Point-of Care Diagnostic Devices in Cancer Detection

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelor of Pharmacy (Hons)

School of Pharmacy
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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis titled "Point-of Care Diagnostic Devices in Cancer Detection" submitted by Rizwana Yasmin, ID: 18146085 of Summer, 2021 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on April 2022.

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Ethics Statement

This study does not involve any kind of human and animal trial.

Abstract

Cancer is the leading cause of mortality in the world, claiming the lives of one in every seven people. It is commonly known that early detection and screening are critical for boosting the chances of recovery. Patients, on the other hand, rarely has the ability to utilize the facilities and services available to them due to the high cost, time commitment, and intrusive nature of many of the present methods and so, cancer remains undetected and death toll rises. Furthermore, as cancer keeps expanding in middle- and low- income countries as a non-communicable illness, it is crucial to find and invest in promising cancer treatment and control strategies. As a result, several researchers are looking into the prospect of developing non-invasive, rapid, and reliable diagnostic technologies that can be utilized in-person or by local healthcare personals at the point-of-care.

Point-of-care device results are more precise, sensitive, and quickly generated, aiding in the choice of the optimum course of treatment for best patient care. Point-of-care diagnostics ought to, in theory, upgrade patient well-being while also lowering cancer-related fatalities. This review paper focuses on affordable POCTs for cancer care and aspires to encourage innovation and further investment in this space.

Keywords: Cancer; POC; Diagnostic; Biomarkers; Resource-limited locations.

Dedication

Dedicated to my parents.

Acknowledgement

I would want to begin by thanking Allah, our creator, for providing me with life, strength, knowledge, wisdom, blessings, and mercy. All glory be to Allah, who has blessed me with tremendous patience and strength in order to complete this undertaking. Without the help of the persons listed above, this project would not have been completed.

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Last but not least, I would like to express my gratitude to my family for always being there for me and encouraging me to work harder in every aspect of my life. I would not have made it this far without their prayers and unwavering love.

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List of Acronyms

BSA	Bovine Serum Albumin
CRP	C-reactive Protein
CTC	Circulating Tumor Cells
HRME	High-Resolution Micro-Endoscopy
LFIA	Lateral Flow Immunoassay
LMICs	Low- and Middle-Income Countries
POC	Point-of-care
POCT	Point-of-care Technology
WHO	World Health Organization

Chapter 1

Introduction

1.1 Cancer

A human body is made up of trillions of cells with the capacity to divide into identical daughter cells over a person's lifetime and these cells divide and grow as the body needed (Gottlieb et al., 2021). So, when these cells become damaged or worn out, apoptosis (self-destruct) occurs. However, when old or abnormal ones don't die in appropriate time as well as new cells gets created from existing ones, cancer starts to invade the body.

Basically, cancer is a group of diseases marked by abnormal cell development which spreads to other parts of body and destroy normal healthy body tissue including organs (Akay, 2009). Numerous external factors as well as internal genetic changes embarks on human cancers. Approximately 93% cancers are non-hereditary and only about 7% of all cancers are hereditary (Seto et al., 2010). Four classes of genes contribute in cancer formation which are: 1. Tumour suppressor genes, 2. DNA-mismatch repair genes, 3. Proto-oncogenes, 4. Apoptotic genes (Parsa, 2012). The classification of cancers is done according to where they start in the body, such as lung cancer. More than 200 types of cancer were identified according to Cancer Research UK and two main categories are:

- Hematologic cancers (e.g., leukaemia, lymphoma, multiple myeloma) and
- Solid tumor cancers.

The cancer burden is growing globally, playing a huge physical, emotional and financial load on patients, exerting strain on families, communities and overall health systems. The health-care system of low- and middle-income countries are not ready to overcome this difficulty. For example, in 2020, Bangladesh, a lower-middle-income country had 1,56,775 new cancer cases

and the number of deaths was 1,08,990. Moreover, huge number of cancer patients globally have least access to timely quality diagnosis and treatment *(WHO*, 2020). Though many types of cancer are preventable; however, cancer is recognized as the second prime cause of death globally as 1 in 6 death is caused by cancer (*Cancer*, n.d.). An estimation of cancer death in 2019 of cancer death in both male and female is given below-

Table 1 Cancer death estimation in male in US

Source: American Cancer Society, Surveillance Report

Lung & Bronchus	76,650	24%
Prostate	31,620	10%
Colon & Rectum	27,640	9%
Pancreas	23,800	7%
Liver & Intrahepatic bile duct	21,600	7%
Leukaemia	13,150	4%
Esophagus	13,020	4%
Urinary bladder	12,870	4%
Non-hodgkin lymphoma	11,510	4%
Brain & other nervous system	9,910	3%
Total	321,670	

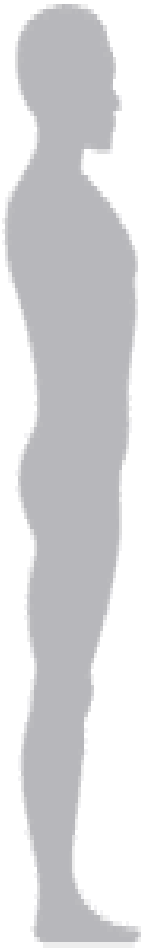

Table 2 Cancer death estimation in female in US

Source: American Cancer Society, Surveillance Report

Lung & Bronchus	66,020	23%
Breast	41,760	15%
Colon & Rectum	23,380	8%
Pancreas	21,950	8%
Ovary	13,980	5%
Uterine Corpus	12,160	4%
Liver & Intrahepatic bile duct	10,180	4%
Leukemia	9,690	3%
Non-hodgkin lymphoma	8,460	3%
Brain & other nervous system	7,850	3%
Total	285,210	

In addition to, the mortality rate is expected to increase 16.1 million due to cancer by 2030 (Thun et al., 2010). On top of that, The UN health agency declared that by 2040, a rise by 81 percent of cancer cases would occur in middle- and low- income countries as there are lack of investment in prevention and care for cancer patients (*WHO Outlines Steps to Save 7 Million Lives from Cancer*, n.d.).

1.2 Point-of-Care Diagnostic Devices

Point-of-Care diagnostic devices are a combination of technologies which is used at or near the patient site, to detect and diagnose diseases quickly and accurately than conventional lab-based testing in order to improve healthcare outcomes. It is thought to be a paradigm shift from current diagnostic procedures as it is considered as a medical laboratory at or near the patient bedside which provides physicians and patient with timely diagnostic particulars and allowing for more informed patient care and treatment decisions (Syedmoradi et al., 2017) (Sandbhor Gaikwad & Banerjee, 2018) (Meyer & Gorin, 2019).

In other words, POC devices are crucial in rapid detection and fast clinical decision-making (rule-in or rule-out), monitoring and prognosis (Lee, 1999). The major goal of POC devices is to manifest multiple biomarkers at the same time on a single platform (Dou et al., 2019) as well as to lay out a reliable, quick and especially low-cost quantitative analysis of biomarkers (Dincer et al., 2017). So, in short, POC devices are-

- Affordable,
- Specific,
- Sensitive,
- Rapid and Robust,
- User friendly,
- Equipment-free and
- Deliverable to end users.

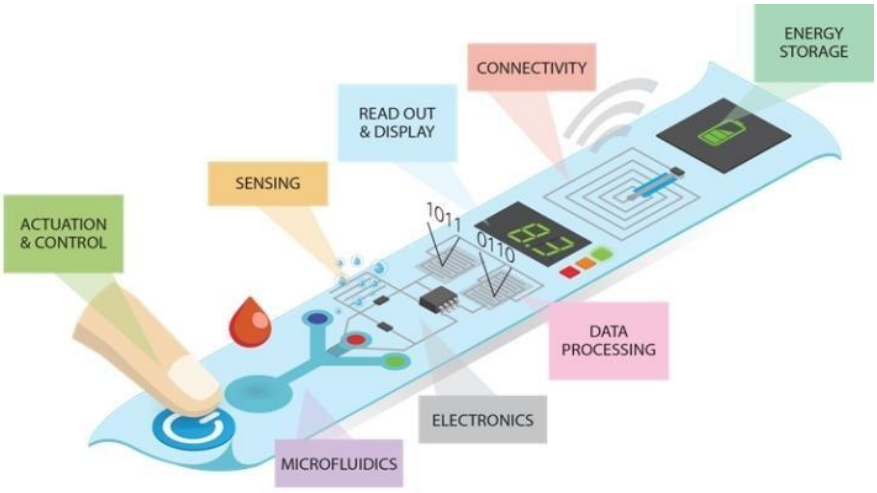

Figure 1 A simplified conceptual view of an automated, integrated POC diagnostic solution. (Smith et al., 2018).

