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Research Article

ROLE OF MRI IN DIAGNOSING AND TNM STAGING OF LUNG CANCER SPECIALLY STAGE 3 AND STAGE 4

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A B S T R A C T

Aim: Lung cancer is increasing at an alarming rate in India. Although smoking is concerned as the primary cause but non smokers too have been found to be affected by it and besides this it is prevalent in both the sexes. The aim of present study was to determine the clinical utility of MRI thorax in TNM staging and detection of lung Cancer specially stage 3 and stage 4.

Materials and methods: the study was conducted on the patients approaching the Radiology Department of AJ Institute of Medical Sciences, Bangalore in a period of two years from January 1, 2015 to December 31, 2017.The study included 30 participants (N= 30)which were known cases of lung cancer (established and Suspected) referred for MRI. Out of 30 participants 18 were males (60%, N=30) and 12 were females (40%, N=30). (MRI of the Lungs was performed using Siemens Avanto MR Machine and images were analyzed by experts

Results: the efficacy of CT and MRI was evaluated in the assessment of TNM staging in patients with small cell carcinoma. The result showed that CT scan was able to detect more stages of lung cancer than MRI. However, stage IIIB showed an increased diagnosis in MRI whereas the level of diagnosis of stage IIIA and IVA remains identical in both the imaging modalities.

Conclusion: CT and MRI diagnosis gives almost similar data for adenocarcinoma while in small cell carcinoma, CT scan gives more detailed picture of carcinoma with peaks at additional stages.

INTRODUCTION

Lung cancer is increasing at an alarming rate in India. Although smoking is concerned as the primary cause but non smokers too have been found to be affected by it and besides this it is prevalent in both the sexes.

Lung carcinoma is a malignant lung tumor typified by uncontrolled cell division in the lung tissues leading to metastasis. [1] Such uncontrolled transformation is due to genetic blueprint where the DNA gets altered and mutated. SCLC is highly malignant tumor derived from cells exhibiting neuroendocrine features. NSCLC is further divided into adenocarcinoma, Squamous cell carcinoma, and large cell carcinoma.[2] Tobacco smoking, both cigarettes and beedis, is the prime risk factor contributing to lung carcinoma in Indian population. Past decade has shown an alarming rise of about 15% in the lung carcinoma cases. [3] Indian youngsters are an easy prey to lung carcinoma then the western countries. Late diagnosis is the major reason of mortality.

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Improved and advanced imaging techniques have led to more accurate staging.

Computed tomography or CT scan gives more detailed and accurate three-dimensional imaging and analysis of the extremely minute tumors. A more recent advancement in the diagnosis is Magnetic Resonance Imaging {MRI} which is ideally suited to evaluate tumor extent and nodal disease. It is more sensitive scan utilized to check the tumor extent and nodal disease. [4]

Compared with CT, the relatively low signal in the lung limits the detection of pulmonary nodules and other lung parenchymal diseases, and noise due to motion has been a frequent and significant problem in thoracic MRI. Because of its superior spatial resolution and ability to detect calcification, CT is better than MRI for the detection and evaluation of lung nodules and mediastinal adenopathy when assessing lung cancer. For the detection of mediastinal invasion or lymph node metastases, CT and MRI generally provide similar information. However, volume averaging problems, which may occur on trasaxial CT, can be avoided or clarified using MRI, and nodes can sometimes be more clearly distinguished from vessels using this technique. If MRI is used selectively as

a secondary imaging study to answer specific questions raised or unanswered by CT, its value can be optimized.

MATERIALS AND METHODS

A prospective study was designed to analyze the role of MRI in diagnosing and TNM staging of Lung cancer specially stage 3 and stage 4 on the patients approaching the Radiology Department of AJ Institute of Medical Sciences, Bangalore in a period of two years from January 1, 2015 to December 31, 2017.The study included 30 participants (N= 30) which were known cases of lung cancer (established and Suspected) referred for MRI. Out of 30 participants 18 were males (60%, N=30) and 12 were females (40%, N=30). (Chart: 1)

