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Technological advances in detection and diagnosis of Cancer: a review

Varahalarao Vadlapudi *[1], Dowluru SVGK Kaladhar[2], Sandeep Kulkarni[1], Sudhakar Meesala[2], Mutyala naidu Laguda [3], Jeyaraj Senthil Kumar[4]

[1]Diabetomics Medical Private Limited, Muppireddypally Village, Medak - 502336, Telangana

[2]Department of Microbiology and Bioinformatics, UTD, Atal Bihari Vajpayee University, Bilaspur-495009, Chattisgarh.

[3]Department of Botany, Adikavi Nannaya University, Rajamahendravanam-533296, Andhra Pradesh

[4] Department of Biotechnology, PSG College of Arts and Sciences, Coimbatore-641014, Tamil Naidu.

*Correspondence: Dr Varahalarao Vadlapudi, E-mail: vvraophd@gmail.com

ABSTRACT

Cancer is a major global health problem and leading cause of death globally. Recent advances in approaches and instrumentation in diagnosis of cancer become accurate, precise and save human lives. Early-stage detection of cancer is essential for the treatment and disease management. There have been several new advancements within radiation oncology in terms of utilizing Positron emission tomography (PET). The most widely used imaging method present for the diagnosis of cancers is the PET and F-FDG-PET/CT. Fluorescence *in situ* hybridization (FISH) procedure is possible to recognize tumor-specific abnormality. Enzyme-linked immunosorbent assay (ELISA) is the most frequently used technique amongst immunoassays for cancer detection and diagnosis. In the coming years, it is expected for molecular diagnostics metabolomics will play a crucial role in cancer detection. Scientists developed affordable, accurate, and simpler ELISA based detection for various cancers. Protein biomarkers for cancer detection typically emerge from the cancer cells. Molecular based techniques Polymerase chain Reaction (PCR), RNA-based assays, Nanotechnology (NT) based, Artificial intelligence (AI) and Bioinformatics based are emerging as more accurate and speedy techniques for early detection of cancer. In Liquid biopsy technique preferred samples are biological fluids such as pleural fluid, cerebrospinal fluid (CSF), ascites, urine, blood, saliva, and stool.

KEYWORDS: Cancer, Polymerase chain Reaction (PCR), Artificial intelligence, Bioinformatics

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INTRODUCTION

Cancer is a major public health problem and leading cause of death globally [1], causing one in six deaths. The major challenge is to accurately diagnose it at an early stage. Recent advances in approaches and instrumentation at molecular level the diagnosis of cancer become accurate, precise and save human lives. Human disease is also considered as the cause of the interaction between genetic and environmental factors. Challenges facing the early detection research fall into mainly five broad categories. 1. Understanding the biology of early cancer 2. Determining risk of developing cancer 3. Finding and validating cancer detection biomarkers 4. Developing accurate technologies for early detection 5. Evaluating early detection approaches. In the coming years, it is expected for molecular diagnostics like bioinformatics and metabolomics will play a crucial role in cancer detection [2,3] one approach for lung cancer detection traditionally followed is Tissue-based histopathological [4]. Molecular diagnostics rely heavily on the detection and quantification of cancer biomarkers. For diagnosing a cancer need potential biomarkers "a biological molecule found in tissues, other body fluids, blood (Circulating tumor DNA, circulating tumor cells, proteins, exosomes, and cancer metabolites) that provides information about a condition or disease and abnormal or normal process of cancer. There is an urgent need to find new signatures or biomarkers for early detection and prognosis. Oral cancers are the sixth most frequent cancer with a high mortality rate than Cervical cancer. Advances in Deep sequencing of circulating tumor DNA detects molecular residual disease and predicts recurrence in gastric cancer [5]. Early diagnosis of cancers and it plays a crucial role in the subsequent treatments and due to the recently new biomarker are found by DNA zyme-assisted aptasensors [6].

Positron emission tomography (PET) based detection

Early detection and staging of recurrence are also essential for optimal therapeutic management. The most widely used imaging method present for the diagnosis of cancers is the PET and F-FDG-PET/CT is the current state-of-the-art diagnostic imaging and has shown accurate staging of nonsmall cell lung cancers, anatomical and functional information of nonoperative head and neck cancer [7,8] and performs better for invasive ductal carcinoma and of staging invasive lobular carcinomas [9]. There have been several new advancements within radiation oncology in terms of utilizing PET scans in conjunction with certain tracers to identify and stage several types of cancer. Other variant FAPI-PET used to detect both the presence and activity of lung fibrogenesis [10]. Detection of Synchronous Esophageal Cancer (SEC) in Pharyngeal Cancer was achieved with high sensitivity [11]. With the help of PET found skeletal metastases in patients with prostate cancer [12,13] or breast cancer [14], in human papillomavirus-associated oropharyngeal cancer [15], pancreatic cancer [16], gastrointestinal stromal tumors [17].