This simplified overview POC device shows that using a small sample of plasma or blood, it can process the sample and subsequently, through sensing and processing steps it reads out the result, and therefore, a digitized result can be obtained which can directly diagnose a targeted disease (Smith et al., 2018).

1.3 Current Diagnostic Methods

Early cancer identification is linked to a higher chance of patient survival. The prognosis for a cancer patient is frequently fatal after the primary tumor is visible or symptomatic during routine cancer screenings. One of the most important steps in improving overall patient survival is early tumor diagnosis (Heyn, 2015). Some of the tests which are often used to help diagnose cancer are discussed below.

1.3.1 Lab Tests

The presence of high or low amounts of specific chemicals in a patient's body can detect the existence of cancer. So, lab tests analyzes these compounds in the urine, blood, or other bodily fluids and can help doctors diagnosing patients. The following are the categories of some

frequent laboratory tests used in cancer medicine (*Understanding Laboratory Tests Fact Sheet - National Cancer Institute*).

- **Blood chemistry test:** It measures the levels of metabolites, electrolytes, lipids, and proteins, including enzymes, which are released into the bloodstream by the body's organs and tissues. Blood urea nitrogen (BUN) and creatinine assays are commonly included in blood chemistry tests. Basically, it is utilized in patient monitoring during and after therapy as well as diagnosis of cancer. Low or high levels of certain chemicals can be symptoms of disease.

- **Cancer gene mutation testing:** The existence of particular hereditary mutations in genes are measured by this test which is linked to the development of cancer. Tests for BRCA2 and BRCA1 gene mutations, which has a part in the growth of ovarian, breast and other cancers, are examples. It is utilized to assess the possibility of cancer.

- **Complete blood count (CBC):** It measures the number of different types of blood cells in a sample of blood, such as white blood cells, red blood cells and platelets. The percentage of total blood volume taken up by red blood cells (haematocrit), the amount of hemoglobin in the blood, the size of red blood cells, and the amount of hemoglobin in red blood cells are all measured in this test. In diagnosis of cancer and monitoring during and after treatment, notably for leukemias, this test is carried out.

- **Cytogenetic analysis:** It assesses chromosome changes in a patient's white blood cells or bone marrow cells, including the quantity and shape of chromosomes. It is used in making a diagnosis and deciding on the best course of action.

- **Immunophenotyping:** It assesses antigens found on the cell surface are used to identify cells. It's used to diagnose, stage, and monitor blood malignancies and other hematologic illnesses, including as lymphomas, leukemias, myeloproliferative

disorders and myelodysplastic syndromes. It is most commonly performed on bone marrow or blood samples, but other biological fluids or biopsy tissue samples may also be used.

- **Sputum cytology:** It checks for the presence of aberrant cells in sputum (mucus and other matter brought up from the lungs by coughing). The usage of this test is Lung cancer diagnosis.

- **Tumor marker tests:** Some tests look for specific genes or proteins in blood, tissue or other physiological fluids that could be indicators of certain benign (non-cancerous) disorders or cancer. A tumor with a higher-than-normal level of a tumor marker may respond to a therapy that targets that marker. Cancer cells having high levels of the HER2/neu gene or protein, for example, may react to treatment with a HER2/neu protein-targeting medication. They are used in diagnosis, therapy selection, assessment of treatment response, and cancer recurrence monitoring.

- **Urinalysis:** The contents of urine, for example- protein, sugar, white blood cells, red blood cells and the color of it are measured. It is used to detect and diagnose kidney cancer as well as urothelial malignancies

- **Urine cytology**: It detects disease by detecting the presence of abnormal cells shed from the urinary tract into urine. It's used to detect and diagnose bladder cancer and other urothelial malignancies, as well as to keep track of patients for cancer recurrence.

1.3.2 Imaging Tests

Imaging tests produce images of places inside a patient's body that assist the physician to determine whether or not a tumor is present. These images can be created in a variety of ways (*How Cancer Is Diagnosed - National Cancer Institute*, n.d):

CT Scanning

A CT scan is a process that requires utilizing an x-ray scanner connected to a computer to take a series of images of organs from different angles. These photographs are utilized to build precise 3-D representations of the body's interior.

Ultrasound

Ultrasound examinations use high-energy sound waves that humans are unable to hear. The sound waves bounce within the body's tissues. These echoes are used by a computer to build images of internal body locations. This image is known as sonogram. During an ultrasound test, a technician glides a device called a transducer across the skin over the portion of the body being checked. A heated gel covers the transducer, making it easier to glide over the skin.

X-rays

To obtain images of the inside of the body, Low levels of radiation are used in X-rays. An x-ray technician will carry out the test by guiding the x-ray beam to the correct part of the body.

Biopsy

In most cases, to detect cancer, a biopsy is a must. A biopsy is a technique in where the doctor removes sample of tissue. A pathologist examines the tissue under a microscope and does additional tests to determine whether it is cancerous. In a pathology report, pathologist's findings are written, including the relevant information regarding patient's diagnosis.

Pathology reports are crucial in identifying cancer and determining therapy options. There are various techniques to collect a biopsy sample:

- **With a needle:** A needle is used by the doctor to extract tissue or fluid. Bone marrow aspirations, spinal taps, and some breast, prostate, and liver biopsies are all done this way.
- **Endoscopy:** It is a procedure in which a doctor examines internal organs using a narrow, illuminated tube known as an endoscope. Endoscopes are inserted into natural body openings like the mouth or the anus. If the doctor notices abnormal tissue during the exam, he will use the endoscope to remove the abnormal tissue as well as part of the surrounding normal tissue. The following are some examples of endoscopic exams-
    - ❖ Colonoscopy
    - ❖ Bronchoscopy
- **With surgery:** During surgery, a surgeon removes an aberrant cell cluster from a patient's body. Excisional or incisional surgery are both options. The surgeon removes the entire area of aberrant cells in an excisional biopsy. A portion of the normal tissue surrounding these cells is frequently removed as well. The surgeon removes only a portion of the suspicious area during an incisional biopsy. A sedative or anesthetic may be required for some biopsies.

1.4 Limitations in Laboratory Based Cancer Detection

In 2019, the approximate national patient economic burden for cancer care was $21.09 billion US dollar (Yabroff et al., 2021). By 2040, because of the aging population, 16.3 million cancer deaths are estimated. In addition to, the occurrence of cancer rate, morbidity, and mortality is

rapidly increasing in developing and least developing country (Kanavos, 2006). So, diagnosis of cancer is one of the most important steps in cancer treatment. But detecting cancer via traditional technique is strenuous. For example- to detect gastrointestinal malignancy, a patient needs to have the following laboratory methods which have several drawbacks-

Table 3 Disadvantages of different laboratory-based methods in detecting gastrointestinal malignancy. (POZIOMYCK et al., 2016)

Method for gastrointestinal malignancy	Disadvantages
Albumin	• Not reliable • Influenced by many factors and conditions
C-Reactive Protein (CRP)	• Higher costs • Alone is not cancer-specific
Pre-albumin	• Higher costs • Non-disease specific • Can be influenced by non-nutritional factors
Retinol Binding Protein (RBP)	• Higher costs • Fewer studies in cancer patients
Adductor Muscle Pollicis Thickness (APM) / Dinamometry	• Does not evaluate the acute effects of cancer malnutrition • Requires the evaluator training

Hence, in brief, there are several hindrances in existing cancer detection technique-

- The traditional cancer detection techniques are all lab-based, invasive or needle-based, time-consuming, and most importantly, expensive. For example, breast cancer is usually detected by ELISA test and mammography. For ELISA testing, blood separation, mixing, incubation, and test reading is needed and also, Mammography is considered painful. Because of the ongoing diagnostic test characteristics, patient abandon basic screening (Nayak et al., 2017).
- Unintended manual errors are common in conventional lab-based detection methods, as there are separate and multiple pre- and post-analytical stages, such as sampling, labelling, etc.
- In middle- and low- income countries, cancer is responsible for 70% of deaths. On top of it, healthcare infrastructure of these countries is lacked in required diagnostic capabilities. (Shah et al., 2019)
- Shortage of highly trained lab practitioners is disadvantageous to the implementation of improvised diagnostic measures.
- Longer analysis time is another roadblock in existing technique.

1.5 Necessity of POC Diagnostic Devices in Cancer

Several analytical procedures (for example, sample preparation, signal amplification, and target detection) can be performed in one automated single unit in the POC system. This system outrun the conventional diagnostic tests as it can detect cancer via novel and coherent sensing platforms in a rapid, cost-effective manner without requiring skilled technicians (Hayes et al., 2018a) (Zarei, 2017).

Therefore, effective Point-of-Care (POC) diagnostic solutions can play an important part to decipher the above-indicated laboratory-based challenges.

