Radiology Section

Comparison of Lung Masses Perfusion Characteristics by Dynamic Contrast Enhanced CT with Histopathology: A Cross-sectional Study

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ABSTRACT

Introduction: The management of lung masses depends upon the nature of the mass i.e., being benign or malignant. The use of contrast based Computed Tomography (CT) scan helps in ascertaining the malignant nature of the lesion. In previous studies, computed tomographic evaluations are done to evaluate pulmonary nodules, but only few studies characterised the lung masses into benign and malignant lesions.

Aim: To evaluate the diagnostic accuracy of a non invasive modality (dynamic contrast enhanced perfusion CT), in the characterisation of lung masses by comparing with histopathology.

Materials and Methods: A cross-sectional observational study was conducted at a tertiary care centre, Lucknow, Uttar Pradesh, India from January 2018 to November 2019 where 62 patients between age group 20-80 years of both sexes with lung masses and no contraindications to the administration of iodinated contrast material were enrolled in the study. Dynamic Contrast Enhanced CT (DCE-CT) perfusion was done which included parameters like Blood Flow (BF) in mL/100 g/min, Blood Volume (BV) in mL/100 g,

Mean Transit Time (MTT) in seconds, and Flow Extraction Product (FEP) in mL/100 mL/min. The DCE-CT features were compared with histopathology to determine the sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV).

Results: Among the 62 lung mass cases included in the study, 30 were histopathologically found to be benign lesions and 32 were malignant lesions. On contrast enhancement, the values of the CT perfusion parameters among the malignant masses were significantly higher as compared to benign (p<0.001). DCE-CT was able to correctly diagnose 31/32 cases of malignant and 26/30 cases of benign lung masses in concordance with histopathology. Thus, the overall, sensitivity, specificity, PPV, NPV, and diagnostic accuracy was 96.90%, 86.70%, 88.60%, 96.30%, and 91.90%, respectively.

Conclusion: The DCE-CT has a high diagnostic value in differentiation of malignant from benign lung masses and thus can be promoted for its use as a non invasive methods for lung masses characterisation.

Keywords: Benign lung masses, Computed tomography, Malignant lung masses, Pulmonary nodules

INTRODUCTION

Lung masses encompass a diverse range of etiologies comprising from benign (Tuberculosis, sarcoidosis, fungal infections, and inflammatory pseudotumour) to malignant (Lung cancer) in nature. The presence and knowledge about any such mass in the lung can be worrisome from the patient point of view especially if it is being diagnosed as lung carcinoma [1].

Epidemiological data of Global Cancer Data (GLOBOCAN) 2018 accounts cancers of the lung, female breast, and colorectum as the top three cancers in terms of incidence where lung cancer tops the list of mortality (1.8 million deaths, 18.4% of the total), because of the poor prognosis for this cancer worldwide [2]. In India, the data from 27 Population Based Cancer Registries (PBCRs) was analysed and the "Three-year Report of Population Based Cancer Registries 2012-2014", was released in May 2016. The report declared that lung was the predominant site for cancer in 10 PBCRs. The number of new cases of lung cancer was projected to be 144,351 in 2020 [3].

Though the gold standard diagnosis is provided by the biopsy driven histopathology, but due to its invasive nature, the role of imaging in detection and characterisation of lung masses into benign or malignant cannot be ignored. Chest X-ray is the first imaging of investigation which provides preliminary information about the disease but the patients are subsequently imaged with CT scan for optimal characterisation and staging. Currently, various modes of CT have been used in this regard. The conventional and spiral

CT [4], Positron Emission Tomography-CT [5], Multidetector CT (MDCT), and recently put to use are the DCE-CT [6].

The use of contrast based CT scan to ascertain the malignant nature of the lesion relies on the transport of intravenously administered iodinated contrast material into the possibly larger number of tissue capillaries and the increased exchange of contrast material between intravascular and extravascular interstitial space owing to an increased fenestration of the basement membrane of tumoural vessels [7]. By using the latest developments in dynamic contrast technology, perfusion parameters characterising both effects can be calculated throughout the entire tumour volume [8].

To note further, the correlation of various CT perfusion parameters with histologic markers of angiogenesis in lung cancer [9], enhances knowledge about the diagnosis, prognosis and guides the appropriate management as to promptly perform surgery in all patients with operable malignant masses and to avoid unnecessary thoracotomy in those patients with benign lesions [8-17]. Therefore, it is essential that one should be able to differentiate malignant from benign nodules in the least invasive manner and make the most specific and accurate diagnosis.