Magnetic resonance spectroscopy (MRS)

MRS is a widely used form of imaging techniques used for the diagnosis of cancer. MRS detects metabolic changes in tumors such as total choline (Cho) levels and ratios with other metabolites in detection of cancer. MRS has a clinical role in grading gliomas along with other imaging features like necrosis enhancement and haemorrhage it can be useful to finding low grade vs glioma high grade glioma. MRS having own limitations like considerable overlap between the spectroscopic appearance of different pathology and lack of definitive imaging findings [18]. Research and Development is currently underway to increase the clinical usefulness of MRS in brain tumor diagnosis and treatment.

Fluorescence in situ hybridization (FISH) and chromogenic in situ hybridization (CISH) based detection

FISH technique developed in 1980s. FISH procedure is possible to recognize tumor-specific abnormality. By comparing the hybridization pattern of cancer cells with the normal cells comparative genomic hybridization (CGH), can identify chromosome losses and gains in tumor cells. Modern concept of FISH technique present microfluidic platforms which are dedicated to the analysis of circulating tumor cells (CTCs) [19]. FISH analysis used in Solid Tumors diagnostics in Lung, breast cancer, soft tissue sarcomas, Ovarian Cancer [20, 21].

Enzyme-linked immunosorbent assay (ELISA) based detection

ELISA, is the most frequently used technique amongst immunoassays. Accurate, rapid, and simple detection methods are required to facilitate early diagnosis of cancer [22]. Cervical cancer is the third most common cancer in women. Scientists developed affordable, accurate, and simpler ELISA based detection for Cervical cancer [23]. microchip ELISA that detects HE4, an ovarian cancer biomarker, from urine using a cell phone integrated with a mobile application for imaging and data analysis [24]. ELISA can used for detection of Salivary interleukin-6 in oral cancer and precancer [25].

Rapid Point-of-Care (POC) detection

Early-stage detection of cancer is essential for the treatment and disease management. In molecular diagnosis, extracellular vesicles play significant role in biomarker discovery of cancer. POC (electrochemical, surface plasma resonance (SPR), Microfluidic systems) devices are simple to use, affordable, quick, and robust to analyse clinical samples at home or at medical diagnostics centre [26]. Protein biomarkers for cancer detection typically emerge from the cancer cells. Due to the poor stability of protein biomarkers of cancer the test should consider the paraments like sensitivity, specificity, and accuracy [27]. Chip and nanotechnology lab devices bring unique physiochemical features to improve the biosensing performance of distinct point of care (PoC) devices.

PCR based detection

Cancer diagnosis at the preliminary stage is challenging, entailing sophisticated diagnostic methods. The emergence of practical applications of molecular biology techniques (PCR and RNA-based assays) are largely attributed for molecular analysis of cancer. Polymerase chain reaction (PCR) require simple instrumentation and infrastructure in clinical DNA testing relatively [28]. Although ELISA is the method of choice in clinical practice for detecting cancer biomarkers in serum/urine samples. iPCR technique is 1000-fold more sensitive than the conventional ELISA and can detect even a single antigen molecule [29]. New method was developed for detecting T790 M point mutations in lung cancer biopsies using PCR-LFA [30]. Colorectal cancer (CRC) is the fourth leading cause of the cancer death worldwide [31]. Many methylation markers associated with colorectal cancer have been reported [32] and Early detection of Circulating tumor DNA-based precancerous colorectal lesions using QClamp XNA-mediated real-time PCR **[**33] and multiplex RT-PCR assay for colorectal cancer detection [34]. Develop a multiplex PCR-based method for detection of circulating tumor cells in peripheral blood of lung cancer (LC) [35].