- The earlier a cancer is detected, the better chance of survival is present. But one of the numerous barriers in early diagnosis is lack of access to screening and diagnostic testing which can delay the treatment (*Guide to Cancer Early Diagnosis*, n.d.). Furthermore, there is variation in survival rate in different cancer types because of late diagnosis. Survival rates of a cancer patient fall off about 30-40% because cancer is diagnosed at a later stage and it spreads to other body parts from the site/organ of origin (Jin & Mu, 2015). In addition to, some cancers, namely-brain cancer and Non-Hodgkin lymphoma are hard to diagnose. So, POC devices comes in handy to solve the imminent need for tools to facilitate preventive screening by detecting the cancer in a fast and ultra-sensitive way. Hence, POC diagnosis plays a significant role in early diagnosing for the better of survival rates.

- Financial barrier is arguably the highest roadblock in cancer screening. In 2019, economic burden of cancer care of patient was more than $21 billion in the United States (Yabroff et al., 2021). Furthermore, cancer exerts a significant economic burden on the US healthcare system, with estimated medical costs in 2020 expected to reach $157.7 billion, a 27% increase from 2010 costs. Hence, POC devices plays an important role to solve the problem of high out-of-pocket costs for cancer screening as it is affordable than most traditional laboratory-based operations.

- In 2019, less than 15% of low-income countries had comprehensive treatment services for cancer in the public health system *(WHO Outlines Steps to Save 7 Million Lives from Cancer, n.d.).* It proves that there is an unacceptable inequality between cancer services in rich and poor countries. Over the next decade, the WHO estimates that at

least 7 million lives could be saved with screening and treatment. On the other hand, POCTs have high potential in its cost-effectiveness, and simplicity and revolutionize cancer diagnosis, detection and treatment, especially for in middle- and low-income countries (Haney et al., 2017). Therefore, Point-of-care (POC) testing of cancer can improve health care provision where there is limited access to health care services.

- Point-of-care technologies (POCTs), devices that can be utilized at or near the time and location of a patient's bed, can improve cancer care by allowing for more individualized treatment or personalized therapy. So, as it is portable, thus it is "fit-for-use" by the patients themselves or by "on-site" medical staff (Yu et al., 2013) (Uludag et al., 2016).

- Most of the time, patients are unwilling for screening as there is underlining fear of invasive approach in traditional technique, for example- biopsy. But minimum invasive method or blood loss occurs in POC diagnostic devices. So, there will be least patient discomfort.

- As POC devices has no complex equipment, highly trained lab practitioners are not necessary. Furthermore, there is least scope in manual error as it is a very simple device.

- POC devices are very rapid and robust. So, it is very convenient in future monitoring of cancer stages and is very time saving for cancer patient as it will be unnecessary to wait for weeks after weeks to get a serial and the result of diagnosis in conventional method.

1.6 Objectives of the Study

The aim of this literature review is to highlight the importance of usage of POC devices in cancer diagnosis and care, especially for developing and under-developed country. Other objectives include assisting with research and increasing interest so that scientists can focus more on developing POC devices using technologies that are mentioned in this review article.

Chapter 2

Research Methodology

To obtain all of the information included in this review study, a thorough literature review was conducted. The data was gathered from a variety of reliable sources, including peer-reviewed publications and an online scholarly database. The following is a list of some of the many databases that were combed through for this study.

 Journal Database

 Professional website

 Newspaper Database

 Library Catalogue

A thorough search of multiple journals, research papers, and review articles from official sites and research databases was conducted in order to gather as much relevant information as possible about point-of-care diagnostic equipment in cancer detection. The information for this review paper was gathered using well-known and trustworthy databases such as PubMed, SCOPUS, and Science Direct. Appropriate key terms, such as; Cancer, Biomarkers, Point-of-care technology, low-resource setting countries etc was used to collect relevant articles. Approximately 170 articles have been evaluated based on the title and key words. Then, after reading the abstracts, 85 articles were whittled down. To construct this review study, 54 papers were chosen and meticulously analyzed. To be respectful of the work or the original writers, Mendeley software was utilized for proper and reasonable reference.

Chapter 3

Different POC Technologies in Cancer Detection

3.1 Lateral Flow Immunoassay (LFIA)

One of the most used technologies in POC diagnostics is lateral flow immunoassay (LFIA). It is a low-cost, simple, rapid and portable detection assay technique (Koczula & Gallotta, 2016). Basically, LFIA diagnostic devices are "dipstick"-like which uses antibodies to discover the existence of an analyte, in this case, cancer biomarkers. It is simple to use because it gives a qualitative yes/no answer to the presence of a biomarker in minutes.

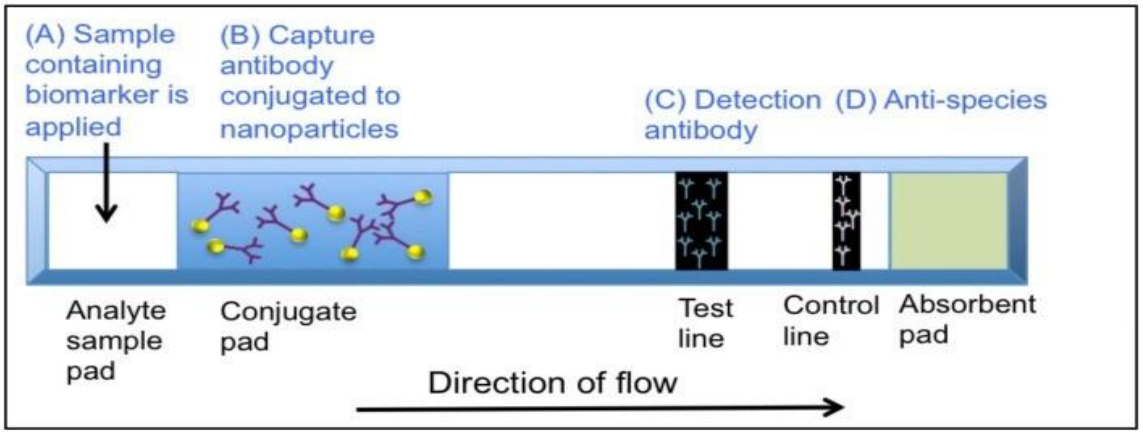

Figure 2 A Schematic representation of lateral flow immunoassay. (Hayes et al., 2018)

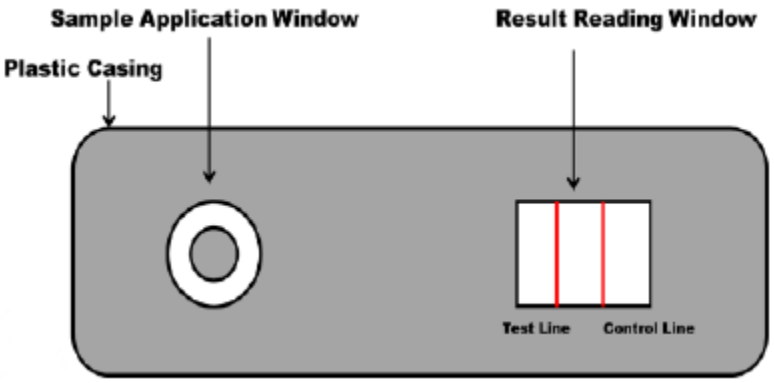

Figure 3 Top view of a LFIA test cartridge (Sharma et al., 2015)

The plastic base of LFIA has mainly four distinctive roles-

A. At position A, sample (serum) is placed.

B. The sample then travels ahead and comes into touch with antibodies against the biomarker of interest (at location B).

C. Then, the antibodies attach with the biomarker and, if the biomarker exists in the sample, a visible line will tun up at the test line zone (position C).

D. The sample proceeds along the single axis to the control line (position D), where anti-species antibodies are used to detect the capture antibodies, and finally, a line appears indicating that the test was successful.

This technology is successfully used in some commercially available POC cancer diagnostic devices. Some of them are-

Table 4 Commercially available LFIA-based POC diagnostic devices for cancer detection. (Sharma et al., 2015)

Cancer	**Cancer Biomarker**	**POC Device**	**Test duration**	**Sample**	**Company**
Prostate	PSA	PSA Semi-quantitative rapid test	15 min	Whole Blood/ Serum/ Plasma	CTK Biotech
Bladder	Nuclear matrix protein 22 (NMP 22)	Alere NMP22® BLADDER CHEK®	30 min	Urine	Abbott (formerly Alere)

Colorectal	Fecal occult blood	FOB Rapid Test CE	5-10 min	Stool	CTK Biotech
Cervical	OncoE6	OncoE6™ Cervical Test	2.5 hour	Cervical Swab	Arbor Vita
Liver	AFP	Medical IVD rapid diagnostic test kits AFP Test kit	10 min	Whole Blood/ Serum/ Plasma	INVBIO (Innovation Biotech)
Colorectal, breast, lung	CEA	CEA Serum Rapid Test	10 min	Serum/ Plasma	Cortez Diagnostics Inc.

