cancer i.e surgery , chemotherapy and radiotherapy. Survival of patients depends on the stage of cancer, overall health condition and some other factors but overall only 14% people survive four to five years after the diagnosis of symptoms of Lung cancer. Symptoms of Lung cancer are:

1. Abdominal pain
2. Shoulder pain
3. Chest and Arm pain
4. Persistent breathlessness
5. Finger clubbing
6. Dysphagia
7. Swelling of face and neck
8. Hoarseness
9. Emphysema
10. Weight loss
11. Bone pain

Lung cancer can develop any where in the lungs and it can damage any part of the respiratory system. Lung cancer may take several years to develop and it usually effect the people who are fifty plus.

Lung cancer is of two major types.

1. Non-small cell lung cancer
2. Small cell lung cancer

These both types of lung cancer spreads in different ways and there treatment is also different. The growth and spreading of Non-small cell lung cancer is slow as compared to small cells lung cancer. Small cell lung cancer grows and spreads more quickly. Its main cause is smoking cigarettes.

Early diagnosis of Cancer:

Early diagnosis consists of three components:

- being aware of the symptoms of different forms of cancer and of the importance of seeking medical advice if you are concerned;
- access to clinical evaluation and diagnostic services; and
- timely referral to treatment services.

Carbon Nanotubes Based Sensor

CNTs are hollow cylindrical nanostructure consist of carbon atoms. CNTs can be classified in single-walled CNTs (SWCNTs) and Multiwalled CNTs (MWCNTs) based on their structural differences [18,19]. These have a regular patterned structure and good sensing properties because of semiconducting modification of CNTs which make them a fundamental material in the sensing of VOCs to diagnose lung cancer [20]. Kumar *et al.* synthesized specified sensors for the detection of VOCs which were named as vapor quantum resistive sensors (vQRS). Two steps were involved in the formation of these sensors. Firstly, CNT layers and the secondly nanometric layer of drop casted polymer was generated to coat CNT. The sensor showed a chemo resistive behavior by which different lung cancer biomarkers were identified at low concentrations [21]. CNTs were bonded to different polyhedral oligomericsilsesquioxanes (POSS) through the covalent and non-covalent bonds. A specific type of chemoresistive sensor was established and QRS of different nano-junctions gap were generated to establish a selective array of sensor which could discriminate different VOC at 6 ppm level [22].

A Chemresistor sensor was developed by using SWCNTS modified with meso-tetraphenylporphyrin. Response was evaluated by exposing the sensor with different classes of VOCs [23]. Zhang *et al*. synthesized a composite of single-walled CNT and MIPs. This composite was fabricated on alumina tube with Au electrode and Pt wires to check gas sensing properites. The response for methanol gas was in the range of 1 ppm level [24]. Janfaza *et al*. constructed a sensor by using MIPs and MWCNTs to diagnose lung cancer by detecting hexanal molecules. The detection limit obtained atroom temperature was 10-200 ppm [25].

Tasaltin and Basarir synthesized a sensor that was based on Au NPs and MWCNTs. Firstly, Polyimide interdigital electrodes were fabricated then Au NPs and MWCNTs were electrosprayed. Sensor investigated different polar and non-polar VOCs [26]. Abraham *et al.* synthesized a surface acoustic wave (SAW) sensor having CNTs as adsorbent substances. In the second model, nanospheres of ZnO and CuO were added into the sensing layer to enhance the response. Second model gave better results than the first model. They suggested that a composite of ZnO-CuO/CNT SAW sensor can be the ideal material to sense VOCs [27]. Interdigital electrode was coated with MWCNTs and **PEG** due to their good adsorption ability for the VOCs. The sensor exhibited good response at room temperature for acetone, ethanol, isopropanol and isoprene [28]. Park *et al.* used ionic liquids (ILs) to establish a distinctive sensor of chemiresistive CNTs. Ionic liquid has several unique properties including high thermal stability and conductivity. Constructed Sensor was functionalized with imidazolium-based ILs to detect cancer related VOCs. Stability is one of the major advantages of this type of sensor [29].