Artificial intelligence (AI) based detection

Early cancer diagnosis and artificial intelligence (AI) are rapidly evolving fields with important areas of convergence and detection was well established [36]. Machine learning (ML), a subdivision of AI. AI comes with several challenges, like data security. Approaches are emerging to improve data security and reduce the risks associated with transferring data across multiple institutions [37]. Deep learning (DL) is a subgroup of ML (Machine learning). AI and its deep learning (DL) have also pervaded the field of breast cancer detection using mammography [38]. CRC, which represents the third most diagnosed malignancy in both men and women [39]. AI algorithms has permeated the medical field with great success for diagnosis of colorectal cancer (CRC). AI has been found to be useful to physicians in the field of image recognition. Gastric cancer is the fifth most common form of malignant tumor and the third leading cause of cancer-related death worldwide [40]. Japanese endoscopists have produced the world's first convolutional neural networks (CNN)-based AI system for detecting gastric and esophageal cancers [41,42]. breast cancer imaging, AI can detect mammographic abnormalities with comparable accuracy 4[3,44]. Lung cancer is one of the most common malignant tumors with the fastest increase in morbidity and mortality and the diagnosis mainly relies on tissue biopsy and computed tomography (CT). AI system can detect malignant pulmonary nodules based on chest CT images [45] and in CT film analysis it is assisting doctors in improving lung cancer screening accuracy. AI system can detect tumor detection but also can be used in staging of lung cancer [46]. AI can improve the efficiency of the cytopathological diagnosis of lung cancer. AI could also be used detecting mutant genes in lung cancer. Data analysis methodologies like AI (ML) tools are also accelerating progress [47,48].

Nanotechnology (NT) based detection

Advances in nanotechnology and medical science have spurred the development of engineered nanoparticles (NPs) and nanomaterials with particular focus on their applications in molecular diagnosis. Nanomaterials and nanotechnologies will greatly enhance the throughput and sensitivity of the identification and screening of potential biomarkers. NPs such as polymeric carbon nanotubes (CNTs), nanoparticles (nanogels, nanofibers, liposomes), calcium nanoparticles (CaNPs), metallic nanoparticles such as gold NP (GNPs), sliver NP (AgNP), graphene, and quantum dots (QDs) have revolutionized cancer diagnostics and defection. QDs (Quantom dots) are a type of semiconductor NPs that can emit fluorescence signals under ultraviolet light (UV) irradiation with a high quantum yield. Potential applications of QDs in molecular diagnostics can be Cancer. In Ovarian cancer biomarker CA125, human epididymis protein 4 (HE4), mucin 1 (MUC1), and prostate identified using NT [49]. Graphene is good at amplifying detection signals, and its derivatives play an important role in the early diagnosis and cancer Novel Graphene-Based Multifunctional Nanomaterials are developed for detection [50].

Bioinformatics (BI) based detection

BI is one of the newest fields of biological research its use of mathematical, statistical, and computational methods for the processing and analysis of biological data. Currently, there is a growing need to convert biological data into knowledge through a bioinformatics approach [51]. Diagnosis and detection of pancreatic cancer early is the key to successful clinical management and improve the patient outcome. In recent years, with the rapid development of bioinformatics, an increasing amount of microarray and sequencing data have provided a convenient to elucidate molecular mechanisms for the cancer diagnosis. [52] analysed prognostic value of PITX1 gene in breast cancer by using BI tools Oncomine, Bc-GenExMiner v4.3, PrognoScan and UCSC Xena. Pancreatic ductal adenocarcinoma (PDA) is one of the most aggressive cancers on globe [53].BI strengthened greatly the research and ITS application of liquid biomarkers. For the studying of liquid biopsies uses alignment of sequences [54]. BI facing another challenge for tumor circulome is to differentiate tumor mutations from background somatic mutations. Metastasis is a serious event in the clinic, leading to most deaths of melanoma patients This study provided a deeper understanding of the molecular mechanisms of melanoma metastasis [55]. In the results, cell mitosis and malignant proliferation were activated, whereas the interaction with the extracellular environment was suppressed during the metastatic process One of study may contribute to the more profound elucidation of mechanisms of melanoma metastasis [56]. Novel and high-performance genomic technologies allow detection of signals from cancers in blood, giving rise to a new paradigm of multi-cancer early detection (MCED). MCED tests analyze genomic features of circulating cfDNA and distinguish these from background genomic signals. New multi-cancer early detection (MCED) tests-using a single blood sample-have been developed based on circulating cell-free DNA (cfDNA) or other analytes. Doctors and Healthcare providers need to consider how to implement MCED testing for large numbers of cancer patients [57].