Although, a number of computed tomographic evaluations have been performed on evaluation of pulmonary nodules, only few studies have been done to characterise the lung masses into benign and malignant lesions [9,18-20]. Hence, the present study was proposed to carry out dynamic contrast enhanced perfusion CT evaluation of lung masses and to compare these findings with histopathology.

MATERIALS AND METHODS

A cross-sectional observational study was conducted in the Department of Radiodiagnosis at Era's Lucknow Medical College (tertiary care centre), Lucknow, Uttar Pradesh, India from January 2018 to November 2019. Ethical clearance for carrying out the study was obtained from the Institutional Ethical Committee (ELMC/R_Cell/EC/2018/59). An informed consent was obtained from all the patients prior to enrollment in the study.

Sample size calculation: The sample size was calculated based on the study of Ohno Y et al., who observed that sensitivity of Extraction Fraction (EF) and BV for predicting malignancy was 88% and 86% respectively and specificity was 82% and 54%, respectively [10]. Taking these values as reference, the minimum required sample size with desired precision of 20%, 90% power of study and 5% level of significance was 60 patients. To reduce margin of error, total sample size taken was 62.

Inclusion criteria: Sixty-two patients of age group 20-80 years of both sexes with clinco-radiologically suspected lung masses and no contraindications to the administration of iodinated contrast material were enrolled in the study.

Exclusion criteria: Patients who were allergic to contrast, pregnant patients, critically ill patients, those with deranged kidney function test, and those with lung pathology (other than lung masses) were excluded from the study.

After obtaining an informed consent, demographic information and nature of complaints were noted on a separate case sheet for every individual. All the patients were subjected to radiological investigations. Lung mass was evaluated and characterised into benign and malignant on Siemen's SOMATOM Force (384 slice) after dynamic contrast enhanced perfusion study. The protocol for dynamic contrast enhanced perfusion CT as defined by Miles KA et al., was followed [11]. The procedure (CT guided needle aspiration/bronchoscopic biopsy) was decided on the basis of site of tumour.

The following CT perfusion parameters were evaluated: BF in mL/10 g/min, which represents flow rate through vasculature in tissue region; BV in mL/10 g, which indicates volume of flowing blood within a vasculature in tissue region; MTT in seconds, which indicates average time taken to travel from artery to vein; and FEP in mL/100 mL/min which indicates the passage of the dye from the intravascular into the extravascular compartment estimating the permeability [12]. Lesion was characterised according to histopathological diagnosis. Central tumour was defined as having contact to the hilum, whereas all other tumours were considered peripheral [13]. The Dynamic contrast enhanced perfusion CT thorax features of lung mass was compared with histopathology. Sensitivity, specificity, PPV, and NPV of DCE-CT to correctly diagnose the features of benign and malignant lung masses was evaluated.

STATISTICAL ANALYSIS

The statistical analysis was done using Statistical Package for Social Sciences (SPSS) software version 15.0. The values were represented in number (%) and mean±SD. The Chi-square test was used for comparison. To test the significance of two means, the student t-test was used. The p-value <0.05 was accepted statistically significant.

RESULTS

Among the 62 cases of lung masses included in the study, 30 were histopathologically found to be benign lesions comprising of 13 cases of tuberculosis, 11 cases of pneumonic consolidation and six cases of hamartoma; and 32 were histopathologically found to be malignant lesions comprising of 11 cases of adenocarcinoma, six cases each

of small cell carcinoma and squamous cell carcinoma, five cases of large cell carcinoma, and two cases each of sarcomatoid carcinoma and metastasis.

Compared to the benign lung masses, patients with malignant lesions had significantly higher mean age 43.93±13.54 vs. 55.94±13.34, p=0.001), with male:female ratio of 1.28:1 for malignant lesions and 1.14:1 for benign lesions (p>0.05), and comparable number of patients with cough, breathlessness, haemoptysis, weight loss, and fever (p>0.05) [Table/Fig-1].