3.1.1 CTK Biotech's "Onsite"

Prostate cancer is the most commonly diagnosed cancer among men in the United States, as well as the second leading cause of cancer death (*Reduce the Prostate Cancer Death Rate — C-08 - Healthy People 2030 | Health.Gov,* n.d.). Some populations have significantly higher rates of prostate cancer death than others. According to studies, regularly monitoring prostate cancer in men who are diagnosed early is an effective way to reduce the death rate from prostate cancer.

CTK Biotech's "Onsite" is based on lateral flow chromatographic immunoassay. Basically, it is a semi-quantitative rapid test for the prostate cancer-associated marker, prostate specific antigen (PSA). This point-of-care diagnostic equipment is an immune-chromatographic test

that can detect PSA at a concentration of 4 ng/mL, which is the "cut-off" level for PSA in blood (if PSA is less than 4 ng/mL, the patient is healthy; if PSA is greater than 4 ng/mL, additional tests should be performed). Furthermore, if the PSA value is greater than 10 ng/mL, a biopsy is strongly advised. (*PSA Semi-Quantitative Rapid Test - CTK Biotech*, n.d.)

Figure 4 PSA Semi-quantitative Rapid Test (PSA Semi-Quantitative Rapid Test - CTK Biotech, n.d.)

3.1.2 OncoE6™ from Arbor Vita

Cervical cancer can be the leading cause of death in the region where women have limited any access to regular check-ups. The OncoE6™ Cervical Test gives the solution from this problem by directly detecting the cancer-causing E6 oncoprotein molecule. Basically, it is a lateral flow cervical cancer POC test device that uses highly specific monoclonal antibodies (mAbs) in a lateral flow immunoassay format to detect the presence of E6 oncoproteins from high-risk forms of human papillomavirus (HPV) types 16 and 18 (Zhao et al., 2013). The POC test has marvellous clinical performance with high specificity and high positive predictive value and so, unnecessary treatment procedures can be easily avoided. Furthermore, this POC test is room temperature stable. Though with its dipstick-like style, the test takes 2.5 hours, which is a considerable time for a POC test, OncoE6™ is -

- simple,
- quick,

- non-invasive and
- no refrigeration is required.

*Figure 5: OncoE6™ Cervical Test – CE-IVD (*OncoE6 - Arbor Vita Corporation*, n.d.)*

Few advantages of this POC device are mentioned below-

• Easy to use as it has "dipstick" (lateral flow) format

• Predictive cancer biomarker test accompanied by high specificity for cervical cancer as well as pre-cancerous lesions.

• Detects strains approximately 70-80% of cervical cancer worldwide (92% in India, 84% in China)

• No refrigeration or complex equipment required

• Low test cost and start-up.

• Test results in about 2 ½ hours.

• Low false negative rate.

• Low false positive rate

• Minimum laboratory training required.

3.1.3 INVBIO's Rapid Diagnostic AFP Test Kit

The sixth most familiar diagnosed cancer is Liver cancer which is the fourth leading cause of cancer-related death worldwide, with approximately 841,000 new cases and about 782,000 deaths annually (Bray et al., 2018). A prime histological subtype of liver cancer is Hepatocellular carcinoma (HCC), accounting for 70–85% of all cases (Xu et al., 2021). Basically, it occurs most often in patients who have history of chronic liver diseases, such as cirrhosis caused by hepatitis B or hepatitis C infection. So, Serum alpha-fetoprotein (AFP) levels and its expression in liver tissue is related with Hepatocellular carcinoma (Durazo et al., 2008).

INVBIO's test to detect alpha-fetoprotein (AFP) is based on a sandwich chromatographic immunoassay format. Mainly, it is a "dipstick"-style diagnostic test that is able to find AFP in human serum plasma or whole blood. As AFP levels can be increased because of production by the tumor or by regenerating hepatocytes, so to detect AFP below 200 ng/mL is very important in the diagnosis of hepatocellular carcinoma.

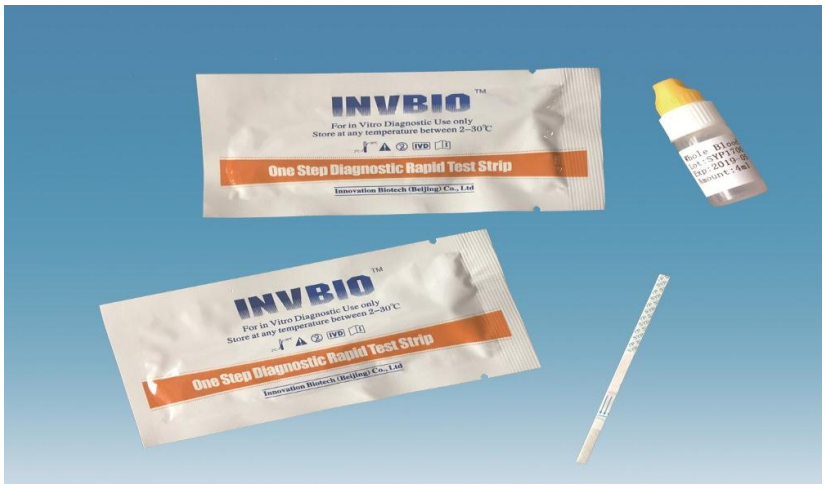

*Figure 6: Medical IVD rapid diagnostic test kits AFP Test kit (*Innovation Biotech (Beijing) Co.,Ltd, *n.d.)*

3.2 Circulating Tumor Cells

When peripheral tumor cells are detached and depart the local location of the tumor, the existence of a cancerous tumor can be observed. Thereafter, then move through lymphatic system or the blood stream (Williams, 2013). However, there is a small probability that these malignant cells (0.01 percent) will spread throughout the body and cause secondary tumors (Yu et al., 2013). Circulating tumor cells (CTCs) are the name given to these cells. As a result, they play a significant role in tumor recurrence. Therefore, it is widely believed that CTC is the primary objective of liquid biopsy.

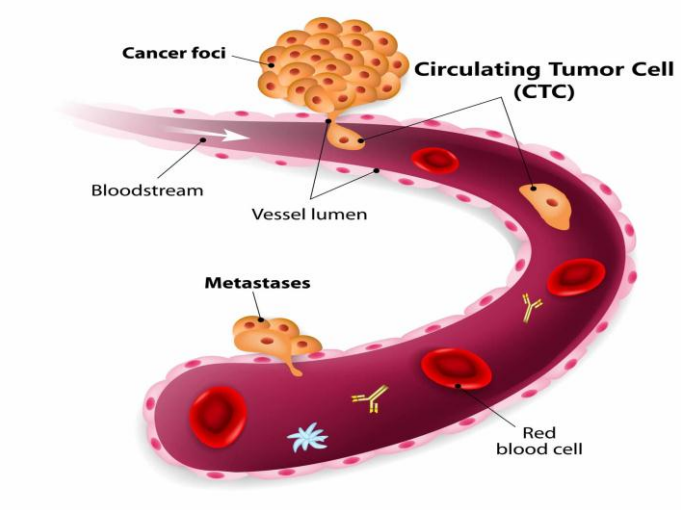

*Figure 7 Circulating Tumor Cells (*Enumerate Circulating Tumor Cells in Whole Blood, Urine, and Spinal Fluids, *n.d.)*

They are highly traceable to POC since they occur in blood, even if they exist in extremely small levels (1 in 107–109 cells/mL) (Song et al., 2014). CTC detection is not commonly employed in clinics at the moment for a variety of reasons. For starters, it necessitates the purchase of a high-priced specialist fluorescence microscope, secondly, professional technicians are required for the output of the results and lastly, it takes a very long period of time, thus limiting its clinical use (Luo et al., 2020). On the other hand, Point-of-care testing

(POCT) determines the size of a target by measuring pressure, distance, color, and other factors. Point-of-care CTC detection is a simple-to-use method that-

- method that allows patients to use the technology with sample input and result output,
- does not need for complex equipment and the testing instrument is portable and small,
- does not involve the use of specialized laboratories or clinical examiners,
- can be performed at the patient's bedside with immediate results.

So, overall, POCT CTC detection is sensitive, quick, inexpensive, and simple to use..

3.2.1 Micro-Hall Detector (μHD)

The Food and Drug Administration (FDA) authorized CELLSEARCH® as one of the first tests for detecting CTCs in cancer patients. (CELLSEARCH® | Home, n.d.) This test can detect metastatic breast, colorectal, or prostate malignancies. A point-of-care device based on a microfluidic chip is being developed to replace CELLSEARCH®, namely the micro-Hall detector (HD).

