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A Review of the Technological Advancements in Detecting Lung Cancer Severity Among the Malaysian Population

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Lungs are the main organs for breathing and are part of the respiratory system. Subsequently, one lethal disease of cancer, known as lung cancer, is a type of malignancy that grows when abnormal cells in one or both lungs proliferate and reproduce uncontrollably. In the detection of lung cancer, some diagnostic assessment modalities can be employed, for instance, chest X-ray, computed tomography scan, and magnetic resonance imaging. Although these modalities are incredibly effective aids, a remarkable advancement in lung cancer diagnostics should be implemented. The main goal of this research is to highlight current diagnostic techniques as well as some advanced diagnostic techniques for lung cancer severity detection among Malaysians. The epidemiology, along with the challenges regarding lung cancer screening, is also emphasised.

Keywords: Lung Cancer Detection (LCD); Chest Radiography (CXR); Liquid Biopsy (LB); Radiomics; Biosensors

I. INTRODUCTION

Lung cancer is the foremost reason of mortality from cancer in Malaysia and around the world. Lung cancer was identified in over 1.8 million people wide-reaching in 2016, resulting in 1.6 million fatalities (Kan & John, 2016). Because of the high rates of smoking, the occurrence of lung cancer and subsequent mortality from the disease is predicted to grow across the subsequent decade. Although tobacco is the primary cause, several Asian countries have documented a significant frequency of female non-smokers with adenocarcinoma (Hassan *et al.*, 2017). The unrestrained, uneven proliferation of cells in lung tissue causes lung cancer, and lung nodules describe these anomalies in lung tissue. They are small, generally spherical masses of tissue ranging from 5 to 30 millimetres (Mahersia *et al.*, 2015). The increased global prevalence of lung cancer is thought to be linked to a lack of public awareness about the disease, resulting in a delay in symptom presentation and, as a result, a late diagnosis (Loh & Tan, 2018).

Lung malignancy is one of the most frequently diagnosed cancers in Malaysia, reported for nearly 10% of all cancers between 2012 and 2016, according to the Malaysia National Cancer Registry Report. For Malaysian males, the hazard over a lifetime is about 1 in 55, with the risk being most significant in Chinese guys (1 in 43), afterwards Malays (1 in 62), and Indians (1 in 103). The hazard is roughly 1 in 135 for women. The National Cancer Registry (NCR) also provided information on the epidemiology of lung cancer. Lung cancer was the third extremely prevalent cancer in the nation in 2007, the second greatest widespread cancer in men, and the fourth most popular cancer in women. In 2020, the data from the WHO showed that the number of lung cancer cases in Malaysia accounted for 10.6% of all malignancies. Fig. 1 indicates the number of new cases in 2020 for both sexes at all ages (Rajadurai *et al.*, 2020).

In Malaysia, several approaches for lung cancer detection (LCD) have been employed. Surveillance with sputum cytology and chest radiography (CXR) has remained used in the past to test for lung cancer (Azizah *et al.*, 2019).

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Furthermore, the imaging modalities, for instance Computed Tomography (CT), Magnetic Resonance Imaging (MRI) with computer-aided diagnostic systems (CAD), and Positron Emission Tomography (PET), have also been utilised to analyse the images and data in detecting lung cancer and determining its aggressiveness. However, CT is the most frequent imaging mode for staging, since it is less expensive than a positron-emission tomography scan, which is usually reserved for patients with stage II or higher infection and is only available in private practice. However, both modalities are studied to be the most utilised aids, while the application of chest radiography and ultrasonography for performance is infrequent (Rajadurai *et al.*, 2020).

The screening of lung cancer for early diagnosis is particularly necessary for those who have no signs or a history of lung cancer since it allows them to discover the disease earlier. The most general suggested lung cancer screening test is low dose computed tomography (LDCT), indicated for adults who are at a high risk of acquiring the condition due to a history of smoking, and it takes only a few minutes and is painless.

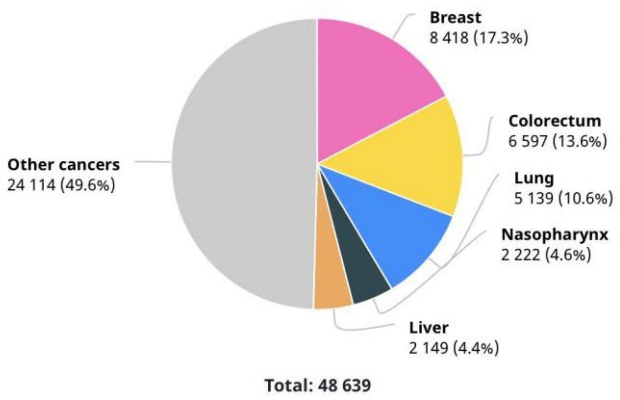


Figure 1. Number of new cases in 2020 for both sexes at all ages (Rajadurai *et al.*, 2020).

II. EPIDEMIOLOGY

According to a World Health Organization statement from 2014, lung cancer caused 19.1 demises per 100,000 people in Malaysia, or 4,088 demises per year (3.22% of all demises), making it the second most mutual source of cancer demise after breast cancer and the eighth-most mutual cause of death overall (Sachithanandan & Badmanaban, 2012). The most prevalent cancer fatality in males in 2014 was cancer of the bronchus, trachea, and lung, which accounted for 24.6 per cent of total cancer deaths in the country. In females, it was the second highly prevalent cancer death after breast cancer, accounting for 13% of all cancer deaths (Kan & John, 2016). According to World Health Organization, the high quantity of male patients detected with lung cancer is attributable to smoking, with over 40% of Malaysian males smoking in 2016.

