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REVIEW ARTICLE

Application of Electrical Impedance Tomography in Cancer Diagnosis

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ABSTRACT
Cancer imposed a social, economical, and physical burden all over the world that required early-stage diagnosis and timely medication. There are several costly and unaffordable diagnostic tools and techniques that create an economic strain over the middle and lower economic class of the society. Therefore, there is a need for some cost-effective and sensitive technique that can be afforded by each class of society. Electrical impedance tomography may be an emerging solution as recently research started for this well-established technique in the detection of premalignant tissue. In this paper, we review the working principle, the basic functionality of EIT as well as its procedure to differentiate the cancerous and non-cancerous tissue. Sensitivity and specificity were also reviewed to evaluate its performance in cancer diagnosis. The previous finding reported the efficacy of electrical impedance tomography in cancer diagnosis with higher sensitivity and specificity and proposed it as a cost-effective tool for early diagnosis of several types' cancer.
Keywords; *Electrical Impedance Tomography, Cancer, Resistivity, Conductivity, Impedance, Sensitivity and Specificity*

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INTRODUCTION

Cancer is a serious and complex disease that can affect any part of the body [1]. It arises from the transformation of normal cells into tumor cells in a multistage process that generally progresses from a pre-cancerous lesion to a malignant tumor [2]. These changes are resulted due to the interaction of genes with some external factors, which includes physical carcinogens (ultraviolet and ionizing radiation), chemical carcinogens such as asbestos, components of tobacco smoke, aflatoxin (a food contaminant), and arsenic (a drinking water contaminant), biological carcinogens, such as certain viruses, bacteria, or parasites [3]. According to WHO, Cancer is the second leading cause of death, accounting for 9.6 million deaths in 2018 [4]. The overall burden of cancer is increasing economically in developing countries as a result of population, aging, and growth besides that the increased adoption of cancer-associated lifestyle including smoking, physical inactivity, etc [5]. The existing technology for cancer diagnosis are computed tomography (CT), magnetic resonance imaging (MRI), single-photon emission computerized tomography (SPECT) and positron emission tomography (PET) etc [6]. These technologies are costly, less accessible, and have patient compliances with side effects. The economic burden of a cancer diagnosis can be replaced by an alternative cost-effective technology electrical impedance tomography with no patient compliances. The aim of this study is to review the application of electrical impedance tomography in cancer diagnosis. Electrical impedance scanning has been generating interest for several reasons including comfort to the patient, relatively low cost, compatibility, and portability [7-8]. Cancer is simply the uncontrolled proliferation of the cells without following the cell cycle norms, because of this cancer cells will have a different material composition ratio as compared to the normal cell. Shreds of evidence are available that the hydrostatic condition of the cancer is different with respect to the normal cells [9-10]. Changes in dielectric media result from a change in impedance characteristics of the cell [11]. Electrical impedance tomography based on Ohm's Law. It measures the impedance or opposition to the flow of an electric current through the body fluids contained mainly in the lean tissue. A small constant current or constant voltage signal administrated inside the body using a surface electrode other side connected to the EIT instrument [12-14]. Output potentials and voltage drop between the electrodes measured concerning mono or multi-frequency current [15-18]. Further, an image constructed using the backend software that indicates resistivity and conductivity of the tissue in the form of an image. Figure 1 is representing a simple working block diagram to understand the working of electrical impedance tomography (EIT).