To detect CTCs in breast cancer patients, this chip was developed. The micro-Hall (-Hall) chip is intended to be a low-cost mobile platform for usage at the point-of-care. It employs magnetic particles labelled with monoclonal antibodies that target the epidermal growth factor receptor (EGFR), mucin-1 and EpCAM, as well as the epidermal growth factor receptor-2 (HER2) in humans (Issadore, 2015). The use of a panel of biomarkers makes it easier to identify a diverse population of CTCs. Furthermore, the -Hall chip was directly compared to CELLSEARCH® (an FDA-approved test), and it was discovered that the chip can detect 100% of patients, but CELLSEARCH® can only detect 25% of patients (Issadore, 2015). So, to sum up, micro-Hall (μ-Hall) chip -

- can directly detect single, immunomagnetically tagged cells in whole blood.
- As the diagnostic is fully automated and the sample is not required processing, it can be used by minimally trained personnel.
- can readily be connected to mobile devices for remote clinical data sharing and epidemiological surveillance (Issadore, 2015)
- even in the presence of a large number of blood cells and unbound reactants, it may detect individual cells.
- with no need of washing or purification steps.
- is cost-effective, single-cell analytical technique is mobile platform.

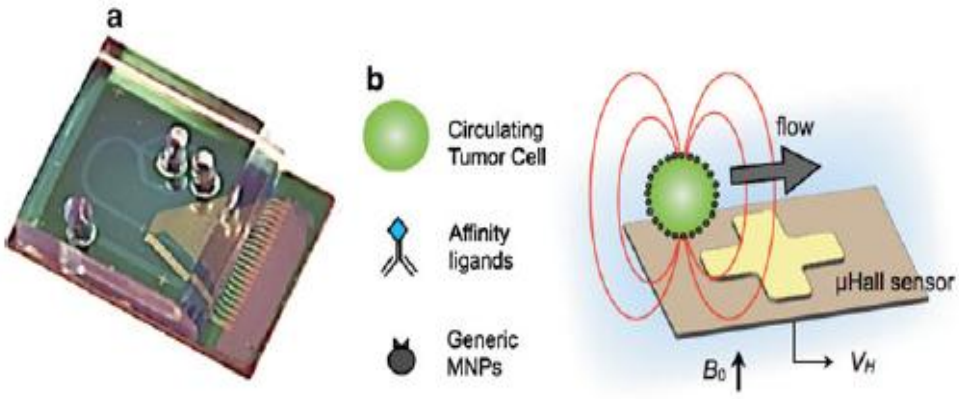

Figure 8: Micro-Hall detector (μHD) (Issadore, 2015).

The detection method of CTC via Micro-Hall detector (μHD) chip is-

A. The hybrid chip consists of a microfabricated Hall sensors with GaAs substrate. It is constructed directly on top of the semiconductor chip is a microfluidic network. It controllably delivers cells to the sensors. Soft-lithography is used to fabricate the microfluidics, which are irreversibly bonded to the GaAs.

B. Magnetic nanoparticles (MNPs) and a panel of relevant cancer biomarkers (EGFR, HER2/neu, etc.) are used to label circulating tumor cell. The cells are passed one-by-one via hydrodynamic flow structures over μHall sensors for highly sensitive detection (Issadore, 2015).

3.2.2 Centrifugo-magnetophoretic System

The Centrifugo-magnetophoretic system, invented by Kirby et al., is a second device with a promising future in POC CTC detection. It combines direct immuno-separation with cost-effective, bright-field detection of cancer cells in whole blood (Kirby et al., 2015). The device is built on a centrifugal disc (CD) platform that uses a centrifugal force on the disc to separate CTCs that are particularly attached to magnetic microbeads. The MCF7 breast cancer cell line was used to simulate CTCs in the study, and cells were successfully recovered from spiked whole blood. The technology is simple to use and requires small sample quantities (18 L/sample), making it ideal for usage in POC and low-resource environments.

In a disposable cartridge all liquid handling takes place with geometry akin to a conventional compact disc (CD). The apparatus needed to process a "lab-on-a-disc" cartridge might be as basic and inexpensive as the rotor on a standard optical disc drive.

- Target cells in a blood sample are initially bound to paramagnetic microbeads in a first step. After that, the sample is put into the disc cartridge and spun.
- In the second step, magnetically tagged target cells are isolated from the background population of numerous blood cells, as well as unattached magnetic beads, by a co-rotating, basically lateral magnetic field. A stream of target cells is centrifugally deposited into a specified detecting chamber through a stationary liquid phase.

- The constant, multi-force immuno separation is carried out gently, with minimal mechanical and hydrodynamic stress applied to the target cells to reduce the danger of cell loss due to collective trapping in the background cells or forceful snapping against a wall.

The extraction of MCF7 cancer cells at concentrations as low as 1 target cell per ll from a background of whole blood, with capture efficiencies of up to 88%. Its short time-to-answer is a notable characteristic of this system, with 10% of target cells collected in the first minute after their loading to the system and the remainder captured within the following 10 min. All the above-mentioned factors synergistically combine to leverage the development of a prospective point-of-care device for CTC detection. So, the system-

- have the potential to improve patient comfort by reducing clinic visits.
- Due to the lower volume needs, gentle blood sampling is used.
- Reduce the financial strain on health-care budgets.
- In clinics and hospitals, mobile illness monitoring has become a primary driver of cell-based medical analysis and above-mentioned system allows this.
- The removal of unbound paramagnetic beads from tagged magnetic cells is a unique aspect of this multi-force separation. Many platforms have used magnetic separation, but none have been able to remove unbound magnetic beads from isolated tagged target cells. This is because such purification, such as through integrated size filtration, is prone to clogging and unspecific trapping, and so may result in the loss of few target cells, making rare cell identification impossible. By design, this system's filter-less, flow-less sedimentation-driven technology eliminates this crucial shortcoming.

3.3 Optical Imaging Technologies

Optical imaging technology allows doctors to examine organs and tissues at the cellular and molecular level. Images are created using non-ionizing radiation such as visible, ultraviolet, and infrared light, which can subsequently be used in real time to detect and treat disease.

Because optical imaging technologies are safe, rapid, and versatile, they are extremely useful in cancer care. They can be used for recurrent operations to track treatment and evaluate disease progression. Rapid, POC imaging, together with image-analysis technologies and appropriate training programs, can transform the landscape of cancer staging and diagnosis in areas where a lack of pathology resources has generated a bottleneck in clinical operations.

3.3.1 High Resolution Micro-Endoscopy (HRME)

HRME (high-resolution micro-endoscopy) allows for in vivo high-resolution, real-time imaging of cells. HRME is now being used in conjunction with other screening methods to improve the diagnosis of precancerous and cancerous lesions in a variety of locations, including the colon, esophagus and cervix, as well as the gastrointestinal tract and mouth cavity (Protano et al., 2015).

HRME could be a beneficial tool for improving screen-and-treat programs, particularly when smartphone-based image analysis techniques improve the imaging modality's diagnostic capabilities. For HRME images, for example, an automated frame selection technique allows for fully automated image analysis at the point of treatment, which is especially significant for technologies utilized in areas with limited infrastructure and specialized skills. While typical imaging procedures such as Lugol's chromoendoscopy (LCE) are lacking in specificity in esophageal cancer, HRME enhances the accuracy of LCE in correctly detecting esophageal squamous cell neoplasia, resulting in fewer unnecessary biopsies.

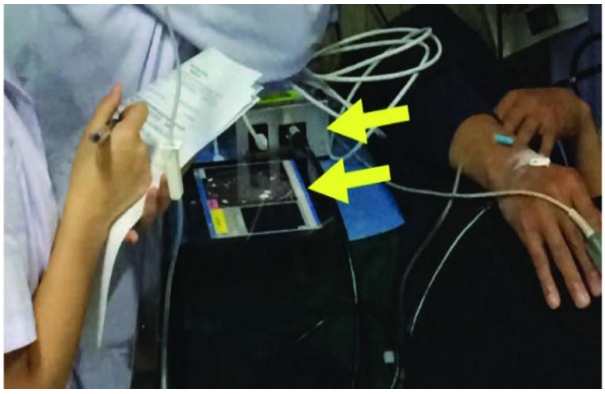

Figure 9: HRME in use during an endoscopic screening study for esophageal squamous cell cancer (Protano et al., 2015).

In colorectal cancer, a combination of HRME and traditional white-light colonoscopy can be utilized to detect colorectal polyp growth as well as differentiate between neoplastic and non-neoplastic colorectal polyps, advising doctors in real time on which lesions should be biopsied for further investigation. HRME is frequently used to screen for cervical cancer in conjunction with the widely used visual examination with acetic acid (VIA) (Protano et al., 2015).

- The technology can be used to provide mobile cancer care to patients in rural areas without requiring a lot of infrastructure, so that patients are able to avoid having to travel to a primary cancer center.
- HRME-based real-time cervical neoplasia diagnosis, evaluation and staging can help doctors determine whether urgent cryotherapy is needed, improve the efficiency of in-clinic see-and-treat and mobile procedures, and minimize overtreatment.