Demographic and clinical parameters	Benign masses n=30 (%)	Malignant masses n-32 (%)	Total n=62 (%)	p- value	Test Performed (*,**)		
Age (Years)	,	,					
21 to 40	15 (50%)	6 (18.8%)	21 (33.9%)		3.515		
41 to 60	10 (33.3%)	11 (34.4%)	21 (33.9%)				
61 to 80	5 (16.7%)	15 (46.9%)	20 (32.3%)	0.001			
Mean±SD	43.93±13.54	55.94±13.34	50.13±14.64				
Range	23 to 71	28 to 75	23 to 75				
Gender distribu	ution						
Male	18 (56.25%)	18 (56.25%)	34 (54.8%)	0.818	0.053		
Female	14 (46.7%)	14 (43.75%)	28 (45.2%)	0.818			
Place of reside	Place of residence						
Rural	9 (30%)	16 (50%)	25 (40.3%)	0.400	2.574		
Urban	21 (70%)	16 (50%)	37 (59.7%)	0.109			
Smoking habit	Smoking habit						
No	26 (86.7%)	16 (50%)	42 (67.7%)	0.002	9.526		
Yes	4 (13.3%)	16 (50%)	20 (32.3%)	0.002			
Clinical profile							
Cough	29 (96.7%)	26 (81.3%)	55 (88.7%)	0.055	3.67		
Breathlessness	16 (53.3%)	15 (46.9%)	31 (50%)	0.611	0.258		
Chest pain	19 (63.3%)	7 (21.9%)	26 (41.9%)	0.001	10.93		
Haemoptysis	23 (76.7%)	22 (68.8%)	45 (72.6%)	0.485	0.488		
Weight loss	14 (46.7%)	22 (68.8%)	36 (58.1%)	0.078	3.101		
Fever	20 (66.67%)	23 (71.9%)	43 (69.4%)	0.657	0.198		

[Table/Fig-1]: Demographic and clinical profile of patients and its correlation with histopathological diagnosis.

On conventional CT, among the malignant and benign lung masses, significantly more lesions were located centrally in malignant (37.5% vs 13.3%) than peripherally (62.5% vs 86.7%) (p=0.03), significantly less calcification was seen in malignant (18.8% vs 46.7%, p=0.019) [Table/Fig-2].

CT findings	Benign masses n=30 (%)	Malignant masses n=32 (%)	Total n=62 (%)	p- value	Test performed (*, **)	
Size						
Mean±SD (mm)	4.89 1.11	5.20±1.25	5.05±1.19	0.318	1.007	
Volume						
Mean±SD	158.93± 60.97	141.25± 70.44	149.81± 66.07	0.296	1.054	
Location						
Central	4 (13.3%)	12 (37.5%)	16 (25.8%)		4.723	
Peripheral	26 (86.7%)	20 (62.5%)	46 (74.2%)	0.03		
Angiogram sign	19 (63.3%)	27 (84.4%)	46 (74.2%)	0.058	3.581	
Spiculated margin	12 (40%)	19 (59.4%)	31 (50%)	0.127	2.325	
Calcification	14 (46.7%)	6 (18.8%)	20 (32.3%)	0.019	5.522	
Pleural effusion	21 (70%)	19 (59.4%)	40 (64.5%)	0.382	0.764	
Lymphadenopathy	17 (56.7%)	30 (93.8%)	57 (75.8%)	0.001	11.61	
Pleural extension	18 (60%)	20 (62.5%)	38 (61.3%)	0.84	0.041	
Mediastinal extension	2 (6.7%)	13 (40.6%)	15 (24.2%)	0.002	9.736	

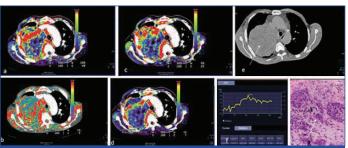
Bone destruction	0 (0%)	17 (53.1%)	17 (27.4%)	<0.001	21.958
Bronchus cut-off	3 (10%)	19 (59.4%)	22 (35.5%)	<0.001	16.489
Metastasis	0	25 (78.1%)	25 (40.3%)	<0.001	39.27

[Table/Fig-2]: CT profile and its correlation with histopathological diagnosis. ": t-test. *": Chi-square test

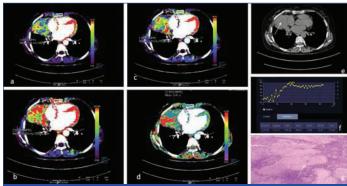
The values of the CT perfusion parameters among the benign and the malignant masses was significantly different with statistically higher values in malignant masses as compared to the benign lesions (p<0.001) as shown in [Table/Fig-3]. The graphical representation of the complete DCE-CT and histopathological findings for the representative benign and malignant case has been shown in [Table/Fig-4,5].