In terms of ages, lung cancer is diagnosed at a typical age of 60 years in Malaysia, with a peak age of diagnosis in the seventh decade. Lung cancer is uncommon in Malaysian individuals under the age of 40, with just about 6.2% having been diagnosed (Sachithanandan & Badmanaban, 2012). Adenocarcinoma with poor prognosis was more common in younger patients than in older patients, based on another record from the World Health Organization (WHO). Younger age groups are more likely to have a late-stage presentation and thus inoperability since they are more likely to be asymptomatic or disregard symptoms. In terms of ethnicity, Chinese patients were overrepresented among those who had been diagnosed with lung cancer. The ethnic division of lung cancer patients was similar in both the younger and older groups (Chinese 71%, Malay 19%, Indian 9%, others 1%) (Kan & John, 2016).

Small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are the two main divisions of lung cancer. Based on categories of Lung Cancer, over 80% of all lung cancer issues are affected by Non-Small Cell Lung Cancer (NSCLC) and include many histological forms such as squamous cell carcinoma (SCC), adenocarcinoma (AC), and large cell carcinoma (LCC) (Bangash *et al.*, 2017). Over the last 20 years, AC lung cancer has surpassed SCC as the most ordinary histological type of lung cancer, reporting for almost 40% of all occurrences. As mentioned before that those patients identified with lung cancer are attributable to smoking, this includes both active and second-hand smoking.

According to the Ministry of Health Malaysia data from 2016, tobacco smoke comprises over 4000 chemical substances, the majority of which have been linked to lung cancer. When compared to non-smokers, smoking 20 cigarettes per day raises the risk by 20 to 25 times. However, the risk of lung cancer is lowered when a smoker stops smoking. After 15 years of no smoking, the threat of lung cancer is said to be the same as it is for non-smokers. Cigar and pipe smoking also raise the threat to develop lung cancer. Table 1 shows the prevalence of current smokers in Malaysia in percentage based on data from 2016 while Figure 2 shows the prevalence of smokers by the state for 2011 and 2015 (MOH, 2018).

Table 1. Prevalence of present smokers in Malaysia (MOH, 2018).

Gender	**2006**	**2011**	**2015**
National	21.5	19.3	22.8
Male	46.4	36.4	43.0
Female	1.6	1.5	1.4
Ethnicity	**2006**	**2011**	**2015**
Malays	24.0	21.5	24.7
Chinese	16.2	12.8	14.2
Indians	13.7	13.0	16.5
Other Bumiputras	24.8	21.9	25.8
Others	23.8	29.2	35.0

2006 (aged 15 years and above)
2011 (aged 10 years and above)
2015 (aged 18 years and above)
Source of data: NHMS

Other triggers of lung cancer include air contamination from vehicles, factories, and other sources, as well as asbestos exposure, which is naturally occurring from fibrous silicate material that significantly raises the risk of lung cancer. Mesothelioma, which is a cancer that develops from the lung pleura, is intimately connected to exposure to asbestos. Lung disorders, including tuberculosis and chronic obstructive pulmonary disease, on the other hand, increase the chance of lung cancer. Other than that, Lung cancer is also increased by radon/radium (a uranium-derived chemical). Occupational contact with arsenic, chromium, nickel, aromatic hydrocarbons, and ether, according to the study, also contributes to the risk (Ghosal *et al.*, 2009). There is currently no cost-effective technology for detecting early lung cancer, and most patients appear at a late stage. As a result, reducing tobacco smoke exposure, whether active or passive/second-hand smoking, is the most effective way to inhibit lung cancer. Other substances, such as those described above, should also be avoided.

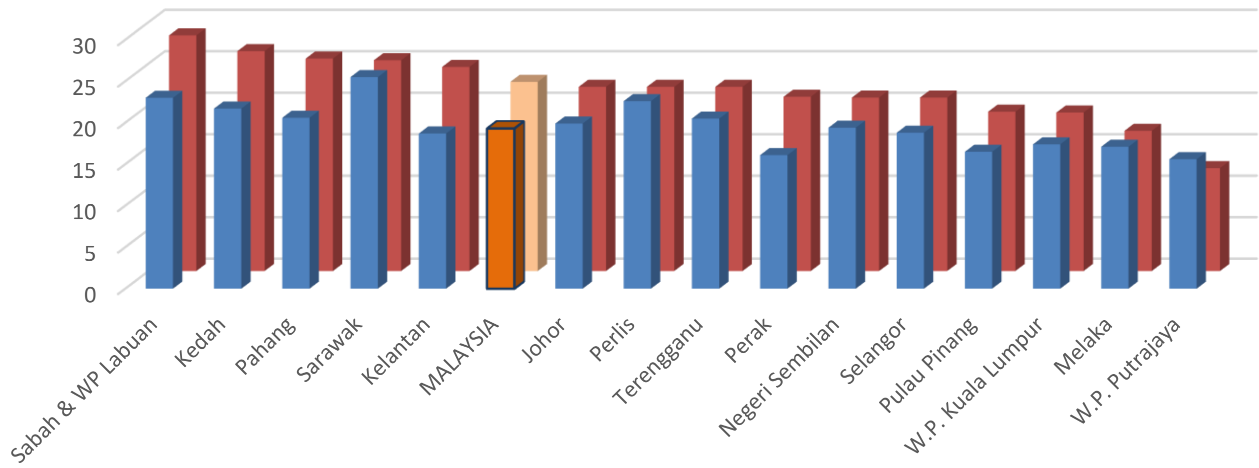
III. PRINCIPLES OF SCREENING

Screening is a crucial medical procedure that identifies a disease in a designated population to enhance health outcomes (Ghosal *et al.*, 2009). It is not primarily a diagnostic test, but it is an important method for the early-stage disease diagnosis, including cancer required for the further diagnostic test. In cancer imaging, there are specific screening aspects that should be stressed.