3.3.2 Low-Cost Microscopy

Low-cost microscopic options based on developments in LEDs (light-emitting diodes) for fluorescence microscopy were first designed for Mycobacterium tuberculosis diagnosis. The Global Focus microscope, for example, is a battery-powered fluorescence microscopy that uses

an LED-based flashlight as a source of light. The microscope produced results comparable to a laboratory fluorescence microscopy in 98.4 percent of TB cases examined and can be constructed for $240 USD against $1875 USD for PrimoStarTM.

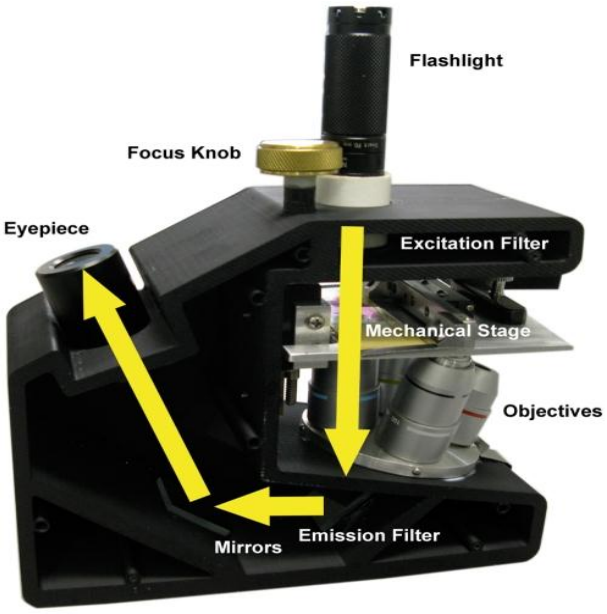

Figure 10: The Global Focus microscope (Miller et al., 2010)

In ex vivo tissue samples, fluorescence microscopy (FM) techniques are playing a pivotal role for cancer diagnosis, detection and monitoring. Implementing and expanding on the previously described low-cost microscopy technologies for infectious disease detection can provide laboratories with the potential to examine biopsies at the spot or point-of-care, allowing for quicker decision-making and treatment of the patient in circumstances where follow-up is minimal. Point-of-care analysis is possible with camera-enabled mobile phones:

- High-resolution LED-based fluorescence microscopy can be performed with mobile phone-mounted microscope extension which has the capability of high-resolution clinical light microscopy.

- Holographic microscope extensions to mobile phone camera device enable for lens-free digital microscopy. An LED illuminates the samples vertically by the phone camera for imaging. The images are later on rebuilt for additional investigation using quick digital processing.

- Smartphone-based chip-scale microscopes rely on the user's hand motion for angular scanning and use ambient light sources. Because this design does not require lenses or a light source, it may be made with a simple modification of a phone's camera module. Images are reconstructed into a high-resolution image for examination in this modality.

Because cell-phones are used as a platform for mobile-phone-based microscopy equipment, their use will likely grow increasingly popular among healthcare providers in low-resource contexts.

Chapter 4

POC Technologies for Use in Cancer Diagnostics in the Future

Various modern methods are quickly establishing themselves as a pioneer in the discovery of tumor markers for early detection of cancer. These cutting-edge technologies is able to diagnosis cancer in real-time where there is resource is constrained, and they can be moved from the conventional lab to the clinic as a cancer therapy point-of-care diagnostic platform

4.1 Molecular Imprinted Membrane as a Sensing Platform

Molecular imprinting is a new technology for constructing unique molecular configurations that uses a lock and key mechanism, allowing interaction of bimolecular. For instance, cross-linking template/imprint molecules with monomer or molecular imprinting of a synthetic polymer by co-polymerizing a feature which lead to the establishment of a complex (via covalent/non-covalent interaction or self-assembly) in which systematically arranged polymeric structure and a strongly cross-linked introduced high intrinsic robustness and stability to the system, accompanied by, the incorporation of molecular memory at binding sites that are able to compliant with (Sandbhor Gaikwad & Banerjee, 2018).

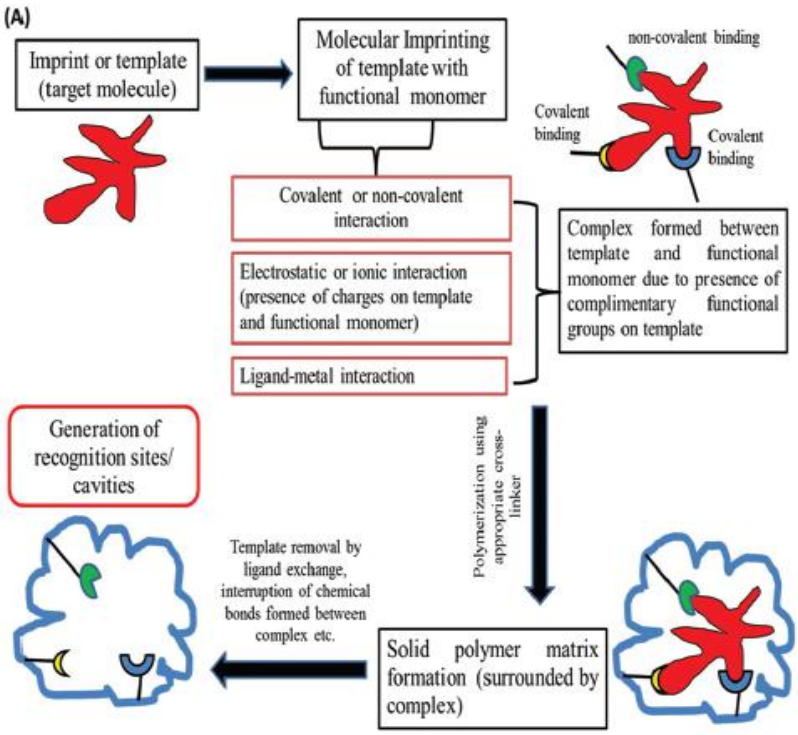

Figure 11: The principle of molecular imprinting technique. (Sandbhor Gaikwad & Banerjee, 2018)

Therefore, because molecularly imprinted materials has great specificity and affinity of binding sites that are similar to an antibody–antigen system, they are often known as "antibody mimics."

4.1.1 A Novel MIP-Based Device Based on an Immune-Polymeric Membrane

A microfluidic chip with a biomimetic immuno-like membrane paired with molecular nano-cavities was developed so that C-reactive proteins can be detected, which could be used as a biomarker in cancer detection and inflammation linked with infections, trauma, tissue necrosis, and, among other things. In three steps, the immuno-like membrane was created: combination, polymerization, and extraction, in which cross-linking and functional monomers were co-polymerized with a template (target molecules) and imprinted nano-cavities were formed when the template was removed. The sensor was made up of a C-reactive protein (CRP) imprinted polymer film that was orderly structured with nano-cavities (from the polymer film, the C-

reactive protein was removed later on) and where antibodies modified on a cyclic olefin co-polymer substrate reacts with C-reactive protein. The surface was modified by creating a layer (gold) on a substrate that had been functionalized with cysteamine and glutaraldehyde, then an immuno-like membrane was integrated into the microfluidic chip. The results revealed that the ordered designed nano-cavities on the immuno-like membrane had unique adhesion forces comparable to the contact forces between CRP and biological CRP antibodies.

As a result, a biomimetic immuno-like membrane was created that is extremely specific and sensitive for detecting the target protein from complex bio-fluids in a matter of seconds (110 seconds), as opposed to traditional ELISA, which requires multiple hours to analyze. As a result, because of its cost-effectiveness and scalability, a proposed technique like this can be employed as an adaptable platform in point-of-care testing so that various protein biomarkers can be identified easily in detecting the cancer (Park et al., 2022).

4.2 Smartphone Controlled POC Diagnostic Platform

The most widely used mobile devices is Smartphone which offers outstanding and consumer-friendly features like easy operation, computing capability, sensitive touch-screen display, major data storage, in-built camera, and, prompting the integration of imaging and sensing features in them so that a possibility to identify and screening of various proteins, metabolites and nucleic acid-based biomarkers in diseases.

