



## Research Paper

# Validity of Computed Tomography in Differentiating Malignant and Benign Lung Lesions

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### Abstract

**Background:** *In the present world, the most common cause of cancer associated death is lung cancer, among both males and females.<sup>1</sup> Computed tomography gives a sharper anatomic and morphologic description of the lung lesion as opposed to plain radiography. Features of benign and malignant lesions are said to be better differentiated using computed tomography.<sup>2</sup> Considering the absence of standardized guidelines for reporting lung lesions, a study to find the validity of computed tomography in differentiating the malignant and benign nature of a pulmonary lesion would be appropriate in this setting.*

**Aim:** *To find the sensitivity and specificity of Computed Tomography in differentiating malignant and benign lung lesions as opposed to its histopathological diagnosis.*

**Materials and Methods:** *Patients sent to the Department of Radiodiagnosis, for imaging and CT guided lung biopsy are chosen for the study. The CECT images of the patient are studied and a radiological diagnosis is made based on the findings. The histopathological report will be correlated with the radiological diagnosis on terms of benign and malignant nature of the lesion. The duration of study is 18 months from January 2018 onwards and the CT equipment used for the study is GE Healthcare Optima CT660 128 slice.*

**Result:** *In this study we have evaluated the sensitivity (83.3%) and specificity (50%) of Computed tomography in differentiating benign and malignant lesions. Overall diagnostic accuracy was determined to be 75%.*

**Conclusion:** *In conclusion computed tomography is useful in differentiation of benign and malignant lung lesions. The differentiation of benign from malignant lung lesions is of great value because the therapeutic approach is different for both entities.*

**Keywords:** *CT, Computed tomography, Thorax, Biopsy.*

### Introduction

In the present world scenario, the most common cause of cancer associated death is lung cancer, among both males and females, of which the most prevalent subtype of lung cancer is the

adenocarcinoma variety.<sup>1</sup> The situation in India is quite similar, with lung cancer being the most common cancer, and also being the most common cause for cancer related deaths.

A proportion of lung tumors present in the form of pulmonary nodules, more commonly as solitary nodules which are usually < 3cm in diameter and rounded. These are quite often missed on radiography and picked up on Computed Tomography (CT) scans.<sup>3,4</sup> Computed tomography gives a sharper anatomic and morphologic description of the lung lesion as opposed to plain radiography. Features of benign and malignant lesions are said to be better differentiated using computed tomography.<sup>2</sup> Reporting of nature of thoracic lesions does not follow any specific guidelines as in case of BIRADS and TIRADS, making the process difficult and thereby many discrepancies can occur when the radiological and post biopsy pathological correlation is being done.<sup>5</sup>

Nearly 94% of patients present with symptoms from the effects of the primary tumor, regional spread, or metastatic disease.

Local effects of the primary tumor account for around 27% of presenting symptoms and vary depending on the location of the tumor. Central tumors are seen to be associated with cough, hemoptysis, dyspnea, chest pain, and pneumonia. Peripheral tumors can however, cause cough, chest wall pain, pleural effusions, lung abscess, Horner's syndrome.

Symptoms due to regional spread include hoarseness of voice from recurrent laryngeal nerve palsy, dyspnea due to phrenic nerve palsy, dysphagia from compression of the esophagus, superior vena cava syndrome from compression or invasion of the superior vena cava, and pericardial tamponade from invasion of the pericardium.

Metastatic disease may present with symptoms of systemic illness (weight loss, loss of appetite, weakness, and malaise) or local manifestations of distant metastases (jaundice, abdominal mass, bony pain or fracture, neurologic deficits, mental status changes, seizures, and soft tissue masses).<sup>6,7,8</sup>

#### **Common Malignant Lesions of Lung are**

**Adenocarcinoma**<sup>9,10,11,12</sup> Adenocarcinomas are around 31% of all lung carcinomas. They are

usually located peripherally and are smaller than 4cm in diameter. Very few of them show cavitation. Half of them show lymphnodal involvement in the hilum and the mediastinum. They show two characteristic appearances on CT, localized ground glass opacity or solid mass type. Adenocarcinomas can be associated with concomitant lung disease like fibrosis, both diffuse or focal and is known to metastasize early. It is also called scar carcinoma as it can develop from pre existing scar tissues.