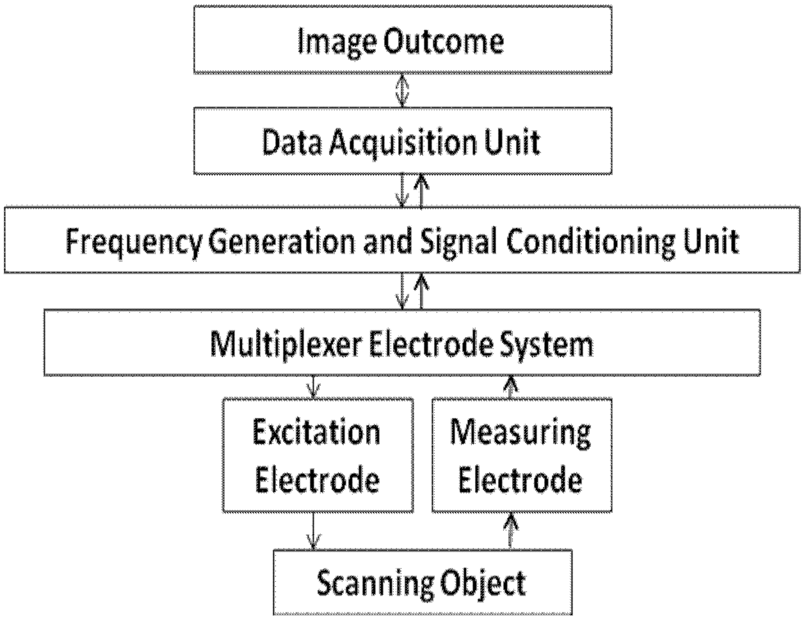

Figure 1: Block diagram of EIT

ELECTRICAL PROPERTIES OF BIOLOGICALTISSUE:

Electrical properties of biological tissues depend on cellular structures. Human tissue consists of an aggregation of cells surrounded by fluids. Each cell has a membrane enveloping intracellular fluid. The cellular membrane is a complex system, containing mainly lipids, proteins, and oligosaccharides, and shows a bi-layer structure. The backbone of this bi-layer cellular membrane is a heterogeneous mixture of different kinds of lipids. Lipids are organic molecules composed of a hydrophilic head group (polar) and a hydrophobic acyl chain (hydrocarbon chain) [19]. Several studies on bilayer cell membranes showed that a cell membrane maintains an ion concentration gradient between the intracellular and extracellular spaces. This electric charge gradient creates an electrical potential difference across the membrane and behaves as an electrical capacitor [20-21] an electrical capacitor is a charge-storing device, which consists of two conducting plates separated by an insulating barrier. The lipid bilayer of the plasma membrane forms an insulating barrier to separate ICF and ECF electrically conductive plates and behaves like a capacitor [22-23 resistor too, therefore, controls the conductance of various ions. This conductance can directly translate to resistance since conductance is simply the inverse of resistance. Therefore, the cell membrane is modeled as a resistor and capacitor in parallel [24], Figure 2.

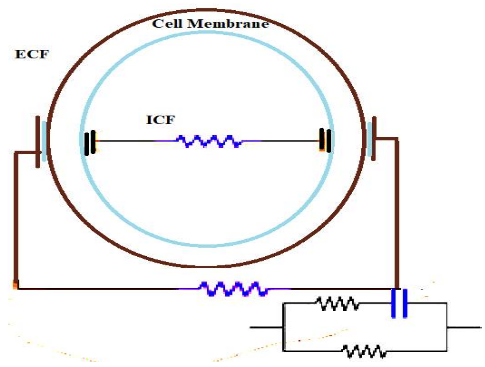

Figure 2: Electrical Equivalent cell model

Since the electrical impedance of the biological tissue contains resistive and capacitive and can be represented as Z(impedance)=R (Resistance)+jX (reactance) in serial representation and Y(admittance)=G (conductance)+j*w (angular frequency)*C (capacitance). However, electrical properties of tissue vary with the frequency of applied electric current and can be seen in the form of alpha, beta, and gamma dispersion [25]. At low frequency (10 Hz–10 kHz) alpha dispersion occurs that is mainly affected by the ionic environment surrounding, the cells or the ions present in the extracellular spaces. The beta dispersion is related to the structure relaxation and occurs in between 10 kHz–10 MHz; at higher frequencies >10MHz, the gamma dispersion found which is related to water molecules. Figure 3 representing the pathways for the low and frequency electrical current within the biological tissues. The alpha and beta dispersion regions are more interesting in medical applications since most changes between pathological and normal tissue occur in this range [26-28]. Any alteration in the permittivity, and hence in the specific membrane capacitance and impedance may be attributed to morphological and/or functional alteration of the membrane. Therefore, changes in membrane bioelectric properties may indicate the aging presence of disease or stress [29-31]. Zohdi *et al.* stated deviation of the permittivity parameter help to characterize the tissue disorders [30]. Several techniques like bioelectrical impedance analysis (BIA), electrical impedance spectroscopy (EIS), electrical impedance plethysmography (IPG), impedance cardiography (ICG), and electrical impedance tomography (EIT) based on electrical impedance of biological tissues are being used for diagnostic purposes also [32-37].