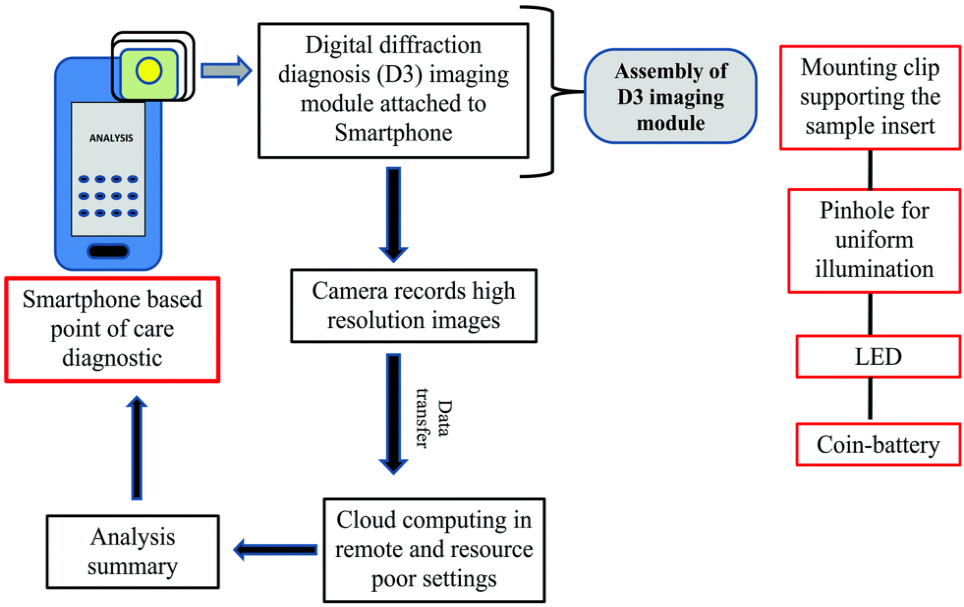

Figure 12: For resource-poor areas, a smartphone-controlled point-of-care cancer detection platform (Sandbhor Gaikwad & Banerjee, 2018)

Because of its portability, affordability, and customer-friendly operation, the mobile health (mhealth) system is used in point-of-care diagnostic applications to send the findings of a lateral flow pregnancy test from a clinical and pre-surgical ward to a real-time laboratory information system (Olla, 2015). Overall, the findings indicated that Smartphone-based point-of-care diagnostics have the possibility to upgrade treatment effectiveness, patient health and standard of living through real-time decision-based assessment.

4.2.1 Smartphone-Based Electrochemical Biosensing System

A smartphone-supervised point-of-care biosensor incorporating electrochemical impedance spectroscopy was created so that immuno-quantification and detection of proteins such bovine serum albumin (BSA) and thrombin can be carried out. For immuno-sensing and protease (thrombin) detection, researchers used a handheld biosensors, detector and a Smartphone (which included a carbon-printed electrode, a single gold electrode and multichannel inter-digital gold electrodes altered with antibodies anti-BSA/BSA and octapeptides with covalently

linked bovine serum albumin). The detection limits for BSA and thrombin were determined to be 1.8 g mL1 and 3 ng mL1, respectively, which were equivalent to available commercially diagnose method, with high stability for long-term analysis (one hour) with real-time detection (Shen et al., 2020).

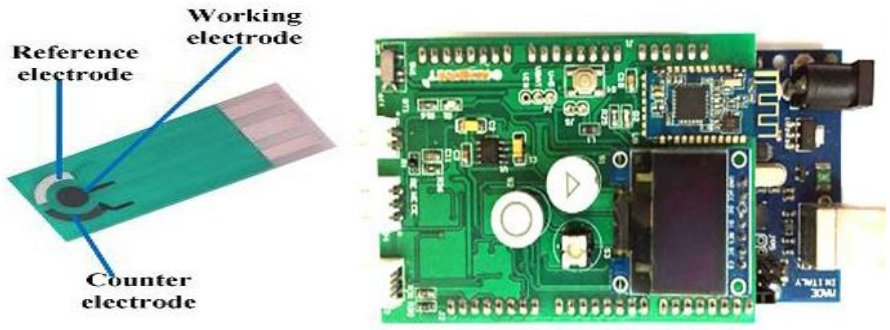

Figure 13: Images of components of the smartphone-based electrochemical biosensing system (Shen et al., 2020).

As a result, the Smartphone-based protease cleavage technique could be used in point-of-care diagnostic applications for the early detection and screening of cancer biomarkers like MMP.

4.2.2 Smartphone-Based Rapid Hematocrit Determination

Based on an ELISA integrated microchip platform, a smartphone/charge-coupled device (CCD) was created as a point-of-care ovarian cancer diagnosis so that human epididymis protein 4 (HE4) can be detected which is a biomarker found in urine samples. A non-lithographic process was used to create the PMMA-based biochip featuring three microchannels. (Jalal et al., 2017).

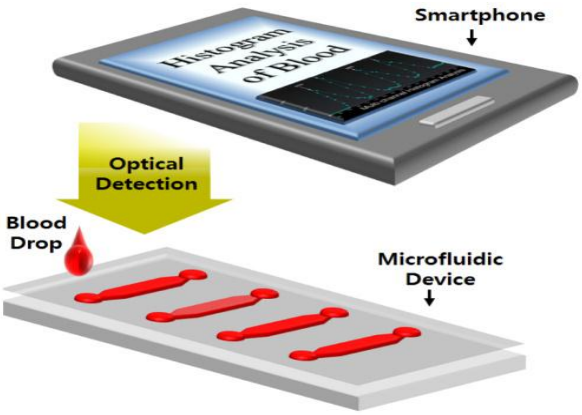

Figure 14: Conceptual view of smartphone-based lab-on-a-chip (LOC) platform for a histogram analysis of blood hematocrit (Jalal et al., 2017).

A smartphone-lensless CCD integrated sandwich ELISA based on TMB/H2O2 colorimetric detection was used to image and quantify the HE4 biomarker, with immune-complexes created via interaction between HE4 (from a capture antibody on the microfluidic chip) and an HRP tagged secondary antibody against HE4. With high specificity and sensitivity, the detection limit was reported to be 19 ng mL-1. A mobile application app was installed on the Smartphone to evaluate the ELISA findings without the use of a computer or microplate reader.

Furthermore, the technology has benefits, for example- ability to differentiate between healthy cells and cancerous cells, as well as transference of data easily via mobile networks, which aids in improving diagnosis by allowing the end-user to consider demographic and epidemiologic variables, followed by efficient disease monitoring as -

- Rapid,
- Real-time,
- Cost-effective and
- Non-invasive point-of-care testing.

4.2.3 Mobile Colposcopy

Colposcopy, or a cervix inspection with a magnifying equipment known as a colposcope, permits doctors to discover aberrant cervical cells for biopsy and further investigation (Mitchell

et al., 1998). A qualified provider, space, proper equipment and time for a pelvic exam as well as a working colposcope are all required for traditional colposcopy. Innovative colposcopy procedures in resource-constrained settings, on the other hand, own the ability to reshape these needs. MobileODT, for instance, is a gadget that employs image capture to let physicians better visualize cervical cells. It's protected by a sturdy casing and runs on batteries for further portability (Lombardi et al., 2016).

Another example is the POCkeT Colposcope. With its tampon-like form that allows deployment into the vagina for cervical image acquisition, the POCkeT Colposcope removes the necessity for a comprehensive pelvic exam. This solution well-suited with task-shifting models that empower community-level caregivers to improve detection of cervical anomalies as soon as possible at the point of care by lowering the level of training necessary for use. (Lam et al., 2015)

Figure 15: Point of Care Tampon (POCkeT) Colposcope (Lam et al., 2015)

4.3 Point-of-care Ultrasound (POCUS) in Cancer Detection

Ultrasonography is a diagnostic and image-guided surgery technique used by radiologists and clinicians to diagnose and treat a variety of disorders, including cancer. However, recent technology breakthroughs have improved conventional ultrasound over the last few decades, making it more affordable, simple, sophisticated, and non-invasive, allowing it to be used in a point-of-care diagnostic platform.

4.3.1 VSCAN

Ultrasound has been found to help women with dense breast tissue detect breast cancer earlier than mammography, and there is rising acceptance for utilizing ultrasound in resource-limited locations as a key method of diagnosis of breast cancer, including the use of ultrasound-guided small needle aspiration. Ultrasound also can be utilize to assist focused biopsies in the detection of prostate cancer, which saves time and money. Ultrasound has the power to contribute a part in targeted treatment and disease surveillance as the advancement potential, reduced-cost contrast agents for image-guided treatments progresses. Ultrasound devices have been promoted in LMICs thanks to hardware changes that improve portability, ease of use, and affordability. There are already various products that are available in the market which have incorporated these variables into consideration and produced positive outcomes, proving that portable ultrasonography may improve patient care and be used by healthcare practitioners of varying levels of training.