**Bronchoalveolar Carcinoma (BAC)**<sup>9,10</sup> 3-7% of all primary pulmonary carcinomas. They can present in solitary pulmonary nodule, dense consolidation or as a localized area of parenchymal consolidation. Bronchoalveolar carcinomas have a characteristic bubble like low attenuation areas within the mass. Lymph nodal involvement is relatively lesser.<sup>11</sup>

**Adenosquamous Carcinoma:** usually presents as a solitary nodule seen in the peripheral region.

**Squamous Cell Carcinoma (SCC)**<sup>8,9,10</sup> 30% of all pulmonary carcinomas, having the best prognosis among all lung malignancies. These carcinomas have a known strong association with smoking. They are usually centrally located and are usually more than 4 cm in size and commonly cavitate. They are also associated with presence of amorphous, punctate calcification within the lesion. There can be invasion of the adjacent recurrent laryngeal nerve.<sup>11</sup>

**Carcinoid Tumour:** This category consists of just 1% of lung cancers. There can be typical and atypical carcinoids. Atypical carcinoids are usually larger and typical carcinoids are more endobronchial in location. Carcinoids in general are central in location and usually contain calcification.

**Large Cell Carcinoma:** This group represents around 10% of lung cancers and is also called giant cell carcinoma. It is a poorly differentiated variety of non-small cell carcinomas. It is known to grow rapidly into a large mass. Usual metastasis is to brain and mediastinum<sup>11</sup>

**Small Cell Lung Carcinoma:** This represents around 20% of all pulmonary malignancies. The characteristic appearance of small cell lung carcinoma is bulky hila along with enlarged mediastinal lymph nodal masses. In around 40% of cases there can be a parenchymal lesion as well. A mass adjacent to the hilum or involving the hilum is highly suspicious for small cell lung carcinoma.<sup>12,13</sup>

#### **Few Benign Lesions of Lung**

**Pneumocytomas** also called Sclerosing Hemangiomas are rare benign tumours that are seen in middle aged women. They demonstrate low density areas, with calcification. Usually these lesions present as smoothly margined homogenously, well enhancing round or oval solid mass<sup>14</sup>

**Inflammatory myofibroblastic tumors:** Most commonly seen within the lung, however they can also appear endobronchially or endotracheally. It is seen as a lobulated mass on CT, however it can also present as consolidation or with spiculations and can mimic lung cancer.<sup>15</sup>

**Tuberculomas** are well defined round or oval focus of parenchymal tuberculosis. Sometimes calcifications and satellite nodules can be seen. They can be seen showing a variable contrast enhancement pattern, and most of them show a central non enhancing necrotic area with ring enhancement of the granulomatous inflammatory tissue in the outer zone. They can also appear as smooth margined round nodules.<sup>42</sup>

**Histoplasmoma** is another pulmonary lesion that merits discussion. It is usually seen as a sharply defined nodule with presence of central or diffuse calcification. There can also be shaggy or irregular edges at times, causing it to mimic lung cancer.<sup>17,18</sup>

**Lung abscess,** usually caused by anaerobic bacteria like Klebsiella and Pseudomonas. On CT it can be seen as single or multiple lung masses or nodules. These can be cavitary lesions as well, which can occur within consolidatory areas.<sup>16,17</sup>

#### **Materials and Methods**

**Study Design:** Observational cross-sectional study.

**Study Setting:** Department of Radio diagnosis – Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala.

**Duration of Study:** From January 2018 to June 2019.

**Sample Size:** Assuming sensitivity of 94% and specificity of 33.3% from previous study, Type 1 error  $\alpha$  as 5% and desired precision as 10%, the sample size is calculated as 48.

The formula used is  $n = (Z\alpha)^2 \times P ( 1-P ) / d^2$   
Where  $n = (a+c)/\text{prevalence}$ , if we consider sensitivity and  $n = (b+d)/ 1- \text{prevalence}$ , if we consider specificity.

**Sampling Technique:** Non probability consecutive sampling.

**Inclusion Criteria:** Patients referred to Department of Radiodiagnosis, PIMS to undergo CT Guided Lung biopsy after initial CT scan of thorax, who have given consent for their results to be used for study.