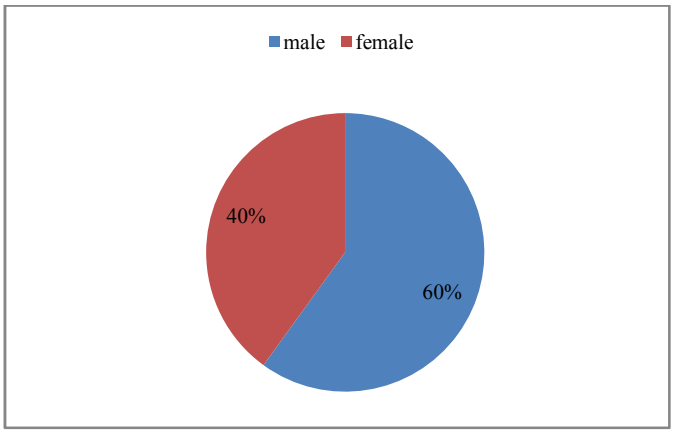

Chart 1 Proportion of participants in Study (N=30)

Inclusion criteria

Patients with established or suspected cases of Lung Cancer were included.

Exclusion criteria

1. Patients in whom MRI is contraindicated like Aneurysm clip, any metallic fragment or foreign body, Cardiac pacemaker, Implanted Cardioverter-defibrillator, Cochlear implants, Known cases of claustrophobia
2. Patients for whom intravenous contrast agents were contraindicated or CT was Inconclusive.
3. Restless, uncooperative patients.
4. Patients not willing to participate.

After obtaining the informed consent, the MRI scan of lungs were performed using Siemens Avanto MR Machine. All images were acquired using either one of two 1.5-T scanners (Sonata and Sonata Maestro, Siemens Medical Solutions, Erlangen, Germany). The standard protocols followed for lung examinations consisted of two components. The first involved a quick whole-lung survey with T2-weighted 2-dimensional half Fourier acquisition single shot turbo spin echo (2D HASTE), using the turbo spin echo technique with double inversion recovery black blood preparation electrocardiogram triggered in axial, coronal, and sagittal orientations with repetition time (TR) of one RR interval, echo time (TE) of 41 ms, flip angle of 160°, slice thickness of 6 mm and matrix of 172 × 256. The examination time was less than 3 minutes (Figure 1).

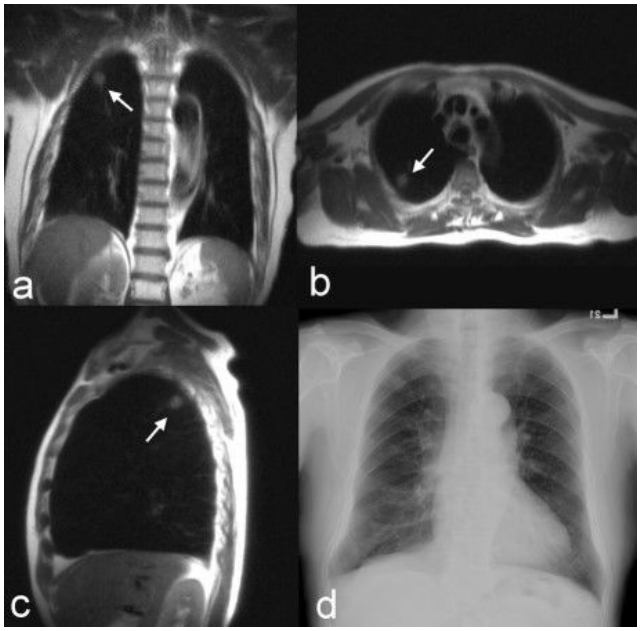

Fig 1 The HASTE images from MRI

(a) coronal, (b) axial, and (c) sagittal images showed an irregular consolidated mass about 1.2 cm in diameter at the posterior segment of the right upper lobe. Under black blood preparation, the lesion easily stood out from the clear background without the appearance of any vessels. (d) The findings from chest radiography were negative. The nodule was surgically proved to be squamous cell carcinoma, stage Ia. The second protocol component was performed with 3-dimensional axial image acquisition using the volumetric interpolated breath-hold examination (3D VIBE) technique with fat suppression, TR/TE of 4.9 ms/2.1 ms, flip angle of 12°, field of view (FOV) of 320-360 mm, matrix of 176 × 256, and slice thickness of 3 mm with 64 slices per breath hold. The duration time for this sequence was less than 3 minutes (Figure 2).