Figure 16: VSCAN portable ultrasound (Schleder et al., 2012)

The ability to use POC ultrasonography to gather samples can improve or introduce novel ways of collecting sample that were earlier inaccessible in low-resource settings. Traditional ultrasound devices are generally prohibitively expensive for health systems in LMICs, with an average cost of $101,865 in 2016 (ECRI Institute 2016 Technology Price Index). (Schleder et al., 2012). Companies are identifying this stumbling block and designing low-cost models to overcome it. The VSCAN Access and the VSCAN Mobile Pocket Ultrasound, both from GE

Healthcare, are priced more than an order of magnitude lower than typical ultrasound equipment. The portable ultrasound versions from SonoScape are equivalent in price. Furthermore, MobiSante's MobiUS SP1 and TC2 Systems provide smartphone and tablet-based ultrasound capabilities, respectively, for increased proven utility and mobility in a number of clinical contexts or application.

Chapter 5 Clinical performance of Newly Designed POC Diagnostic Devices against Traditional Methods

5.1 OSTEOMARK®NTx Vs ELISA

A point-of-care diagnostic tool is OSTEOMARK®NTx Point of Care Rx Home Use. It has been documented in metastatic bone cancer patients (n = 136) utilizing lab setting ELISA tests for the identification of a protein biomarker, known as NTX or the N-terminal peptide bound crosslink of type-I collagen. (Lester et al., 2010).

Figure 17: OSTEOMARK®NTx (Lester et al., 2010)

In order to evaluate the frequency of bisphosphonate medication, the patients were divided into three groups: 0–50, 50–100, and >100 nM bone collagen equivalent per milimole (BCE per mM) creatinine. The results revealed that 231 devices (84.9 percent) out of 272 had the potential to record a value greater than the reported amount. According to the Bland and Altman analysis, point-of-care devices had values that were 25.9% greater than lab tests, with moderate agreement (Kappa 0.508) between the two tests.

5.2 Concile® Vs UBC-ELISA

A UBC Rapid test method was developed with a photometric reader tool Concile® Ω100 as a quantitative point-of care device. On 177 bladder cancer patients, the device's practicality and accuracy were tested in the clinic and compared to UBC-ELISA. For suspicious lesions, all patients went through transurethral and cytoscopy resection, and UBC rapid assays were used

to classify them into three groups: 1, 2, and 3 of any band, good visible band, and strong band, respectively, and later on, bladder cancer biomarkers was detected by using a photometric Concile® 100 reader. Only 45 people out of 177 were found to have bladder cancer, according to the findings. Cut-offs 1. 2 and 3 had sensitivities and specificities of 60 percent, 56.1 percent, and 51.1 percent, and 81.1 percent, 31.1 percent, and 87.8 percent, respectively, according to visual inspections. The quantitative test results showed an area under curve of 0.643 and 57.8% sensitivity and specificity at the best cut-off of 12.3 ng mL-1, respectively, whereas UBC-ELISA showed best cut-off and an area under curve of 31 ng mL-1 and 0.559, respectively, with 32.5 percent and 85.3 percent sensitivity and specificity.

5.3 Smartphone based SPR Detection Vs Clinical Detection

Recently, a Smartphone system that relies on angle-free and label-free SPR detection was created, which used optical detection and conditioned lighting from a cell phone. When the surface plasmon coupling requirements in an SPR biosensor fitted with the angle of incident monochromatic light, surface plasmon resonance was excited by the inherent illumination, at the surface of a thin golden metal film, producing in a distinctive dip in reflection.

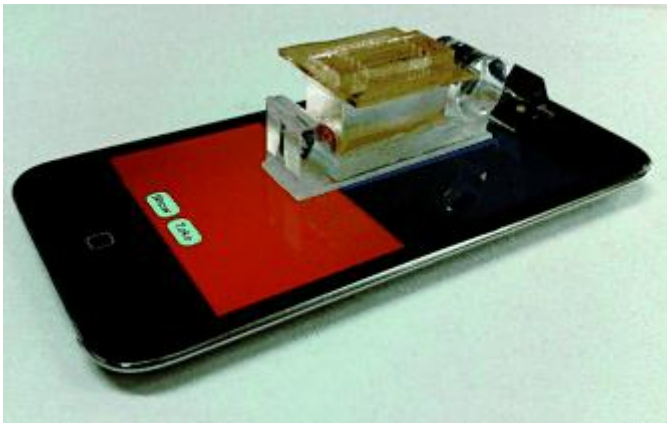

Figure 18: Smartphone Based SNR detection (Preechaburana et al., 2012)

Small variations in the refractive index were induced by the biomolecules adsorbing on the surface, which were detected by calculating the angular variation where the characteristic dip emerged in reflection. For indicators like beta-2 microglobulin, the device had a detection limit of 0.1 g mL1, which was comparable to the performance necessary for clinical use.

Chapter 6

Limitations of the POC Detection

POCT has many advantages over central laboratory testing, including faster turnaround times, no sample transportation, and simplified sample needs and processing. By delivering treatment right away, POCT can increase diagnostic testing accessibility and uptake, enabling physicians to provide prompt guidance, and reduce the need for follow-up visits by providing treatment right from the start.

Despite its benefits, POCT face some challenges that must be addressed to implement them in any healthcare environment.

- **Quality standard assurance:** Quality concerns can be a serious challenge because most POCT kits are utilized outside of a controlled setting. Extreme climatic conditions are also predicted to have an impact.
- **Manual errors:** There is potential of errors due to a lack of understanding of the need of quality assurance and quality control processes as POCT is conducted by clinical staff rather than laboratory qualified and trained professionals. Therefore, because the examinations are conducted by less experienced individuals, there is a greater risk of judgemental errors (Shaw, 2016).
- **Economies of scale:** It's crucial to compare the volume of applications and the availability of reimbursement to lab-based diagnostics. In general, POC tests are more suited for quick screening during epidemics such as illness. It's critical to build and promote a POC solution for chronic disorders like cancer, not just for detection but also for entire management, which includes prevention, detection, monitoring, and treatment efficacy measurement. But, large scale production of POC devices are rare.

- **Difficulty in reporting:** Because the majority of POC testing methodologies lack a good reporting interface, there is a risk of losing important patient data as well as manual reporting errors. Basically, a clinical report is a complete explanation of a patient's symptoms, signs, diagnosis, therapy, and follow-up. From a clinical reporting standpoint, companies developing POCT solutions for cancer must ensure sufficient technology enablement.

- **Single biomarker dependant:** Given the progressive nature of cancer, simultaneous detection of numerous clinical parameters, such as blood analytes, electrolytes, signaling molecules, and metabolites, is critical. But most of the POC devices rely on single biomarker. Cinical evidence based on single biomarker discovery is insufficient to evaluate tumor heterogeneity since the tumor continues to mutate.

- **Wrong clinical result**: Inaccurate POCT results may raise total healthcare expenditures by prompting more diagnostic testing and procedures, or they may miss a serious problem (Nichols, 2004).

Some of my suggestions that can include POCT in cancer detection, especially in low-resource-settings are mentioned below-

- Healthcare providers should continue to relocate routine laboratory testing to the point of care, aided by this ever-expanding POC test menu, to enjoy the benefits of efficiency and cost savings.

- Institutions must rethink their overall care approach, striking a new balance between central and decentralized testing while also addressing the practical problems of implementing POCT, including quality control.

- To get the most dependable results, a healthcare institution must implement a solid POC governance model and POC coordinators who are empowered by actionable data.

As technology progresses and point-of-care testing equipment improve, the accuracy aspects related with POC testing are expected to be rectified. The perks of fast results and simplicity of assessment are likely to be seen as significant and acceptable, as well as commonplace, as more knowledge and experience of point-of-care technology is achieved.

Chapter 7

Conclusion

A point-of-care platform with low-cost, dependable, and user-friendly diagnostic instruments that allow near-bedside diagnosis can deliver instantaneous and quick results, allowing for real-time cancer detection and screening. Due to lack of specificity, low sensitivity, expensive analysis, long assay times and difficulty of access in remote and resource-limited locations, traditional point-of-care diagnostics for cancer have limited practical relevance. Because of their inherent perks such as simplicity in use, miniaturization, portability, higher potential in integration with ultra-sensitivity and diagnosis accuracy, successful ease of access in resource-limited, remote locations as well as robust and rapid multiplexing analysis, breakthrough in microfabrication and nano-technologies have brought about a paradigm shift in point-of-care diagnostic platforms. Furthermore, as they have ability to do glycoprofiling, lectins and aptamers have been introduced into POC testing. ELLAs, which use lectins instead of antibodies, were found to have alike sensitivity and specificity as antibody-based ELISAs, as well as the capacity to differentiate between patterns of glycosylation. Though they have obvious benefits of being easy to manipulate and compact, aptamers are still in the early stages of development in diagnostics.

Several of point-of-care diagnostic innovations are presently in use in clinical settings, while others are still under research or being evaluated. As a result, the commercialization and clinical application of such point-of-care cancer diagnostic devices or tools for accurate and early diagnosis with real-time surveillance of burden of disease to enhance the treatment outcomes and mortality has a lot of potential.

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