**Exclusion Criteria:** .1.Patients who have had previous lung resection/ who have hydatid/cystic disease/coagulopathies/pulmonary arterial hypertension/respiratory failure, patients on anticoagulants / mechanical ventilation and seropositive patients.

2.Inability of the patient to cooperate in the study.

**Equipment:** The CT equipment used at the institute is GE Healthcare Optima CT660 128 slice.

#### **Procedure Done**

Consent will be obtained from the patient who is referred to the department for biopsy for permission to use their results for the study. The Contrast enhanced CT (CECT) images will be reviewed and the plain CT of the area concerned will be taken as part of routine procedure before biopsy. The lesion characteristics are noted from the CECT image for the purpose of study as well as for choosing the needle path. A straight pathway is generally chosen, with the needle crossing the pleura perpendicularly optimally.

Sedation and IV analgesics are usually not warranted for, however local anesthetics are used. Local anesthetic is given, deep into the intercostal muscles. Low dose CT screening will be done throughout the procedure to make sure the trocar is in proper position. The slice thickness will depend on the size of the lesion. The needle entry point is marked on the patient's skin. 16 gauge introducer needle is used with coaxial technique. The automatic cutting needle is chosen at a size 18G which fits into the introducer needle.

Once the tip is in position, the needle is fired and the tissue sample is obtained. This is done during suspended respiration. Post biopsy scanning is done to check for possible complications that may arise due to biopsy being done.

The patients are monitored post procedure by routine for 6 hrs in the emergency department.

#### Method of Data Entry and Statistical Analysis

All data will be documented in spreadsheet and analyzed and presented as sensitivity and specificity of CT in differentiating malignant and benign lung lesions. The association of lesional and technical factors, with the occurrence of complications during biopsy will be assessed using Chi Square or Fischer's exact test. Logistic regression of all these factors and their association.

Significant figures;

- Suggestive significance (P value:  $0.05 < P < 0.10$ )
- Moderately significant (P value:  $0.01 < P$  less than or equal to  $0.05$ )
- Strongly significant (P value: P less than or equal to  $0.01$ ).

#### Statistical Tests Used

Categorical and quantitative variables were expressed as frequency (percentage) and mean  $\pm$  SD respectively. Chi square test was used to find association of Pneumothorax and Hemorrhage with selected variables. Diagnostic statistics such as Sensitivity, Specificity, PPV, NPV and accuracy were used to find the predictive power

CT in detecting malignancy when Histopathology is gold standard.  $p < 0.05$  was considered the threshold for statistical significance. Statistical analyses was performed by using a statistical software package SPSS, version 20.0.

#### Results and Analysis

- 48 patients are included in the study and they had 48 lesions in total.
- 12 cases were benign lesions, and the rest of 36 cases were malignant lesions based on CT findings.
- 7 lesions had smooth margins, 32 had speculated margins, 3 had ill-defined margins and the rest had well defined margins.
- 26 of the cases had bronchus cut off and 9 of the cases had pleural effusion.
- 10 cases had cavitation within the lesion, while 14 cases had air bronchograms within.
- 32 cases had enlarged mediastinal lymphnodes and 22 cases had necrotic areas within.
- 25 of the lesions assessed were less than or equal to 5 cm in size on maximum dimension and 23 of the lesions were above 5 cm in size in maximum dimension.
- 25 of the cases were at a depth of less than 2 cm from the chest wall, while 23 cases were more than or equal to 2 cm in depth, from the chest wall.
- Among the histopathological diagnoses, 8 cases came as adenocarcinoma of lung, 6 came as small cell carcinoma, 11 came as squamous cell carcinoma, 3 came as mucinous adenocarcinoma, 3 came as non-small cell carcinoma, 2 came as organizing pneumonia, Ig G4 related disease and pure benign cells each.
- There were single proven cases of thyroid neoplasm extending to the lung field, thymoma, soft tissue sarcoma, solitary fibrous tumour, pleomorphic carcinoma, neurofibroma, lymphoma, fibrinous pneumonia, aspergillosis and acinar adenocarcinoma. There was also a case which

was given as inconclusive diagnosis, with malignant cells within, which was categorized as malignant however.