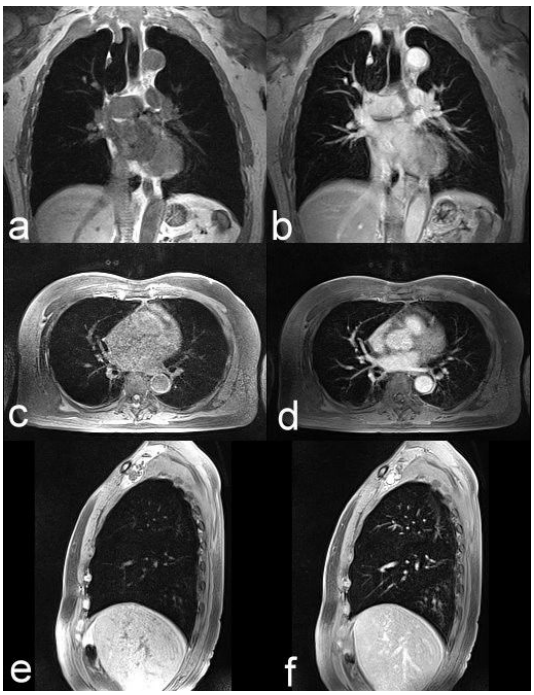

Fig 2 Comparison of VIBE images from MRI without and with the use of contrast.

The (a) noncontrasted coronal, (b) contrasted coronal, (c) noncontrasted axial, (d) contrasted axial, (e) noncontrasted sagittal, and (f) contrasted sagittal VIBE images can display clear branches of pulmonary vessels and bronchial tree with minimal pulsation artifacts in normal lung parenchyma.

For examinees who had additional contrasted MRI, HASTE was applied before contrast agent injection, and VIBE was applied after contrast agent injection using 0.5 mmol/kg of gadodiamide (Omniscan) at an injection rate of 3 mL/sec.

Image Analysis

All images were viewed by 1 of 5 experienced radiologists (HCC, JSK, YCC, PWL, WCL) and classified as well as defined all lesions as (1) normal or extrapulmonary abnormality: negative result in lungs or lesions in the extrapulmonary area, for instance, in the neck or abdomen, (2) lung abnormality of little clinical significance: pulmonary lesions rather than nodules, for instance, pleural thickening or fibrosis, (3) probable benignancy: lung nodules measuring ≤ 0.5 cm with well-defined border and visible only by VIBE and not by HASTE, (4) indeterminate nodules: lung nodules measuring ≤ 0.5 cm with mild irregular border and visible only by VIBE and not by HASTE, (5) possible malignancy: lung nodules measuring > 0.5 cm and <1 cm and visible only by VIBE and not by HASTE, (6) probable malignancy: lung nodules visible by both VIBE and HASTE; or lung nodules measuring ≥ 1 cm; or newly developed lung nodules at the second or more MRI examinations. The latter three were considered to be suspicious lung nodules. [5, 6]

Statistical analysis was accomplished using SPSS version 11.0 statistical software. Appropriate statistical tests were used wherever required.

RESULTS

Out of total 30 participants 14 were smokers and 16 were non smokers, with 46.7% and 53.3% respectively. Among the 30 participants there were no missing cases. Henceforth the valid percentage obtained is 46.7% and 53.3% for smokers and non smokers respectively. (Chart: 2)

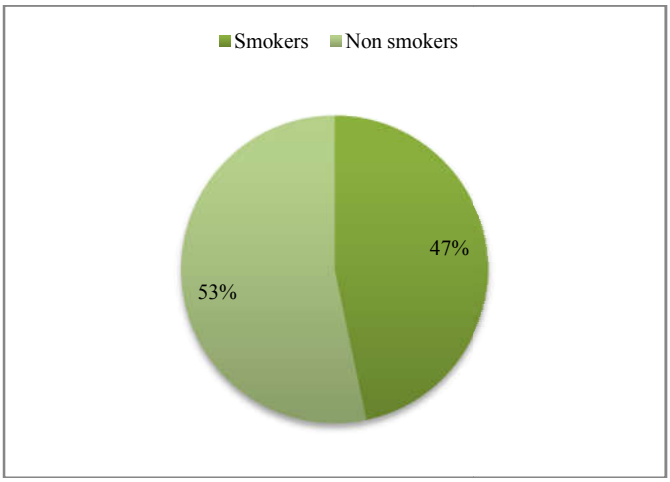

Chart 2 Proportion of smokers and non-smokers in Study (N=30)

Chart: 3 represent the comparative evaluation of TNM stage for adenocarcinoma by CT scan and MRI. The graph shows identical peaks for both MRI and CT scan diagnosis. At stage IVA of TNM showed increased visibility followed by stage IIIB and stage IIA of adenocarcinoma. Therefore, from the graph it is clear that diagnosing levels of adenocarcinoma at stage IVA, IIIB and stage IIA of TNM is identical and give similar data for both CT and MRI scan.