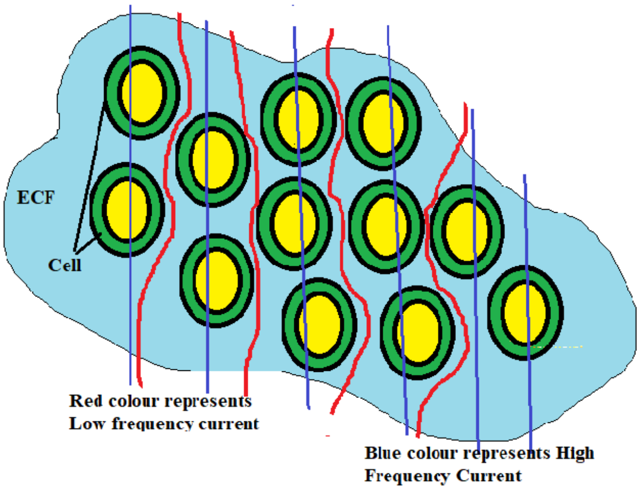

Figure 3: Pathways for Low and High Frequency current

ELECTRICAL IMPEDANCE TOMOGRAPHY FOR CANCER DIAGNOSIS:

Breast cancer is a medically and socially serious issue worldwide that needs early detection for effective treatment. Electrical impedance tomography used as a supplement to the existing technique. There are several studies to evident its application in breast cancer diagnosis. Raneta et al., 2012 randomly selected patients 18-94 (mean 54) years with breast cancer were also confirmed breast cancer using X-ray mammography and ultrasonography. Electrical Impedance Tomography performed using MEIK developed Russian Academy of Sciences. Results shows sensitivity and specificity of EIT87%, 89% and 85%, X-ray mammography (MMG) 91% and 91%; ultrasonography (USG) 91% and 84%. Sensitivity increased to 96% and 98%, respectively, when combinations EIT+MMG and EIT+USG were used. The specificity increased to 79% for EIT+MMG and 71% for EIT+USG. EIT+MMG and EIT+USG NPV remained the same. PPV was 65% and 58%, respectively for the EIT+MMG and EIT+USG combination [38]. Another study by Pak *et. al.*, 2012 also reported 87.39%. the efficiency of EIT in breast cancer diagnosis [39]. Murillo *et al.*, 2020 demonstrated the use of mono frequency electrical impedance mammography (EIM) in the detection of breast cancer with 85 % sensitivity and 96% specificity. This analysis was performed on 1200 women between 25 and 70 years old using MEIK electro impedance v.5.6. (0.5 mA, 50 kHz), developed and manufactured by PKF SIM-Technika® [40]. Halter et al., 2015, demonstrates the 81% specificity and 77%.sensitivity of EIT technique in cancer diagnosis [41].

A preliminary clinical study carried out by Wan *et al.*, 2013 demonstrated higher conductivity of cancerous tissue and reported potential benefits of electrical impedance measurements. A study of EIS (electro interstitial scan) system using bioimpedance and chronoamperometry was performed. Wan et al., 2013 examined three hundred men with prostate cancer where EIS system had a very good specificity of 85.2% and 62.5%sensitivity. Integration of bioimpedance and chronoamperometry with EIS raises the sensitivity from 73.9% to 91.5% in prostate cancer imaging. EIS spectra differ for benign and malignant tissues [42], it can be used for the grading of low and high-grade malignant tissues [43]. Impedance tomography techniques are also proposed for cervical cancer diagnosis based on decreased resistivity and increased conductivity with 81% sensitivity and 71% specificity [44-46]. Another group of studies demonstrated the difference in melanomatous and non-melanomatous skin tumors with very high sensitivities > 95% [47-49]. Overall studies reported the application of electrical impedance tomography in oral, bladder, Liver, and Lung cancer detection [50-54].