- There were smooth margins in 7 cases, of which 4 turned out to be benign and 3 turned out to be malignant.
- Spiculated margins were noted in 32 cases, of which 27 came as malignant and 5 came as benign.
- 3 of the lesions had ill-defined margins, of which 2 of them came as benign and 1 was malignant.
- 6 lesions had well defined margins, of which 5 were proven to be malignant and 1 was benign.
- 26 of the lesions demonstrated bronchus cut off, of which 23 of them came as malignant and 3 lesions were proven as benign.
- 9 cases had pleural effusion, of which 6 were proven to be malignant and the remaining 3 were benign.
- There were 10 cases with cavitation / calcification within, of which 7 came as malignant and 3 benign.
- Air bronchograms were present in 14 of the cases, of which 5 turned out to be benign and 9 turned out to be malignant.
- Enlarged mediastinal lymphnodes were present in 32 of the cases, of which 27 were proven to be malignant cases and the rest 5 were proven to be benign cases.
- Metastatic lesions were reported in 11 cases, of which 9 cases were proven malignant, while 2 cases were proven to be benign however.
- Necrosis was reported in the lesion in 22 of the cases, of which 16 cases turned out to be malignant and 6 cases were proven benign.
- There were 16 cases with homogenous attenuation, of which 13 cases were proven to be malignant, and 3 cases were proven as benign. The remaining 32 cases of the study had heterogenous attenuation of which 23 cases were proven malignant and 9 cases were proven benign.

- In our study 36 lesions were given as malignant lesions, based on CT scan study, of which 30 of them were proven as malignant by histopathology and 6 of them were proven as benign lesion.
- Of the 12 lesions given as benign on CT scan, 6 of them were proven to be malignant, while 6 of them were proven as benign on histopathology.
- There was a sensitivity of 83.3 in the diagnostic accuracy of CT in differentiating malignant and benign lesions, and a specificity of 50.
- False negative value was 16.7 and false positive value was 50.
- Positive predictive value is 83.3 and negative predictive value is 50.
- Positive likelihood ratio was 1.7 and negative likelihood ratio was 0.3.
- Overall diagnostic accuracy was determined to be 75%.

**Table 1** Percentage distribution of the sample according to CT report

CT Diagnosis	Count	Percent
Benign Etiology	7	14.6
Malignant Etiology	18	37.5
Bronchogenic Carcinoma	14	29.2
Lung Abscess	2	4.2
Small cell carcinoma	1	2.1
Lymphoma	1	2.1
Post Radiation changes	1	2.1
Pancoast Tumour	1	2.1
Necrotising Pneumonia	1	2.1
Bronchocele	1	2.1
BAC	1	2.1

**Table 2** Percentage distribution of the sample according to Benign / Malignant based on CT Report

Benign / Malignant	Count	Percent
Benign	12	25.0
Malignant	36	75.0



**Table 3** Percentage distribution of the sample according to Margins

Margins	Count	Percent
Smooth	7	14.6
Spiculated	32	66.7
Ill defined	3	6.3
Well defined	6	12.5

**Table 4** Percentage distribution of the sample according to selected variables

Variable	Count	Percent
Bronchus Cutoff	26	54.2
Pleural Effusion	9	18.8
Cavitation / Calcification	10	20.8
Air bronchogram	14	29.2
Nodes	32	66.7
Mets	11	22.9
Necrosis	22	45.8

**Table 5** Percentage distribution of the sample according to attenuation

Attenuation	Count	Percent
Homogenous	16	33.3
Heterogenous	32	66.7

**Table 6** Percentage distribution of the sample according to histopathology report

Pathology report	Count	Percent
Adenocarcinoma	8	16.7
Small cell carcinoma	6	12.5
Squamous Cell carcinoma	11	22.9
Mucinous adenocarcinoma	3	6.3
Non Small cell carcinoma	3	6.3
Organizing pneumonia	2	4.2
IgG4 related disease	2	4.2
Benign changes	2	4.2
Thyroid neoplasm	1	2.1
Thymoma	1	2.1
Soft tissue sarcoma	1	2.1
SFT	1	2.1
Pleimorphic Carcinoma	1	2.1
Neurofibroma	1	2.1
Lymphoma	1	2.1
Inconclusive, with no benign cells	1	2.1
Fibrinous Pneumonia	1	2.1
Aspergillosis	1	2.1
Acinar Carcinoma	1	2.1