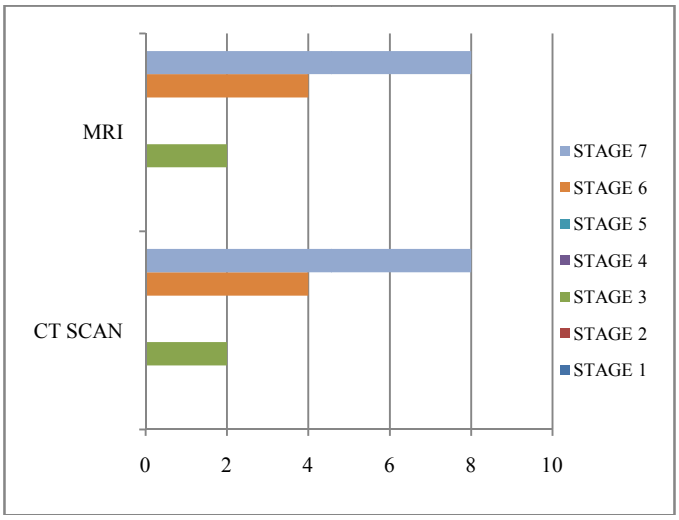

Chart 3 Graphical representation showing comparison of Diagnosis Given by CT Scan and MRI Based on TNM Staging for Adenocarcinoma

Chart: 4 represent the comparative diagnosis of CT scan and MRI in small cell carcinoma based on TNM stages. In MRI scan three stages/substages were detected, stages IVA, IIIB and IIIA respectively. Stage IVA and IIIB are almost identical followed by a decrease at stage IIIA. In CT scan five stages were observed, stage IVA, IIIB, IIIA, IIA and IA respectively. Stage IVA has shown increased diagnosis followed by IIIA stage. Stages IIIB, IIA and IA has shown identical peak in CT scan.

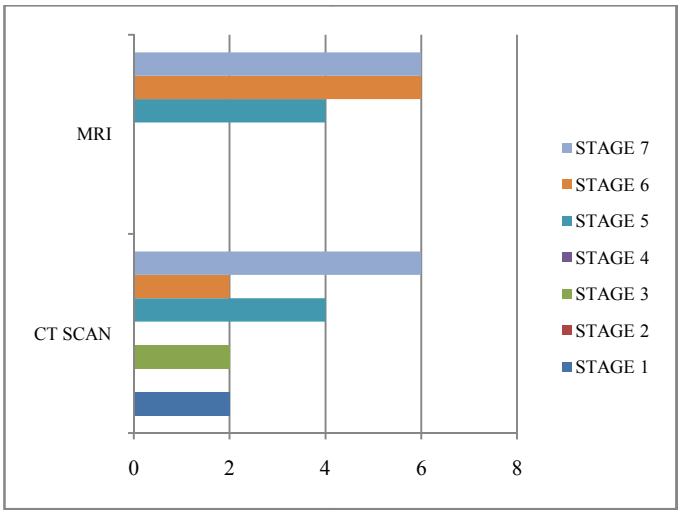

Chart 4 Graphical representation of comparison of diagnosis given by CT Scan and MRI Based on TNM Staging for Small Cell Carcinoma

Table: 1 illustrates case processing summary of biopsy stages performed by CT and MRI scan. Total 30 participants with history of carcinoma were selected for the study. Out of 30 participants there were no missing cases reported, hence, accomplishing the valid percentage to 100% for both CT and MRI stages.

Table 1 Case processing summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
BIOPSY * CT STAGES	30	100.0	0	0	30	100.0
BIOPSY * MRI STAGES	30	100.0	0	0	30	100.0

In table: 2 biopsy study was conducted on smokers and non smokers. Diagnosis of the separated mass was conducted on two categories. Biopsy 1 was performed on smokers with adenocarcinoma comprising of 14 participants; biopsy 2 performed on non smokers with small cell carcinoma comprising of 16 participants. Three parameters were considered in each category i.e. percentage within biopsy (examining isolated stained mass under microscope), percentage within CT stage and sum of both the diagnosis. Total four stages/substages of cancer was taken into account i.e. stage IA, stage IIA, stage IIIA, stage IIIB and stage IVA. Number of participants at each stage preferred was 0,2,0,4 and 8 respectively.