CONCLUSION

The aim of this study was to review the application of electrical impedance tomography in cancer diagnosis. Previous studies reported the change in impedance and conductivity of malignant tissue from normal tissue. Therefore, resistivity, conductivity, and impedance are major monitoring parameters in electrical impedance tomography. Overall, this technology is painless, cost-effective, compatible, portable, user-friendly technique with no side effect. Cost-effective characteristic with a higher value for specificity and sensitivity to several types of malignant tissue make it suitable for cancer diagnostic for the economically weaker section of the society. It can be used for the earlier diagnosis of cancer with no side effect that further leads to the treatment of cancer.

REFERENCES

1. National Institutes of Health. (2007). NIH curriculum supplement series.
2. Khimavath UN. (2018). Prediction Comparative Study on Cervical Cancer Analysis in Women using Machine Learning Algorithms.
3. Parsa N. (2012). Environmental factors inducing human cancers. Iranian journal of public health, 41(11): 1.
4. Cai Z, & Liu Q. (2019). Understanding the Global Cancer Statistics 2018: implications for cancer control. Science China Life Sciences, 1-4.
5. Fitzmaurice C, Dicker D, Pain A, Hamavid H, Moradi-Lakeh M, MacIntyre MF., ... & Hamadeh RR. (2015). The global burden of cancer 2013. JAMA oncology, 1(4), 505-527.
6. Bouchelouche K, Turkbey B, Choyke P, & Capala J. (2010). Imaging prostate cancer: an update on positron emission tomography and magnetic resonance imaging. Current urology reports, 11(3): 180-190.
7. Lobo B, Hermosa C, Abella A, & Gordo F. (2018). Electrical impedance tomography. Annals of translational medicine, 6(2).
8. Bera TK. (2018, March). Applications of electrical impedance tomography (EIT): a short review. In 3rd international conference on communication systems (ICCS-2017) (Vol. 331).
9. Ford HL, & Pardee AB. (1999). Cancer and the cell cycle. Journal of Cellular Biochemistry, 75(S32): 166-172.
10. Shortt J, & Johnstone RW. (2012). Oncogenes in cell survival and cell death. Cold Spring Harbor perspectives in biology, 4(12): a009829.
11. Miklavčič D, Pavšelj N, & Hart FX. (2006). Electric properties of tissues. Wiley encyclopedia of biomedical engineering.
12. Zou Y, & Guo Z. (2003). A review of electrical impedance techniques for breast cancer detection. Medical engineering & physics, 25(2):, 79-90.
13. Pathiraja AA, Weerakkody RA, von Roon AC, Ziprin P, & Bayford R. (2020). The clinical application of electrical impedance technology in the detection of malignant neoplasms: a systematic review. Journal of Translational Medicine, 18(1):1-11.
14. van Weereld JJA, Player MA, Collie DAL, Watkins AP, & Olsen D. (2001). Flow imaging in core samples by electrical impedance tomography. SCA Society of Core Analysts.
15. Hope TA, & Iles SE. (2004). Technology review: the use of electrical impedance scanning in the detection of breast cancer. Breast Cancer Research, 6(2): 69.
16. Yang Y, & Jia J. (2017). A multi-frequency electrical impedance tomography system for real-time 2D and 3D imaging. Review of Scientific Instruments, 88(8): 085110.
17. Bera TK. (2018). Applications of Electrical Impedance Tomography (EIT): A Short Review. IOP Conf Ser. Mater Sci Eng. 90.
18. Yao J, Wang L, Liu K, Wu H, Wang H, Huang J, & Li J. (2020). Evaluation of electrical characteristics of biological tissue with electrical impedance spectroscopy. Electrophoresis, 41(16-17): 1425-1432.
19. Verma A, Uzun O, Hu Y, Hu Y, Han HS, Watson N, ... & Stellacci, F. (2008). Surface-structure-regulated cell-membrane penetration by monolayer-protected nanoparticles. Nature materials, 7(7): 588-595.
20. Tyler SE. (2017). Nature's electric potential: A systematic review of the role of bioelectricity in wound healing and regenerative processes in animals, humans, and plants. Frontiers in physiology, 8: 627.
21. Grimnes S & Martinsen OG. (2011). Bioimpedance and bioelectricity basics. Academic press.
22. Rudolph JL, & Stewart J. (1998). Evolution and the nature of science: On the historical discord and its implications for education. Journal of Research in Science Teaching: The Official Journal of the National Association for Research in Science Teaching, 35(10):1069-1089.
23. Kyle AH, Chan CT, & Minchinton AI. (1999). Characterization of three-dimensional tissue cultures using electrical impedance spectroscopy. Biophysical journal, 76(5): 2640-2648.