A. The Condition Ought to be an Imperative Health Problem

The most effective usage of screening necessitates a basic grasp of the most frequent sources of death (Nielsen & Lang, 1999). Screening for diseases or illnesses with a high degree of morbidity and mortality is regarded as reasonable. Government mortality statistics can provide such information. Heart illnesses, lung and breast malignancies, strokes, and influenzas are the top causes of death for the general population year after year. These prevalent conditions should be the focus of screening methods in general. If cancer can be identified at an early stage, it is critical that proper mediation can be made at that time to change the course of the disease. Early treatment or intervention should, ideally, be supported by substantial evidence from well-conducted clinical trials.

B. There Should be a Latent Phase of the Disease



2011 (%)	23	21.7	20.6	25.5	18.7	19.3	19.9	22.6	20.5	16.1	19.4	18.8	16.5	17.4	17.1	15.6
2015 (%)	28.4	26.5	25.6	25.4	24.6	22.8	22.2	22.2	22.2	21	20.9	20.9	19.2	19.1	16.9	12.4

2011 (%) 2015 (%)

Figure 2. Prevalence of current smokers by the state for 2011 and 2015 (MOH, 2018).

There must be a latent phase of the disease that can be detected before it progresses to an advanced stage for it to be susceptible to screening (Nielsen & Lang, 1999). Most cancers grow slowly, and many have a pre-invasive or precursor stage during which early therapy can prevent invasive cancer from developing. Lung cancers usually present themselves when a patient develops symptoms, therefore, the cancer is usually advanced by the time the symptoms appear. The goal of screening is to catch these tumours early.

C. The Disease or Disorder must Consume a Readily Accessible and Satisfactory Treatment

The purpose of diagnosis is to alter the disease or condition being checked in the changing of the natural outcome of the disease. As a result, if an illness or condition is found through screening, relevant treatments should be accessible to affect the disease's or condition's final course (Nielsen & Lang, 1999). In general, cancer screening tries to discover cancer at an earlier stage than would be the case if the patient waited until symptoms appeared because lower-stage malignancies are generally easier to treat and cure.

D. The Screening Test Ought to be Precise (Sensitivity and Specificity)

An excellent diagnostic test has a great sensitivity (few false-negative results) and a great specificity, which results in a larger number of positive outcomes (few false-positive results). A Test's sensitivity and specificity are frequently associated with a gold standard, also known as a conclusive test. Pathologic tissue is frequently used as the gold standard for disorders like cancer. One study investigated the psychosocial effects of false-positive colorectal screening and found that, in addition to the discomfort and anxiety associated with a positive test result, participants were more ambivalent about future exams (Nielsen & Lang, 1999).

E. The Diagnosis Practice Ought to have an Acceptable Cost (Health and Financial Risk)

The financial expense of a diagnosis involvement must be justified by the advantages (Nielsen & Lang, 1999). The variables that go into determining the cost-efficiency of clinical preventive care are numerous and complicated. The expense of the screening assessment, physician visit, continuation diagnostic testing, side effects, and iatrogenic problems, missed work time, and possible savings from prevented disease and incapacity are all factors to consider. Uninsured or underinsured individuals, as well as those with a poor socioeconomic position, may be less likely to receive screening or early diagnosis.

F. The Screening Process has to be Satisfactory to the Patient and the Public

Since screening trials are also carried out on asymptomatic people, they should be relatively secure (Nielsen & Lang, 1999). Complications from presently acknowledged screening intrusions are quite rare. Because one part of rightness is the test's functionality, the idea that an appropriate early detection test or examination that is acceptable to the general public is strongly related. Furthermore, if the screening method is particularly invasive, cumbersome, or horrible, it may have a lower achievement rate since many people will reject to take the test.

IV. BASIC DIAGNOSTIC IMAGING TECHNIQUE OF LUNG CANCER

Small cell and non–small cell lung cancers are two categories of lung cancer based on histology. Cough, dyspnoea, haemoptysis, and general symptoms such as weight loss and anorexia are the generally ubiquitous symptoms of lung cancer. Chest radiography (CXR) must be worked on high-risk patients who appear with these indications (Latimer & Mott, 2015). Although less effective, chest radiography is used regularly and widely. Computed tomography and potentially positron emission tomography must be employed if a likely other diagnosis is not found. Figure 3 illustrates the radiograph of a tumour in the lung using CXR, where the red arrow indicates the area of the tumour.

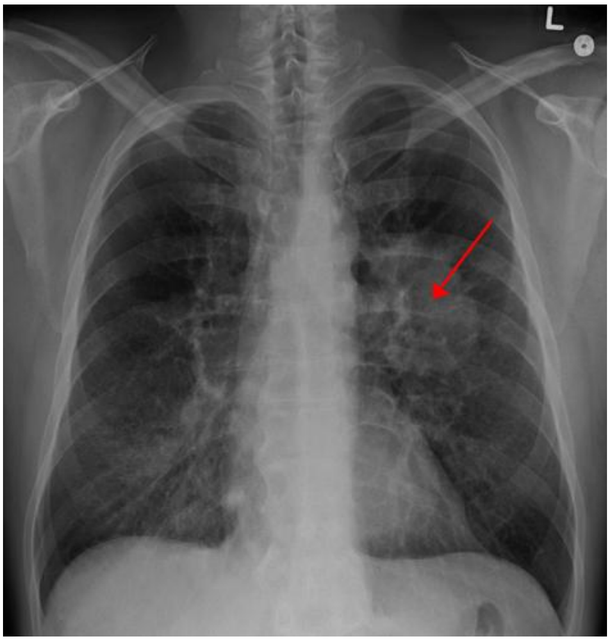


Figure 3. A Chest x-ray displaying a tumour in the Lung (Latimer & Mott, 2015).