**Table 7** Percentage distribution of the sample according to Benign/ Malignant based on Histopathology

Benign / Malignant	Count	Percent
Benign	12	25.0
Malignant	36	75.0

**Table 8** Diagnostic accuracy of differentiating malignant and benign lung lesions as opposed to its histopathological diagnosis

CT Diagnosis	Histopathology Diagnosis		
	Malignant	Benign	Total
Malignant	30	6	36
Benign	6	6	12
Total	36	12	48

Sensitivity	83.3
Specificity	50.0
False Negative	16.7
False positive	50.0
Positive Predictive value	83.3
Negative Predictive value	50.0
Positive Likelihood ratio	1.7
Negative Likelihood ratio	0.3
Accuracy	75.0

**Discussion**

Our study confirms the previous reports suggesting that CT imaging is indeed helpful in differentiating benign and malignant lung lesions as opposed to their histopathological biopsy report. 48 patients were included in the study and they had a total of 48 lesions, with one patient having bilateral lesions. Final diagnosis was made with the help of histopathology.

There was a sensitivity of 83.3 % in the diagnostic accuracy of CT in differentiating malignant and benign lesions, and a specificity of 50%. False negative value was 16.7% and false positive value was 50%.

Positive predictive value is 83.3% and negative predictive value is 50%. Positive likelihood ratio was 1.7 and negative likelihood ratio was 0.3.

Overall diagnostic accuracy was determined to be 75%.

The value of reassuring a patient that a lesion detected on CT scan is benign or probably of an infective etiology, cannot be underestimated, as the patients are also avoided unnecessary surgery and follow up imaging and anxiety. The positive accuracy of CT scan in differentiating malignant and benign lesions is useful for clinicians as well as they can plan further management and appropriate treatment can be initiated at the earliest. Referrals to higher centres can be

arranged based on the scenario, in case a lesion is reported as malignant and aggressive.

Our study has thereby echoed the previous study done by Zhang C et al, in proving that Computed tomography indeed has good sensitivity in differentiating malignant and benign lung lesions, however there was a disparity in the specificity obtained in this study as compared to previous studies. We obtained a specificity of 50% which is lower than the specificity obtained in the study by Zhang C et al, which was 70%.<sup>19</sup>

The study done in 2007 by Kim SK et al<sup>2</sup> had found a sensitivity of 93% and a specificity of only 31%. The sensitivity we had obtained is comparable to that of done in previous studies.

A study done in 2016 by González-Pérez VCAD et al<sup>1</sup> had obtained that the most common malignancy in their study was adenocarcinoma (58.2%) followed by metastasis and squamous cell carcinoma. In our limited study of 48 patients, we had obtained 11 cases of squamous cell carcinoma which comprised 22.9% followed by adenocarcinoma (16.7%).

The most common benign etiology we had obtained is organizing pneumonia which comprised 2 cases which amounted to 4.2%.

84% of the proven malignant cases in this study had spiculated margins, and 5 malignant cases had well defined margins as well which amounted to 83.3% among the 6 cases with well-defined margins. Majority of the proven malignant cases had bronchus cut off and pleural effusion. Enlarged mediastinal nodes were also seen in 84.4% of the proven malignant cases among the 32 cases which had enlarged lymphnodes.

The pretreatment determination of the location, size, nature of the lesion and approachability for biopsy is becoming increasingly important as the treatment options for lung masses are more sophisticated and more patient specific.

### Conclusion

- In this study we have evaluated the sensitivity (83.3%) and specificity (50%) of Computed tomography in differentiating benign and

malignant lesions. False negative value was 16.7 and false positive value was 50.

- PPV is 83.3 and NPV is 50. Positive likelihood ratio was 1.7 and negative likelihood ratio was 0.3.
- Overall diagnostic accuracy was determined to be 75 %.
- In conclusion Computed tomography is useful in differentiation of benign and malignant lung lesions.
- The differentiation of benign from malignant lung lesions is of great value because the therapeutic approach is different for both entities.

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