Graphene-based sensor

Graphene consists of a hexagonal structure in which carbon atoms are sp^2 hybridized forming a two-dimensional nanomaterial layer. Single carbon sheet is formed by the arrangement of carbon atoms in a single layer while in multilayer graphene, several sheets are arranged at each other [30-32]. Graphene materials are being used as semiconductors, transistors and other sensing fabrics due to their transparency, conductivity, strength, and flexibility [33,34].

Zhang *et al*. synthesized a graphene-based sensor for diagnostic purposes. Graphene oxide was synthesized by the modification of Hummer's method and characterized by different characterization tools [35]. Multi-layer graphene (MLG) was fabricared for the detection of lung cancer molecules including ethanol, isopropanol, and acetone. Substances were evaluated by using flat MLG (f-MLG) and patterned MLG (p-MLG) electrodes, where the electrical conductivity of p-MLG was enhanced by acetone. Both sensors showed a good response towards the chemical substance especially the f-MLG sensor exhibited high selectivity for acetone [36]. Nag *et al.* developed an electronic nose by using reduced graphene oxide (RGO). GO was wrapped with functionalized β-cyclodextrin to enhance its functional ability. Supramolecular assembly was established by modifying chemically functionalized cyclodextrin with RGO non-covalently. Pyrene-adamantane was used as a linker in this reaction. Chemical modification was made by using cyclodextrin to make the sensor more selective. RGO has greater surface area and good electrical conducting ability which made QRS sensor selective and sensitive for VOCs [37].

Rattanabut *et al.* synthesized a composite of graphene and poly(methyl methacrylate) (GR/PMMA) for sensing purposes. The GR/PMMA sensor composite examined different VOCs [38]. Similalry, a GO/polypyrene composite based sensor was fabricated to examine toluene. The constructed sensor was sensitive at 9.87×10^{-4} ppm^{-1} level [39]. A chemical sensor was formed for the detection of organic vapor by composing a layer of graphene (transducer layer) with a MIP layer. The gas sensor was further embedded within a smidgen antenna and results were evaluated [40].

GO were modified and reduced with amine ligands which lead to the formation of functionalized rGO. Unmodified rGO and modified functionalized rGO were arranged to develop a chemiresistive arrayThe lowest detection limit was 25 ppm with the ability to differentiate between different VOCs [41]. GO layer was coated on the SiO_2 sensor with Pt bed electrodes. GO was reduced at the desired amount in a specific environment. Reduction of GO affects the sensitivity of sensor in response to various VOCs [42].

Vessalli *et al.* fabricated graphene composite with ZnO nanorods (NR). Firstly, ZnO NR was prepared and coated at Au interdigital electrodes. GO sheet was also embedded with ZnO-NR to develop a composite of GO/ZnO-NR. Selective detection of acetone, benzene, ethanol, and methanol was performed [43]. Liu *et al*. prepared a smartphone-based sensor by measuring and analyzing AC impedance. Graphene and ZnO were used to modify interdigital electrode. Nitrocellulose was also coated to enhance sensing ability. It was a great achievement that VOCs could be detected by smart mobile phone. The concentration of VOCs was also measured by a specific android program. The lowest detection limit for acetone of was 1.56 ppm. VOCs were also differentiated through AC impedance spectroscopy [44].

II CONCLUSION

Lung cancer diagnosis is still a challenging task. There are several hurdles in the detection of lung cancer related VOCs because there is still need to improve the sensitivity and selectivity of the carbon based sensors. Carbon nanotechnology is a hope that researchers will fabricate an effective and commercial sensor for the detection of breath related VOCs.

ACKNOWLEDGEMENT

All the Author would like to acknowledge Mr. Muhammad Ali for his technical support for the data collection, data refining and the Preparation of this Article.

REFERENCES

1. Cancer — World Health Organization (2019). https://www.who.int/news-room/fact-sheets/detail/cancer. Date accessed: March 21, 2021.