A. Computed Tomography (CT)

Computed Tomography (CT) scanning is a very common approach to identify lung cancer using X-ray beams (Hadavi *et al.*, 2014). CT was originally presented in 1973, and the first image scanner built on CT could scan an 80 cm x 80 cm area in 5 minutes, whilst the most recent equipment can scan a 512 cm x 512 cm sector in 1 second. CT scan efficiency has increased by more than a billion times since its invention because of advancements in machinery (Rubin, 2014). The typical CT scan instrument has a superior radiation disclosure rate of roughly seven millisieverts (mSv), therefore, Low-Dose Computed Tomography (LDCT), which has a radiation exposure rate of 1.6 mSv, was invented to limit the exposure to high-intensity radiation.

In research published in 2013, the National Lung Screening Trials (NLST) discovered that chest radiography has a sensitivity of 91.3%, while LDCT has a sensitivity of 73.5%, indicating that chest radiography is extra susceptible than LDCT (New England Journal of Medicine, 2013). Thus, the low sensitivity of LDCT indicates that it is a good diagnostic test that has a little false-negative results. Even though CT scan imaging is the top imaging implement in the medical sector, clinicians find it challenging to translate and spot cancer from CT scan images. As a result, a computer-assisted diagnostic is an important tool that can assist clinicians in properly identifying malignant cells.

Furthermore, because CT scans use ionising radiation to create images, specialists in this field sometimes use the term "effective dose" to explain how greatly radiation absorbs by the body (Fisher & Fahey, 2017). However, the equivalent dose(H) for individual organs needs to be calculated first as in “(2)” by multiplying the absorbed dose (D) as “(1)” with radiation weighting factor (W_R) where the value then can be used to find the effective dose by multiply the tissue weighting factor (W_T) with the equivalent dose (H) as in “(3)”. The absorbed dose (D) is the quantity of energy accumulated in mass by radiation. The unit that has been used to measure the effective dose is in millisievert (mSv). For the lung cancer screening, the amount of radiation that will be absorbed is about 1.5 mSv which is equivalent to about 6 months of experience radiation.

$$\textit{Absorbed Dose, } D = E\ (\mathrm{J})\ /\ M\ (\mathrm{kg}) \qquad (1)$$

$$\textit{Equivalent Dose, } H = D \times W_R \qquad (2)$$

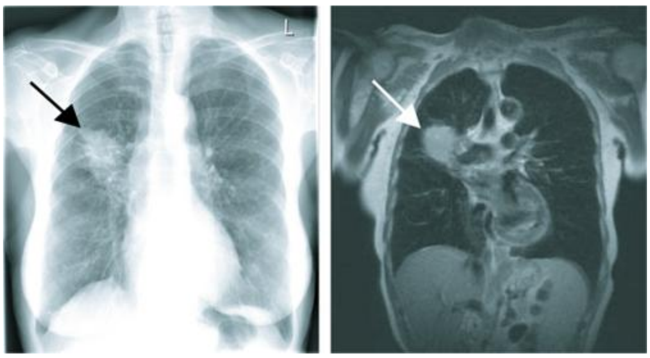
$$\textit{Effective Dose} = H \times W_T \qquad (3)$$

B. Magnetic Resonance Imaging (MRI)

Lung magnetic resonance imaging (MRI) has come to be a viable option to CT due to constant technological advancements such as greater gradients, corresponding imaging, and shorter echo time (Biederer *et al.*, 2017). Lung MRI can detect nodules with a size of 3-4 mm, according to experimental and clinical studies, with exposure rates of 60% - 90% for lesions of 5-8 mm and nearly 100% for lesions of 8 mm or larger. However, the high propensity of MRI to motion artifacts (pulsation and breathing), the intrinsic small proton density of lung parenchyma, and the reduction in signal intensity owing to air-soft tissue interfaces are all limits of MRI of the lung (Kim *et al.*, 2015). Due to these limitations, MRI's position as a problem-solving device in the examination of the mediastinum and chest wall has been limited following CT. The comparison of the CXR with the MRI images of the lung tumour can be seen in Figure 4, which depicts a big tumour that originated in the upper right lobe of the lung (arrows). The pictures indicate that the patient was diagnosed with adenocarcinoma (NSCLC).

The main benefit of MRI is the natural soft tissue contrast that occurs deprived of the introduction of contrast material. As a result, the approach can be recommended for individuals who are allergic to iodine contrast media which is a contrast agent that comprises iodine atoms applied for X-ray-based imaging modalities (Erasmus *et al.*, 2005). Breath-hold acquisitions and gating methods are two recent advancements that have enhanced overall image quality in MRI. Furthermore, gadolinium chelates, which promote reflexivity, are utilised to augment tumours and may aid in the evaluation of treated lesions during follow-up. Other than that, novel contrast agents containing ultrasmall iron oxide particles have been intended to increase the specificity of MRI in detecting mediastinal nodal invasion (Bellin *et al.*, 2000). Although these agents have been found to enhance nodal detection in pelvic and cervical cancers, the outcomes of clinical trials in chest evaluation have been negative. Many radiologists still reserve MRI for the evaluation of improved sulcus cancers and situations where spinal cord canal invasion is suspected. Lung cancer can be detected and staged using MRI, which could be a good replacement for CT or PET/CT in the examination of lung cancer and other disorders.

Figure 4. Standard chest X-ray (left) and MRI scan (right) of the patient (Kim *et al.*, 2015)



C. Positron Emission Tomography (PET)

A lung positron emission tomography (PET) scan, unlike magnetic resonance imaging (MRI) and computed tomography (CT) scans, which reveal the structure of the lungs, can indicate how well the lungs and their tissues are performing (Hochhegger *et al.*, 2015). A small amount of radioactive tracer is required for a PET scan. A vein (IV) is used to administer the tracer, which is commonly on the inside of the elbow. It circulates in the bloodstream before settling in organs and tissues. The tracer aids the doctor and radiologist in gaining a better understanding of certain locations or disorders. PET has a lot of potential as a non-invasive implement for evaluating lung cancer.