24. Amin M, & Isa Z. (2008). An examination of the relationship between service quality perception and customer satisfaction. International Journal of Islamic and Middle Eastern Finance and Management.
25. Dean DA, Ramanathan T, Machado D, & Sundararajan R. (2008). Electrical impedance spectroscopy study of biological tissues. Journal of electrostatics, 66(3-4): 165-177.
26. Geddes LA, Baker EL. (1967). The specific resistance of biological material-a compendium of data for the biomedical engineer and the physiologist. Med Biol Eng, 5:271–93.
27. Asami K. (2014). Low-frequency dielectric dispersion of bacterial cell suspensions. Colloids and Surfaces B: Biointerfaces, 119:1-5.
28. Asami K. (2002). Characterization of biological cells by dielectric spectroscopy. Journal of Non-Crystalline Solids, 305(1-3): 268-277.
29. Youm JB. (2015). Electrophysiological properties and calcium handling of. Jung, 67:368-388.
30. Zink MD, Weyer S, Pauly K, Napp A, Dreher M, Leonhardt S, ... & Mischke K. (2015). Feasibility of bioelectrical impedance spectroscopy measurement before and after thoracentesis. BioMed research international, 2015.
31. Pérez Camargo D. A, Allende Pérez S. R, Verastegui Avilés E., Rivera Franco MM, Meneses García A, Herrera Gómez Á., & Urbalejo Ceniceros VI. (2017). Assessment and impact of phase angle and sarcopenia in palliative cancer patients. Nutrition and Cancer, 69(8): 1227-1233.
32. Zohdi TI, & Wriggers P. (2008). An introduction to computational micromechanics. Springer Science & Business Media.
33. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, ... & Scharfetter H. (2004). Bioelectrical impedance analysis—part II: utilization in clinical practice. Clinical nutrition, 23(6): 1430-1453.
34. Kushner RF. (1992). Bioelectrical impedance analysis: a review of principles and applications. J Am Coll Nutr, 11(2): 199-209.
35. Jakicic JM, Wing RR, & Lang W. (1998). Bioelectrical impedance analysis to assess body composition in obese adult women: the effect of ethnicity. International journal of obesity, 22(3): 243-249.
36. Danford LC, Schoeller DA, & Kushner RF. (1992). Comparison of two bioelectrical impedance analysis models for total body water measurement in children. Annals of human biology, 19(6): 603-607.
37. Rutherford WJ, Diemer GA, & Scott ED. (2011). Comparison of Bioelectrical Impedance and Skinfolds with Hydrodensitometry in the Assessment of Body Composition in Healthy Young Adults. ICHPER-SD Journal of Research, 6(2): 56-60.
38. Raneta, O, Ondruš, D, & Bella, V. (2012). Utilisation of electrical impedance tomography in breast cancer diagnosis. Klin Onkol, 25(1), 36-41.
39. Pak DD, Rozhkova NI, Kireeva MN, Ermoshchenkova MV, Nazarov AA, Fomin DK, & Rubtsova NA. (2012). Diagnosis of breast cancer using electrical impedance tomography. Biomedical Engineering, 46(4): 154-157.
40. Murillo-Ortiz B, Hernández-Ramírez A, Rivera-Villanueva T, Suárez-García D, Murguía-Pérez M, Martínez-Garza S, ... & López-Partida X. M. (2020). Monofrequency electrical impedance mammography (EIM) diagnostic system in breast cancer screening. BMC cancer, 20(1):1-10.