2. Krishnaiah, V., Narsimha, G., & Chandra, D. N. S. (2013). Diagnosis of lung cancer prediction system using data mining classification techniques. *International Journal of Computer Science and Information Technologies*, *4*(1), 39-45.

3. Moujaess, E., Kourie, H. R., & Ghosn, M. (2020). Cancer patients and research during COVID-19 pandemic: a systematic review of current evidence. *Critical reviews in oncology/hematology*, 102972.

4. Cassim, S., Kidd, J., Rolleston, A., Keenan, R., Aitken, D., Firth, M., & Lawrenson, R. (2021). Hā Ora: Barriers and enablers to early diagnosis of lung cancer in primary healthcare for Māori communities. *European Journal of Cancer Care*, *30*(2), e13380.

5. Li, Z., Shu, J., Yang, B., Zhang, Z., Huang, J., & Chen, Y. (2020). Emerging non-invasive detection methodologies for lung cancer. *Oncology letters*, *19*(5), 3389-3399.

6. Koureas, M., Kirgou, P., Amoutzias, G., Hadjichristodoulou, C., Gourgoulianis, K., & Tsakalof, A. (2020). Target Analysis of Volatile Organic Compounds in Exhaled Breath for Lung Cancer Discrimination from Other Pulmonary Diseases and Healthy Persons. *Metabolites*, *10*(8), 317.

7. Chen, X., Muhammad, K. G., Madeeha, C., Fu, W., Xu, L., Hu, Y., & Yurievna, G. O. (2021). Calculated indices of volatile organic compounds (VOCs) in exhalation for lung cancer screening and early detection. *Lung Cancer*, *154*, 197-205.

8. Tsou, P. H., Lin, Z. L., Pan, Y. C., Yang, H. C., Chang, C. J., Liang, S. K., & Li, Y. K. (2021). Exploring volatile organic compounds in breath for high-accuracy prediction of lung cancer. *Cancers*, *13*(6), 1431.

9. Hua, Q., Zhu, Y., & Liu, H. (2018). Detection of volatile organic compounds in exhaled breath to screen lung cancer: A systematic review. *Future Oncology*, *14*(16), 1647-1662.

10. Sun, Y., Chen, Y., Sun, C., Liu, H., Wang, Y., & Jiang, X. (2019). Analysis of volatile organic compounds from patients and cell lines for the validation of lung cancer biomarkers by proton-transfer-reaction mass spectrometry. *Analytical Methods*, *11*(25), 3188-3197.

11. Jia, Z., Zhang, H., Ong, C. N., Patra, A., Lu, Y., Lim, C. T., & Venkatesan, T. (2018). Detection of lung cancer: concomitant volatile organic compounds and metabolomic profiling of six cancer cell lines of different histological origins. *ACS omega*, *3*(5), 5131-5140.

12. Pargoletti, E., & Cappelletti, G. (2020). Breakthroughs in the design of novel carbon-based metal oxides nanocomposites for VOCs gas sensing. *Nanomaterials*, *10*(8), 1485.

13. Tomić, M., Šetka, M., Vojkůvka, L., & Vallejos, S. (2021). VOCs Sensing by Metal Oxides, Conductive Polymers, and Carbon-Based Materials. *Nanomaterials*, *11*(2), 552.

14. Seekaew, Y., Pon-On, W., & Wongchoosuk, C. (2019). Ultrahigh selective room-temperature ammonia gas sensor based on tin–titanium dioxide/reduced graphene/carbon nanotube nanocomposites by the solvothermal method. *ACS omega*, *4*(16), 16916-16924.

15. Nasir, S., Hussein, M. Z., Zainal, Z., & Yusof, N. A. (2018). Carbon-based nanomaterials/allotropes: A glimpse of their synthesis, properties and some applications. *Materials*, *11*(2), 295.