Hochhegger *et al.* (2015) further explain that PET scans using fluorodeoxyglucose (F-FDG) are currently used to characterise lung lesions, stage non–small cell lung cancer (NSCLC), identify distant metastases, and diagnose recurring disease. When utilised in conjunction with traditional radiologic imaging, PET imaging has been presented to cause in substantial shifts in the clinical management of NSCLC patients. Particularly, standard PET imaging can aid in initial performance as well as surgical and radiation planning, while the repetition of PET imaging after chemoradiotherapy can foresee tumour response and assist in tailoring treatment. It also has a higher diagnostic accuracy for detecting tumour reappearance after final therapy than other imaging modalities (Ambrosini *et al.*, 2012). The goal of a study that combined PET and CT to determine the malignancy of tumours was to improve accuracy and precision. Tracer components like 18-fluorodeoxyglucose (FDG) and Fluorine-18-methyltyrosine are used in the imaging, both of which are currently being studied. The CT scan has two drawbacks, which are poor patient cooperation and less accurate detection. Standard procedures like CT and PET are widely utilised, however, they have significant downsides or restrictions, such as cost and the presence of radioactive substances. Figure 5 illustrates the small cell lung cancer (SCLC) for chest CT scan (a) and subsequent CT/PET image (b) that shows the mass in the left lung (top arrow) with passionate radiotracer uptake on the PET/CT image.

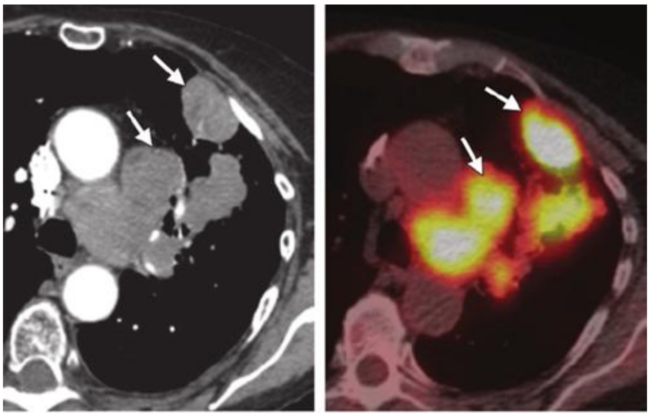


Figure 5. SCLC for chest CT and corresponding CT/PET image (Ambrosini *et al.*, 2012).

V. THE ADVANCED TECHNIQUE USED IN THE RECOGNITION OF LUNG CANCER IN MALAYSIA

In this era, there has been a remarkable advancement in the subject of lung cancer diagnosis. Main procedures such as computed tomography imaging, biopsy, and bronchoscopy were modified, while sophisticated implements and practices such as biosensors, radio genomics, artificial intelligence, and others were introduced (Prabhakar *et al.*, 2018). This is because the conventional approaches have the disadvantages of low patient compliance and are very expensive.

A. Biosensors

The first advanced technique in the recognition of lung tumours reviewed is the use of Biosensors. In terms of medical application, biosensors have become common tools for cancer diagnosis, and advanced sensor development has been realised (Jeffree *et al.*, 2020). Pairing the biological and electronic elements to achieve a qualified signal during evaluation is a critical part of the biosensor created due to the function itself in the screening or diagnosis, which is a device that translates chemical signals into an electrical reaction. It is essentially a device that detects and quantifies biomarkers. The biosensor device is made up of three main parts, which are a bio-recognition surface, a transducer, and an electrical signal amplifier, as well as other related mechanisms of the biosensors, as illustrated in Figure 6.

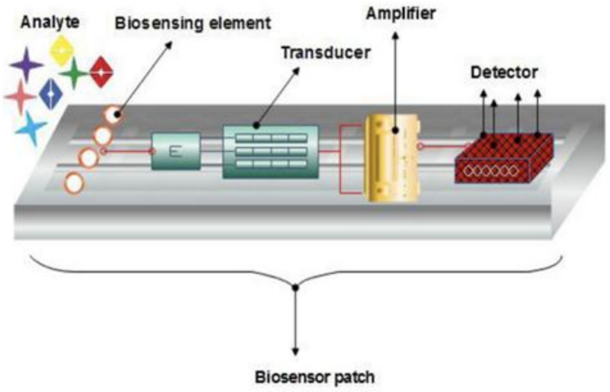


Figure 6. The components of the Biosensors (Perumal & Hashim, 2014).

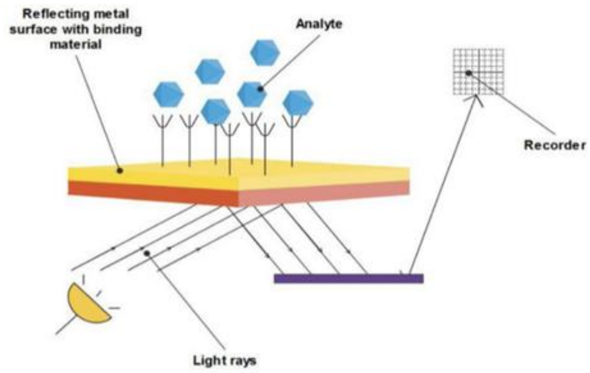


Figure 7. Schematic illustration of an Optical Biosensor (Kaur *et al.*, 2022).

The choice of a conducting surface on which the bio-identification features (e.g., enzymes, nucleic acids, receptors, antigens, proteins, or antibodies) are restrained is the first step in the design of a biosensor. If the result achieved is to be visually examined, the bio-recognition element must be immobilised on a clear conducting surface. The biomolecules of the analyte bond to the bio-recognition site, and the transducer element detects and processes changes in the site. The electrical system then amplifies and displays it. Biosensors are helpful in diagnosis since they are non-intrusive and deliver precise data. Biosensors can be applied not only to diagnose cancer early but also to observe the repetition of cancer during follow-up since they can identify particular biomarkers efficiently (O'Sullivan, 2002).