	Benign masses (n=30)	Malignant masses (n=32)	Total (n=62)		Test
Parameter	Mean±SD	Mean±SD	Mean±SD	p-value	performed
Blood Flow (BF)	14.97±2.24	61.39±9.82	38.93±24.46	<0.001	t-test; 25.27
Blood Volume (BV)	6.43±1.67	10.24±3.57	8.4±3.44	<0.001	t-test; 5.19
MTT	5.2±0.58	8.95±1.32	7.13±2.15	<0.001	t-test; 14.32
FEP	11.39±1.33	16.74±3.46	14.16±3.77	<0.001	t-test; 7.94

[Table/Fig-3]: Comparison of dynamic contrast enhanced perfusion CT assessment between benign and malignant lung masses.



[Table/Fig-4a-g]: A 55-year-old case of malignant lung mass with CT perfusion maps generated on image post-processing. The colour scale (a-d) indicates range of perfusion parameters from high (red) to low (blue). Representative colour coded perfusion maps of lung mass shows: a) high BF; b) MTT; c) FEP; d) high BV; e) Non contrast CT showing a large left lung mass (white arrow); f) Receiver operating characteristic curve drawn with a free hand technique; g) histopathology of the lung mass revealed large tumour cells infiltrating the stroma lying singly and in groups with a large irregular hyperchromatic nucleus, suggestive of large cell carcinoma (White arrow).



[Table/Fig-5a-g]: A 45-year-old case of benign lung mass with CT perfusion maps generated on image post-processing. The colour scale (a-d) indicates range of perfusion parameters from high (red) to low (blue). Representative colour coded perfusion maps of lung mass shows: a) low BF; b) MTT; c) FEP; d) low BV; e) Non contrast CT showing a left lung mass, (white arrow); f) Receiver operating characteristic curve drawn with a free hand technique; f) histopathology of the lung mass revealed caseating granulomas with giant cells suggestive of tuberculosis (White arrow).

Statistical analysis showed that the perfusion parameters BV, BF and MTT were significantly different among malignant masses but FEP was comparable [Table/Fig-6]. The results of Receiver Operating Characteristic (ROC) curve analysis showed that a threshold cut-off value of $\geq\!31.9$ for BF had a projected sensitivity and specificity of 100%; a threshold cut-off value of $>\!6.05$ for MTT had a projected

CT parameters	Blood Flow (BF)	Blood Volume (BV)	MTT	FED			
Benign							
Hamartoma (n=6)							
Mean±SD	14.67±1.5	5.88±1.22	5.15±0.34	10.87±0.92			
Median(IQR)	14.4 (13.575- 15.075)	6.35 (5.875- 6.6)	5.25 (5.125- 5.3)	10.95 (10.075- 11.45)			
Range	13.3-17.3	3.5-6.7	4.5-5.5	9.8-12.1			
Pneumonic consolidation (n=11)							
Mean±SD	16.04±2.8	7.13±1.47	5.42±0.73	11.74±1.32			
Median (IQR)	15.1 (13.4-19)	7.3 (6.35-8.2)	5.1 (4.85-6.15)	11.7 (10.5- 13.05)			
Range	13.2-19.3	4.1-8.7	4.5-6.5	9.8-13.2			
Tubercular (n=1	13)						
Mean±SD	14.22±1.7	6.09±1.9	5.04±0.5	11.33±1.49			
Median (IQR)	13.3 (13.1- 15.1)	6.7 (4-7.9)	5 (4.7-5.5)	11.9 (9.9-12.5)			
Range	13.1-18.1	3.5-8.3	4.3-5.9	9.4-13.2			
p-value	0.064	0.129	0.508	0.427			
Test performed	Chi- square=5.476	Chi- square=4.096	Chi- square=1.352	Chi- square=1.698			
Malignant							
Adenocarcinon	na (n=11)	I	I				
Mean±SD	71.34±5.48	10±0.71	9.85±1.4	17.68±4.18			
Median (IQR)	72.2 (69.35- 74.4)	10.3 (9.75- 10.4)	10 (9.8-10.35)	18.9 (13.9- 19.7)			
Range	58.1-78.3	8.8-11.1	6.1-11.5	12.2-25.4			
Large cell carci	inoma (n=5)	T		ı			
Mean±SD	55.72±6.03	8.34±1.39	8.26±0.57	15.08±2.5			
Median (IQR)	54.3 (52.5- 60.1)	8.3 (7.6-9.2)	8.1 (7.8-8.7)	15.6 (15.5- 16.2)			
Range	48.3-63.4	6.5-10.1	7.7-9	10.8-17.3			
Metastasis (n=2	2)						
Mean±SD	48.5±3.96	6.8±0.14	8.45±0.78	14.35±1.63			
Median(IQR)	48.5 (47.1- 49.9)	6.8 (6.75-6.85)	8.45 (8.175- 8.725)	14.35 (13.775- 14.925)			
Range	45.7-51.3	6.7-6.9	7.9-9	13.2-15.5			
Sarcomatoid (n	=2)	ı	I	ı			
Mean±SD	46.85±3.32	7.7±0.28	7.7±0.14	16.85±0.78			
Median (IQR)	46.85 (45.675- 48.025)	7.7 (7.6-7.8)	7.7 (7.65-7.75)	16.85 (16.575- 17.125)			
Range	44.5-49.2	7.5-7.9	7.6-7.8	16.3-17.4			
Small cell carci	noma (n=6)			1			
Mean±SD	57.25±7.15	7.35±1.52	8.4±1.25	17.6±4.82			
Median (IQR)	56.5 (52.225- 58.9)	7 (6.3-8.525)	8.75 (8.375- 9.05)	16.7 (14.4- 20.125)			
Range	50.1-69.9	5.6-9.4	6-9.5	12.1-25.2			
Squamous cell	carcinoma (n=6)	I					
Mean±SD	61.15±5.53	17.13±0.86	9±1.26	16.3±1.49			
Median (IQR)	59.95 (59.45- 63.3)	16.8 (16.65- 17.775)	9.35 (8.925- 9.7)	16.4 (15.475- 16.95)			
Range	53.4-69.9	16.2-18.3	6.6-10.1	14.2-18.5			
p-value	0.0006	0.0002	0.011	0.647			
Test performed	Chi- square=21.507	Chi- square=24.211	Chi- square=14.837	Chi- square=3.343			
[Table/Fig-6]:	Comparison of D	ynamic contrast e	nhanced perfusio	n CT			