41. Halter RJ, Schned AR, Heaney JA, & Hartov A. (2011). Passive bioelectrical properties for assessing high-and low-grade prostate adenocarcinoma. The Prostate, 71(16): 1759-1767.
42. Wan Y, Borsic A, Heaney J, Seigne J, Schned A, Baker M, ... & Halter R. (2013). Transrectal electrical impedance tomography of the prostate: spatially coregistered pathological findings for prostate cancer detection. Medical physics, 40(6Part1): 063102.
43. Halter RJ, Hartov A, Paulsen KD, SchnedA, & Heaney J. (2008). Genetic and least squares algorithms for estimating spectral EIS parameters of prostatic tissues. Physiological Measurement, 29(6): S111.
44. Mohr P, Birgersson U, Berking C, Henderson C, Trefzer U, Kemeny L, ... & Reinhold U. (2013). Electrical impedance spectroscopy as a potential adjunct diagnostic tool for cutaneous melanoma. Skin Research and Technology, 19(2): 75-83.
45. Åberg P, Birgersson U, Elsner P, Mohr P, & Ollmar S. (2011). Electrical impedance spectroscopy and the diagnostic accuracy for malignant melanoma. Experimental dermatology, 20(8): 648-652.
46. Rocha L, Menzies SW, Lo S, Avramidis M, Khoury R, Jackett L, & Guitera P. (2017). Analysis of an electrical impedance spectroscopy system in short-term digital dermoscopy imaging of melanocytic lesions. British Journal of Dermatology, 177(5):1432-1438.
47. Murdoch C, Brown BH, Hearnden V, Speight PM, D'Apice K, Hegarty AM, ... & Thornhill MH. (2014). Use of electrical impedance spectroscopy to detect malignant and potentially malignant oral lesions. International journal of nanomedicine, 9: 4521.
48. Sarode GS, Sarode SC, Kulkarni M, Karmarkar S, Patll S, & Auciustine D. (2015). Bioimpedance assessment of oral squamous cell carcinoma with clinicopathological correlation. The journal of contemporary dental practice, 16(9):715-722.
49. Ching CTS, SunTP, Huang SH, Hsiao CS, Chang CH, Huang SY, ... & Chen CY. (2010). A preliminary study of the use of bioimpedance in the screening of squamous tongue cancer. International journal of nanomedicine, 5: 213.
50. Keshtkar A, Keshtkar A, & Smallwood RH. (2006). Electrical impedance spectroscopy and the diagnosis of bladder pathology. Physiological Measurement, 27(7): 585.
51. Wilkinson BA, Smallwood RH, Keshtar A, Lee JA, & Hamdy FC. (2002). Electrical impedance spectroscopy and the diagnosis of bladder pathology: a pilot study. The Journal of urology, 168(4): 1563-1567.

52. Keshtkar A, Salehnia Z, Keshtkar A, & Shokouhi B. (2012). Bladder cancer detection using electrical impedance technique (Tabriz Mark 1). Pathology research international, 2012.
53. Laufer S, Ivorra A, Reuter VE, Rubinsky B, & Solomon SB. (2010). Electrical impedance characterization of normal and cancerous human hepatic tissue. Physiological measurement, 31(7): 995.
54. Prakash S, Karnes MP, Sequin EK, West JD, Hitchcock CL, Nichols SD, ... & Povoski SP. (2015). Ex vivo electrical impedance measurements on excised hepatic tissue from human patients with metastatic colorectal cancer. Physiological measurement, 36(2): 315.