One form of biosensor, known as an optical biosensor, is commonly used to identify certain biomarkers in lung cancer and other types of cancer, such as leukaemia (Monosik *et al.*, 2012). The finding of a difference in optical density of reflected light is the basis of the optical biosensor mechanism. There is a bio-identification factor in an optical biosensor to which the analyte binds. As the analyte attaches to the binding material, a permanent beam of light is shone on the reflecting surface, with the angle and intensity of the light changing as the analyte adheres to the binding material. This occurs because of a difference in the surface's optical density, which is documented as an electrical signal. Figure 7 depicts a graphic representation of an optical biosensor.

B. Radiomics

The second advanced technique that can also be utilised in the imaging of lung cancer is Radiomics (Thawani *et al.*, 2018). Radiomics is the computerised withdrawal of data from radiologic pictures, and it can speed up and enhance lung cancer diagnosis using system learning algorithms. The quantitative parameters investigated express subvisual aspects of pictures that are linked to illness progression. Based on the types of visual qualities they collect, these showcases are divided into four classifications: intensity, structure, texture/gradient, and wavelet. Much research has been done to indicate a link between these characteristics and a nodule's malignant potential on a chest CT. These nodules have characteristics that be able to be linked to a cancer patient's prognosis and mutation condition.

Radiomics is the process of extracting sub-visual but quantitative picture attributes from radiological images to create searchable databases (Lambin *et al.*, 2012). Tumour descriptions derived from radiological data, for instance, CT and MRI scans, can be utilised in oncology to unveil diagnostic, predictive, and prognostic correlations in cancer patients by linking them to objective response measures like survival or treatment response (Wilson & Devarage, 2017). Nodule volume, intensity patterns, nodule shape, and a variety of "texture" factors are frequently pursued for extraction and assessment in this environment. The picture analysis is fully automated, and these elements are obtained automatically and at a high rate. The use of radiomics in lung cancer screenings has aroused a lot of interest, intending to improve sensitivity and specificity while lowering radiologists' workload. In precision medicine, radiomics is also utilised to forecast prognosis and therapeutic response in addition to diagnosis (Kumar *et al.*, 2012). Radiomics is a four-step process that involves converting radiographic pictures into data that can be mined: i) image collection and reconstruction, ii) region of interest segmentation, iii) feature extraction and quantification, iv) predictive and prognostic model development as seen in Figure 8. Radiomics has several advantages, one of which is that it should not substantially affect the clinical roadmap. Radiology technicians recreate pictures taken by a physician for diagnostic purposes into 2D or 3D images. Following that, the area of interest, such as the nodule, is segmented, and quantitative features are extracted and examined from this region.

Furthermore, Kumar *et al.* (2012) mention that segmentation can also be automated by measuring homogeneity with sudden variations in grey level (consequent to edges) and resemblance in grey level, albeit this may not be as accurate as manual segmentation. In contrast to something like 2D texture, segmentation is more important for assessing the structure of the nodule. It's also important to be able to distinguish between textural shapes within the nodule and the peri-nodular space and lung parenchyma. Quantitative elements may then be retrieved spontaneously and with high output from the region of interest, allowing machine learning-based models to be built. Radiomics analysis employs quantitative features, which are techniques that can be employed to illustrate regions within a radiologic picture. There are several techniques for this objective, however, the most prevalent radiomic features are now classified as intensity-based, structural, texture/ gradient-based, and wavelet-based.

After all the characters have been retrieved, a variety of numerical models are frequently employed to select a subset of top showcases that connect with the hypothesis-driven result (Parmar *et al.*, 2017). The use of top-ranking characteristics minimises the problem's dimensionality and enhances prediction accuracy. Feature selection can be accomplished using either univariate or multivariate statistical models. Multivariate approaches look into interactions between multiple features and choose the best ones by balancing association and redundancy. Multivariate methods examine relations within various characteristics and pick them after assessing both association and redundancy. Univariate methods simply rely on characteristic association and ignore redundancy. Among other statistical models, the Chi-squared test, Fisher score, and Wilcoxon are frequently employed for feature assortment.

Regardless of the lack of uniformity between groups, the data advocating the utility of radiomics in lung cancer diagnosis is plentiful and encouraging, signalling that computer-assisted diagnosis and management will play a role in clinical oncology in the future.

C. Liquid Biopsy

The use of liquid biopsies (LB) is the third imaging approach. LB is a new approach for detecting lung cancer that employs circulating tumour DNA (ctDNA) in the blood (Liang *et al.*, 2018). Whole blood, serum, saliva, pleural fluid, peritoneal fluid, tears, amniotic fluid, breast milk, bronchial lavage, plasma, sputum, urine, colostrum, and cerebrospinal fluid are examples of liquid specimens that are not tissue, which indicates the liquid biopsy. It is a minimally invasive approach that improves patient compliance and is commonly regarded as non-invasive and useful in molecular diagnostics. Liang *et al.* (2018) further explain that liquid biopsy, which involves taking a monotonous blood sample and extracting tumour-related evidence from the blood using several practices, has the potential to overcome the boundaries of outdated tissue-derived biomaterials gained through surgery or needle biopsy, and to become a common experimental practice in the recognition of early lung cancer, through the following substantial advantages: The procedure is non-invasive, objectively accessible, and repeatable.