16. Fernández-García, J. M., Evans, P. J., Filippone, S., Herranz, M. Á., & Martín, N. (2019). Chiral molecular carbon nanostructures. *Accounts of chemical research*, *52*(6), 1565-1574.

17. Liu, H., Zhang, L., Yan, M., & Yu, J. (2017). Carbon nanostructures in biology and medicine. *Journal of Materials Chemistry B*, *5*(32), 6437-6450.

18. Anzar, N., Hasan, R., Tyagi, M., Yadav, N., & Narang, J. (2020). Carbon nanotube-A review on Synthesis, Properties and plethora of applications in the field of biomedical science. *Sensors International*, *1*, 100003.

19. Rahman, G., Najaf, Z., Mehmood, A., Bilal, S., Mian, S. A., & Ali, G. (2019). An overview of the recent progress in the synthesis and applications of carbon nanotubes. *C—Journal of Carbon Research*, *5*(1), 3.

20. Pargoletti, E., & Cappelletti, G. (2020). Breakthroughs in the design of novel carbon-based metal oxides nanocomposites for VOCs gas sensing. *Nanomaterials*, *10*(8), 1485.

21. Kumar, B., Castro, M., & Feller, J. F. (2013). Quantum resistive vapour sensors made of polymer coated carbon nanotubes random networks for biomarkers detection. *Chem. Sens*, *3*(20), 1-7.

22. Nag, S., Sachan, A., Castro, M., Choudhary, V., & Feller, J. F. (2016). Spray layer-by-layer assembly of POSS functionalized CNT quantum chemo-resistive sensors with tuneable selectivity and ppm resolution to VOC biomarkers. *Sensors and Actuators B: Chemical*, *222*, 362-373.

23. Liu, S. F., Moh, L. C., & Swager, T. M. (2015). Single-walled carbon nanotube–metalloporphyrinchemiresistive gas sensor arrays for volatile organic compounds. *Chemistry of Materials*, *27*(10), 3560-3563.

24. Zhang, J., Zhu, Q., Zhang, Y., Zhu, Z., & Liu, Q. (2016). Methanol gas-sensing properties of SWCNT-MIP composites. *Nanoscale research letters*, *11*(1), 522.

25. Janfaza, S., Nojavani, M. B., Nikkhah, M., Alizadeh, T., Esfandiar, A., & Ganjali, M. R. (2019). A selective chemiresistive sensor for the cancer-related volatile organic compound hexanal by using molecularly imprinted polymers and multiwalled carbon nanotubes. *MicrochimicaActa*, *186*(3), 137.

26.Tasaltin, C., & Basarir, F. (2014). Preparation of flexible VOC sensor based on carbon nanotubes and gold nanoparticles. *Sensors and Actuators B: Chemical*, *194*, 173-179.

27. Abraham, N., Krishnakumar, R. R., Unni, C., & Philip, D. (2019). Simulation studies on the responses of ZnO-CuO/CNT nanocomposite based SAW sensor to various volatile organic

chemicals. *Journal of Science: Advanced Materials and Devices*, *4*(1), 125-131.

28. Liu, Z., Yang, T., Dong, Y., & Wang, X. (2018). A room temperature VOCs gas sensor based on a layer by layer multi-walled carbon nanotubes/poly-ethylene glycol composite. *Sensors*, *18*(9), 3113.

29. Park, C. H., Schroeder, V., Kim, B. J., & Swager, T. M. (2018). Ionic Liquid-Carbon Nanotube Sensor Arrays for Human Breath Related Volatile Organic Compounds. *ACS sensors*, *3*(11), 2432-2437.

30. Farjadian, F., Abbaspour, S., Sadatlu, M. A. A., Mirkiani, S., Ghasemi, A., Hoseini-Ghahfarokhi, M., & Hamblin, M. R. (2020). Recent developments in graphene and graphene oxide: Properties, synthesis, and modifications: A review. *ChemistrySelect*, *5*(33), 10200-10219.