Volatile organic compound (VOC) analysis

The detection and quantification of volatile organic compounds (VOCs) within exhaled breath used for diagnosis of cancer [58]. Most pancreatic cancer patients are diagnosed at an advanced stage Field asymmetric waveform ion mobility spectrometry (FAIMS) was used for VOC and evaluated FAIMS to discriminate between pancreatic cancer and healthy controls in a urine sample [59]. VOCs used as new biomarkers for colorectal cancer detection [60]. Lung cancer is the world's deadliest cancer, but early diagnosis helps to improve the cure rate and thus reduce the mortality rate and based on LC-MS/MS VOCs Lung Cancer was detected. Studies suggested VOC signatures emanating from urine can be detected in patients with CRC using ion mobility spectroscopy technology (FAIMS) [61]. [62] studied Hepatocellular Carcinoma was detected using VOC. No reliable diagnostic methods are available for gallbladder cancer (GBC) but [63] assessed whether VOCs could be used as a diagnostic tool for GBC.

Liquid biopsy (Lb) based detection

In the molecular profiling of cancer there is a growing need to use liquid biopsies. Lb technology provides key insights into mechanisms of drug resistance and tumor evolution. Tumors release ctDNA/cfDNA and CTCs into the blood stream. In this method there are minimally invasive and provide a methodology for obtaining tumor-derived information about circulating tumor DNA (ctDNA), Circulating extracellular nucleic acids (cell-free DNA; cfDNA), and circulating tumor cells (CTCs) in body fluids (liquid samples). Current evidence suggests that Lb may be best used as a second-line or complementary diagnostic tool. There are multiple potential future directions that are emerging for liquid biopsies. There are limitations and challenges in this field such as analyte validation, standardization of Lb assessments and regulatory considerations for their use as a biomarker in clinical trials [64, 65]. Lb is a powerful, multifaceted tool to help improve management of different cancers Breast Cancer [66], Colorectal Cancer [67], gastric cancer [68, 69], Pancreatic Cancer [70]. Single biopsy provides limited snapshot of the tumor. Among all samples tissue biopsy remains the gold standard identification of tumor [71]. Lung cancer is one of the deadliest forms of cancer, with an extremely high mortality rate of around 18% of all cancer-related deaths [72, 73]. Non-small cell lung cancer (NSCLC) is the leading cause of cancer deaths globally and detected by using Liquid biopsy-based Biosensors [74]. Worldwide Ovarian cancer (OC) is the most lethal gynecologic malignancy, and the main challenge is the late detection which results in poor survival [75]. For the last few decades there has been an ongoing search for prognostic, detection, diagnostic, or predictive biomarkers to improve management of ovarian cancer. There is emerging evidence supporting the potential of Lb to enhance ovarian cancer management. Lb can also capture the heterogeneity of ovarian tumours more comprehensively compared to conventional tissue biopsy.

Biosensors based detection

Biomarker-based cancer diagnosis may significantly improve the early diagnosis of different cancers. They are easy to use, portable, and can-do analysis in real time. For cancer biomarker detection they used different approaches like electrochemical, mass-based transduction and optical systems [76]. Electrochemical biosensors are the most sensitive category of biomolecule detection sensors with significantly low concentrations down to the atomic level. based biosensing devices hold great promise for clinical innovations to conquer the unbeatable fort of cancer metastasis. An ultrasensitive biosensing system has proved to be an excellent candidate for automatic, rapid, sensing and analysis of cancer [77]. Analytical biosensing devices for early-stage cancer detection is considered the future of clinical advancements [78]. Tumour-associated Exosomes (TEXs) have been reported to play a significant role in tumorigenesis and currently, clinical trials aiming to directly identify TEXs from body fluids by using micro-fluidic and electrochemical biosensing devices [79, 80].

CONCLUSION

Now a days proactive approach to detecting cancer at an early stage can make treatments more effective, with fewer side effects and improve long-term survival of human race. In this review, we have explained various types of systems for detection and diagnostics of cancer in detailed using novel and emerging techniques. AI play a vital role in cancer detection. AI comes with several challenges, including algorithmic fairness, data bias, ethical considerations, and data security. Despite the challenges mentioned, the implications of AI for early cancer diagnosis are highly promising, and this field is likely to grow very rapidly in the coming years. Over the past few years, innovative and significant progress been made in liquid biopsy technology. Compared with other traditional tissue biopsy, liquid biopsy provides several significant advantages.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed reviewing this of this article.

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