Various distributing cancer biomarkers are currently accessible for liquid biopsy (Kqueen, 2016). The two primary forms of biomarkers detected in liquid biopsies are cell-free DNA (cfDNA), also known as circulating tumour DNA (ctDNA), and the other one is circulating tumour cells (CTCs). Circulatory tumour cells (CTCs) are tiny DNA fragments released into the bloodstream by tumours and are 100 times more prevalent than ctDNA. Cell-free DNA fragments dropped into the bloodstream by tumour cells during necrosis, apoptosis, or active secretion events are known as ctDNA. It is tumour-specific and delivers molecular hints regarding tumour cells' shattered DNAs and mutations.

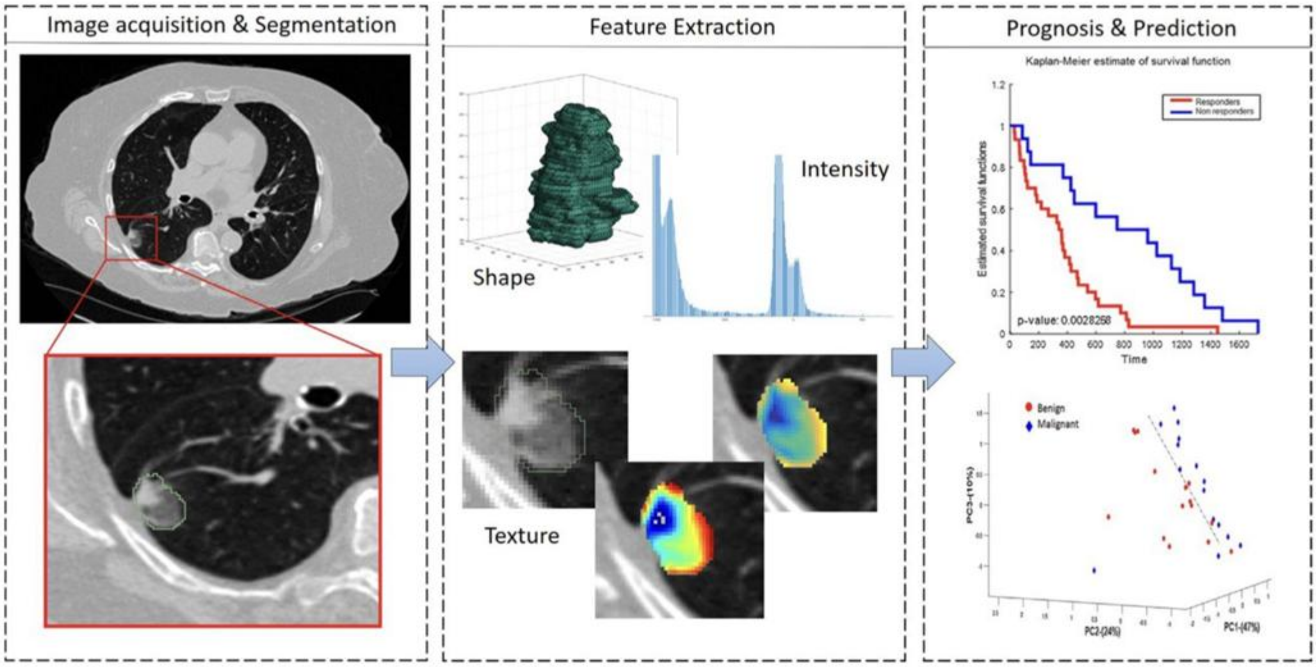


Figure 8. Overview of typical Radiomic Workflow (Kumar *et al.*, 2012).

Furthermore, CTCs are cancer cells that float in the bloodstream after being shed from initial tumours sites and/or metastatic locations. They can be extracted as single cells or bunches. After detaching from epithelial sheets, these cancer cells frequently experience epithelial-mesenchymal transition (EMT) and turn out to be intrusive and motile. They enter the bloodstream by conquering the vessel walls to which they ordinarily attach, becoming CTCs, and then invading and proliferating at distant places. However, their low blood concentrations (1-10 CTCs per 10 mL) and efficiency of cancer-specific surface markers (particularly after EMT) result in a small early detection rate, offering severe problems in CTC identification in early diagnosis. Consistent with the National Cancer Institute, a biomarker is a biological molecule present in the blood, other body fluids, or tissues that is an indicator of a normal or aberrant procedure, or a medical illness (Henry & Hayes, 2012). Diagnostics, prognostics, therapies, and theragnostic all benefit from biomarkers. Because false positives are scarcer with ctDNA and because it has a half-life of fewer than two hours, it provides a sharper picture of a tumour's present rather than its past. The above-mentioned liquid biopsy-based biomarkers provide a wealth of genetic, proteomic, and other information about tumour growth. Because lung cancer is a very dissimilar malignancy in conditions of genesis and progression, single-type detection of these indicators is restricted due to the low analysis of all types of lung cancer. To increase the sensitivity and specificity of lung cancer diagnosis, the constraints are expected to be solved by blending multiple markers along with reasonably great recognition efficiency. Liquid biopsy's immediate clinical applications for initial lung cancer include disease secondary analysis and screening.

To begin, once a shady lesion was discovered via CT scan, the qualities of the lesion might be validated through liquid biopsy (Veronesi *et al.*, 2016). Most research currently focuses on the importance of liquid biopsy as an auxiliary diagnostic implement to increase CT scan efficacy due to cost, but the rapid advancement of artificial intelligence in medical care may quickly blur such requirements.

Second, and perhaps most importantly, liquid biopsy is being developed to replace CT scan as an innovative lung cancer diagnosis method, because biomarkers are noticeable for the identification of early-stage lung cancer and exist early enough in the circulation, even before aberrant pictures arise. Thus, liquid biopsy can produce useful data on cancer genetic traits in real-time due to a large range of interesting biomarkers.