Table 2 Biopsy and CT stages

		CT Stages					Total
		1	3	5	6	7	
Biopsy1	Count	0	2	0	4	8	**14**
	% Within Biopsy	0.0%	14.3%	0.0%	28.6%	57.1%	**100.0**%
	% Within CT stages	0.0%	50.0%	0.0%	66.7%	57.1%	**46.7**%
	% Of Total	**0.0%**	**6.7%**	**0.0%**	**13.3%**	**26.7%**	**46.7**%
Biopsy 2	Count	2	2	4	2	6	**16**
	% Within Biopsy	12.5%	12.5%	25.0%	12.5%	37.5%	**100.0%**
	% Within CT stages	100.0%	50.0%	100.0%	33.3%	42.9%	**53.3%**
	% Of Total	**6.7%**	**6.7%**	**13.3%**	**6.7%**	**20.0%**	**53.3%**
Total	Count	2	4	4	6	14	**30**
	% Within Biopsy	6.7%	13.3%	13.3%	20.0%	46.7%	**100.0%**
	% Within CT stages	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
	% Of Total	**6.7%**	**13.3%**	**13.3%**	**20.0%**	**46.7%**	**100.0%**

In table: 3 the study was conducted on MRI diagnosis similar to that of CT scan with slight variations. Four stages/substages have been considered in MRI. Stage IIA, IIIA, IIIB and IVA. Number of Participants at each stage varied from that of CT scan as 3,5,6 and 7 respectively.

Table 3 Biopsy and MRI stages

		MRI Stages				Total
		3	5	6	7	
Biopsy1	Count	2	0	4	8	14
	% Within Biopsy	14.3%	0.0%	28.6%	57.1%	100.0%
	% Within MRI stages	100.0%	0.0%	40.0%	57.1%	46.7%
	% Of Total	6.7%	0.0%	13.3%	26.7%	46.7%
Biopsy 2	Count	0	4	6	6	16
	% Within Biopsy	0.0%	25.0%	37.5%	37.5%	100.0%
	% Within MRI stages	0.0%	100.0%	60.0%	42.9%	53.33%
	% Of Total	0.0%	13.3%	20.0%	20.0%	53.3%
Total	Count	2	4	10	14	30
	% Within Biopsy	6.7%	13.3%	33.3%	46.7%	100.0%
	% Within MRI stages	100.0%	100.0%	100.0%	100.0%	100.0%
	% Of Total	6.7%	13.3%	33.3%	46.7%	100.0%

However, to sum up the overall trend, the percentage diagnosis of adenocarcinoma and small cell carcinoma through CT and MRI scan is similar, with slight variations observed as follows; in CT scan 100% diagnosis was arrived at stage IA (with 2 non smoker participants) and stage IIIA (with 4 non smoker participants). In MRI scan 100% result obtained at stage IIA (with 2 smoker participants) and stage IIIA (with 4 non smoker participants).

DISCUSSION

In the developed countries lung cancer deaths are leading cancer related deaths for both men and women. Despite the tremendous effort in treating this dreadful disease the overall survival rate for this cancer is dismally low at 15%. [7] Till date, Computed Tomography (CT) scan of the chest was the cornerstone of lung cancer imaging based on which further management is decided. [8] Similar to other malignant diseases in lung cancer also, therapeutic options, as well as patients' prognoses strongly, depending on the proper tumor staging. [9] Thus, accurate tumor staging encompassing the entire body is of essential importance. Magnetic resonance imaging (MRI) is gaining more importance in tumor staging in comparison to CT because of its high spatial resolution and soft tissue contrast. Its advantages over computed tomography (CT) and other imaging procedures have been determined for detection of parenchymal and osseous lesions. [10, 11]

In this present study, we tried to evaluate the importance of MRI of the thorax in the detection of lung cancer in suspected lung cancer patients and also in TNM staging of the tumor.

Smoking and lung cancer

Quantitative association between smoking and lung cancer is well established by numerous epidemiological studies. The assessment of trends in smoking-related mortality for 50 years revealed that death from lung cancer among male smokers was about 12 times higher than that in non-smokers. The absolute mortality from lung carcinoma was found to be higher in men than women throughout the study period and was independent of smoking status. [12] A systematic review and meta-analysis of 287 studies by ***Lee P N et. al.*** revealed a strong association of smoking to lung cancer. The risk is strongly associated with factors such as the amount of tobacco smoked, duration of smoking, earlier starting age, tar level and a shorter quit period. [13] A pooled analysis by ***Pesch B et. al***. on 29, 179 subjects (13,169 cases and 16,010 controls) revealed that the most prevalent lung cancer subtype in non-smokers was adenocarcinoma. He also revealed that smoking induces some irreversible damage to the lung tissue. [14] A systematic review by ***Parsons A et. al.*** assessed the effect of cessation of smoking on mortality due to lung cancer. The results indicated the reduction in mortality is attributed to reduced progression of cancer on cessation of smoking. [15]