31. Zhao, Z., Bai, P., Du, W., Liu, B., Pan, D., Das, R., & Guo, Z. (2020). An overview of graphene and its derivatives reinforced metal matrix composites: Preparation, properties and applications. *Carbon*.

32. Kang, J., Huang, S., Jiang, K., Lu, C., Chen, Z., Zhu, J., & Zhuang, X. (2020). 2D Porous Polymers with sp2-Carbon Connections and Sole sp2-Carbon Skeletons. *Advanced Functional Materials*, *30*(27), 2000857.

33. Rouf, H. K., & Haque, T. (2021). Sensitivity Enhancement of Graphene-MoSe 2–Based SPR Sensor Using Ti Adhesion Layer for Detecting Biological Analytes. *Plasmonics*, 1-10.

34. Pan, S., Pei, Z., Jing, Z., Song, J., Zhang, W., Zhang, Q., & Sang, S. (2020). A highly stretchable strain sensor based on CNT/graphene/fullerene-SEBS. *Rsc Advances*, *10*(19), 11225-11232.

35. Zhang, X. F., Zhang, Z. W., He, Y. L., Liu, Y. X., Li, S., Fang, J. Y., Zhang, X.A., & Peng, G. (2016). Sniffing lung cancer related biomarkers using an oxidized graphene SAW sensor. *Frontiers of Physics*, *11*(2), 116801.

36. Kovalska, E., Lesongeur, P., Hogan, B. T., & Baldycheva, A. (2019). Multi-layer graphene as a selective detector for future lung cancer biosensing platforms. *Nanoscale*, *11*(5), 2476-2483.

37. Nag, S., Duarte, L., Bertrand, E., Celton, V., Castro, M., Choudhary, V., Guegan, P., & Feller, J. F. (2014). Ultrasensitive QRS made by supramolecular assembly of functionalized cyclodextrins and graphene for the detection of lung cancer VOC biomarkers. *Journal of Materials chemistry B*, *2*(38), 6571-6579.

38. Rattanabut, C., Wongwiriyapan, W., Muangrat, W., Bunjongpru, W., Phonyiem, M., & Song, Y. J. (2018). Graphene and poly (methyl methacrylate) composite laminates on flexible substrates for volatile organic compound detection. *Japanese Journal of Applied Physics*, *57*(4S), 04FP10.

39. Zhang, L., Li, C., Liu, A., & Shi, G. (2012). Electrosynthesis of graphene oxide/polypyrene composite films and their applications for sensing organic vapors. *Journal of Materials Chemistry*, *22*(17), 8438-8443.

40. Adams, J. D., Emam, S., Sun, N., Ma, Y., Wang, Q., Shashidhar, R., & Sun, N. X. (2019). A Molecularly Imprinted Polymer-Graphene Sensor Antenna Hybrid for Ultra Sensitive Chemical Detection. *IEEE Sensors Journal*.

41. Liu, B., Huang, Y., Kam, K. W., Cheung, W. F., Zhao, N., & Zheng, B. (2019). Functionalized graphene-based chemiresistive electronic nose for discrimination of disease-related volatile organic compounds. *Biosensors and Bioelectronics: X*, 100016.

42. Ahn, H. S., Jung, B. K., Park, J. R., & Joo, J. C. (2015). Graphene oxide based selective VOCs sensor for indoor air quality monitoring. In *Materials Science Forum* (Vol. 804, pp. 39-42).Trans Tech Publications.

43. Vessalli, B. A., Zito, C. A., Perfecto, T. M., Volanti, D. P., & Mazon, T. (2017). ZnOnanorods/graphene oxide sheets prepared by chemical bath deposition for volatile organic compounds detection. *Journal of Alloys and Compounds*, *696*, 996-1003.

44. Liu, L., Zhang, D., Zhang, Q., Chen, X., Xu, G., Lu, Y., & Liu, Q. (2017). Smartphone-based sensing system using ZnO and graphene modified electrodes for VOCs detection. *Biosensors and Bioelectronics*, *93*, 94-101.