D. Microwave Imaging

Microwave Imaging is the next advanced technique approach for the recognition of lung cancer. Microwave imaging is defined as observing an object's internal structure using electromagnetic fields at microwave frequencies ranging from 0.3 to 30 GHz (Babarinde *et al.*, 2014). Microwave imaging techniques can give a diagnostic imaging system with significant cost savings in terms of operation and procurement, speed of image generation, sensitivity, and specificity to distinguish tumour types and non-exposure to ionising radiation among others. An antenna array for sending signals, a microwave source, a receiver, and a radio frequency switch to switch between separate antenna elements of the antenna array are also included in the microwave imaging equipment. Moreover, microwave imaging techniques are allocated into three categories: active, passive, and hybrid (Abdul, 2012). In active microwave imaging, a system of antennas transmits low-power microwave signals into the tissue, which are then backscattered or transmitted across the imaged tissue to generate an image. Microwave tomography, holography, and ultra-wideband (UWB) pulsed radar imaging techniques are examples of active microwave imaging.

Cancerous tissues are more vigorous and produce more warmth than normal tissue in the host. Furthermore, malignant tissues lose their thermoregulatory capacity, and the passive microwave imaging approach uses this temperature contrast to generate its image. In Microwave Imaging, the temperature variations between malignant and normal tissue are used to provide passive imaging. The method employs a radiometer, and the procedure is known as radiometry (Babarinde *et al.*, 2014). When microwaves are used to heat tissues, especially those with malignancies, pressure waves are created when the heated tissues expand. Ultrasound transducers detect these pressure waves, and it has been discovered that tumour tissues store more energy than normal tissues, resulting in more pressure waves from tumour tissues that can be separated from normal tissues and processed to form an image (Nikolova, 2012). This process forms the origin of hybrid microwave imaging techniques. Microwave-induced ultrasound imaging, thermo-acoustic tomography, and microwave elastography are examples of hybrid microwave imaging techniques. Figure 9 shows an example of a microwave system for determining sample tissue (tumour).

Microwave imaging can identify the lung cancer because malignant tissues have different dielectric characteristics than normal tissues at microwave frequencies (Lazebnik *et al.*, 2007). Relative permittivity and conductivity are used to describe the dielectric characteristics of different tissues. The interchange of EM signals will alter for different tissues due to the differences between normal and malignant tissues as a result, tumour detection is accomplished using a microwave imaging technique that compares the dielectric properties of regular and malignant tissues. The determination of dielectric characteristics of normal and malignant lung tissues, which influence microwave signal propagation, is an important part of microwave imaging technology (Muhammad *et al.,* 2020). Conductivity and permittivity are used to describe the various dielectric properties. In general, conductivity relates to the electron's free route length and speed inside the substance. Permittivity, on the other hand, is linked to the molecule's dipole moment per volume.

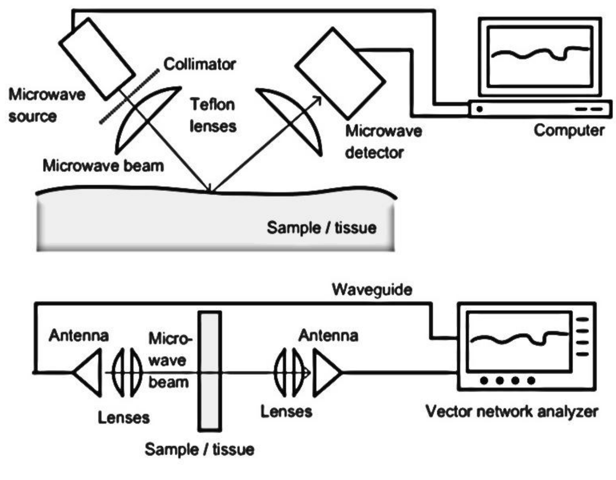


Figure 9. Microwave system for determining sample tissue of tumour (Topfer & Oberhammer, 2017).

Muhammad *et al* (2020) further state that the significant dielectric characteristics difference among malignant and normal tissues at microwave frequencies is the basis for microwave imaging. Due to changes in electrical characteristics, microwaves traveling across the chest tend to disperse. The sensed energy will change at the receivers and transmitters. The images are then produced utilising the details of detected energy as seen in Figure 10.

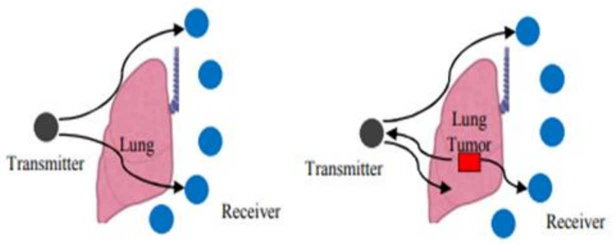


Figure 10. Signal broadcast of lung cancer detection (Alwan *et al.,* 2014).

This suggests tomography and Ultra-Wide Band (UWB) radar imaging as two diagnosis imaging methodologies in microwave imaging screening. The transmitter and recipient antennas will be positioned around the item being studied in microwave tomography. Each antenna that served as a transmitter and receiver in the quantification approach generates combination antennas (Alwan *et al*., 2014). The system reconstructs the image using UWB radar imaging from mirrored waves of the bodies. The reflection that occurs because of changes in the dielectric characteristics of healthy and malignant tissues is utilised. This approach offers various advantages, including the ability to measure backscattered signals and avoid the inverse scattering problem.

VI. CONCLUSION

In conclusion, Malaysia should take bold steps to advance cancer detection technologies, particularly for early-stage lung cancer screening. While current methods have limitations, these can be addressed through continuous technological innovation. In resource-limited settings, challenges to effective cancer care can be overcome through practical, evidence-based strategies tailored to local conditions. The World Health Organization emphasises the importance of adapting clinical guidelines to each region's resources. By optimising existing infrastructure, training healthcare workers, and improving public awareness, countries can enhance access to diagnostic tools and implement better cancer staging practices.

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