The present study finds more non-smokers suffering from lung cancer whereas the pathophysiological connection between smoking and lung cancer is well established and supported by several studies. However, this observation does not contradict the established association between smoking and cancer. It is just an incidental finding of these small sample size included in this study.

CT and MRI as a diagnostic modality and staging tool

The strongest prognostic indicator in lung carcinoma is to determine the resectability of the tumor. To avoid unnecessary surgery, a therapeutic evaluation and pre-operative staging are critical for designing further treatment goal. Even with the advent of high technological advances in imaging studies such as Magnetic Resonance Imaging (MRI), CT still remains the gold standard for staging and evaluation of lung cancer. MRI helps to solve the specific problem when CT becomes equivocal or helps the problem a specific problem in diagnosis that cannot be solved through CT scan. Moreover, MRI studies are more critical to interpreting due to motion and susceptibility artifacts. [16]

Whole body PET-CT was found more accurate by ***Marom E.M. et. al.*** in their study delineating the staging in Non-Small Cell Lung Cancer (NSCLC). In their study, they found staging was more accurately diagnosed (in 83% patients) compared to conventional imaging studies (in 65% patients. [17]

Fischer B. et. al. demonstrated a similar result that showed a faster and accurate staging was achieved using combined PET-CT (8). Although staging by PET-CT was not able to reduce overall mortality, it reduces the number of futile thoracotomies. Moreover, pre-operative staging may help in designing the therapeutic strategy in lung cancer. [18]

According to a review by ***Purandare C N and Rangarajan V*****,** CT scan remains the gold standard for T staging. T1, T2, T3, and some of the T4 tumors are clinically resectable and for those resectable tumors, certain clinical descriptors must be conveyed to the physician such as proximity of the tumor to the main pulmonary artery and whether it crosses the fissures etc for successful surgical planning. [19] CT imaging can diagnose intrathoracic metastases (M1a) with the high degree of precision and no other imaging modality is required. However, CT scan is not the optimum imaging modality for the evaluation of mediastinal nodal disease (2). The detection rate for adrenal metastases (M1b) can be as high as 20% at presentation. [20, 21] ***Quint LE and Francis IR*** reported the sensitivity of CT scan for the same to be 38 to 87% and the specificity varies from 40 to 90%. [22]

Similarly, MRI also shows a good range of sensitivity (63-90%) and a specificity of 84-86% as reported in the studies by *Padovani B et. al.* and *Webb WR et. al.*[23, 24] ***Pieterman M R et. al.*** showed that 18F-fluorodeoxyglucose PET/CT scan (FDG PET/CT) is able to provide a more accurate classification of the stage in patients with resectable NSCLC. In this study, two adenocarcinoma cases were not detected in PET/CT whereas those were clearly visible in conventional CT scan. [25] ***Chin A Yi et. al.*** compared the efficacy of integrated positron emission tomography (PET)/computed tomography (CT) and 3.0-T whole-body magnetic resonance (MR) imaging in describing TNM staging in NSCLC. The results showed acceptable accuracy and comparable diagnostic efficacy for both CT and MR imaging in staging NSCLC. [26]

While comparing CT and MR imaging ***Musset D et. al.*** found no statistically significant difference between the two imaging modalities in the evaluation of either T3 tumors or N2 adenopathies in patients with bronchogenic carcinoma. [27]

In this study, the efficacy of CT and MRI was evaluated in the assessment of TNM staging in patients with small cell carcinoma. The result showed that CT scan was able to detect more stages of lung cancer than MRI. However, stage IIIB showed an increased diagnosis in MRI whereas the level of diagnosis of stage IIIA and IVA remains identical in both the imaging modalities.

CONCLUSION

To conclude CT and MRI diagnosis gives almost similar data for adenocarcinoma while in small cell carcinoma, CT scan gives more detailed picture of carcinoma with peaks at additional stages. As the accuracy and sensitivity of imaging modality vary for the different histological subtype of lung cancer, more studies are warranted to assign specified diagnostic modality for a particular lung cancer subtype.

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