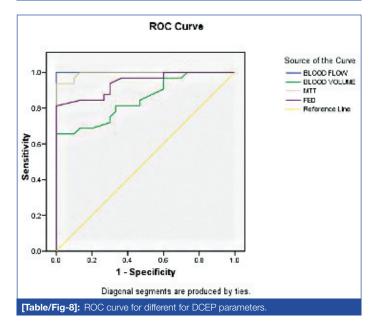
[Table/Fig-6]: Comparison of Dynamic contrast enhanced perfusion CT parameters between benign and malignant histopathological subtypes.

sensitivity and specificity of 96.9% and 90%, respectively [Table/Fig-7,8].

The DCE-CT was able to correctly diagnose 31 cases of malignant and 26 cases of benign lung masses in concordance with

Parameter	Area under curve±SE (p-value)	Projected cut-off value	Projected sensitivity	Projected specificity
Blood Flow (BF)	1.00±0.00 (p<0.001)	>31.90	100	100
Blood Volume (BV)	0.85±0.049 (p<0.001)	>7.35	81.3	66.7
MTT	0.99±0.006 (p<0.001)	>6.05	96.9	90
FEP	0.94±0.028 (p<0.001)	>13.65	81.3	100

[Table/Fig-7]: Receiver-Operator Characteristic (ROC) curve analysis to assess discriminant value of different dynamic contrast enhanced perfusion CT parameters for diagnosis of malignancy.



histopathology. Thus the overall, sensitivity, specificity, PPV, NPV and diagnostic accuracy was 96.90%, 86.70%, 88.60%, 96.30%, and 91.90%, respectively [Table/Fig-9].

Dynamic contrast enhanced	Histopathological diagnosis			
perfusion CT diagnosis	Malignant	Benign		
Malignant	31	4		
Benign	1 26			
Sensitivity	96.90%			
Specificity	86.70%			
Positive predictive value	88.60%			
Negative predictive value	96.30%			
Accuracy	91.90%			

[Table/Fig-9]: Distribution of cases according to DCE-CT diagnosis and its concordance with histopathological diagnosis.

DISCUSSION

The malignant prediction of increased perfusion parameters with contrast enhancement on CT scan as seen in the index study was in line with few previous studies [14-16]. It was owing to the increased vascularity and increased interstitial space fluid volume among the malignant lung masses [17].

The current study results depict the adjunctive role of contrast enhancement towards conventional CT. Conventional CT scan was able to determine the anatomical and structural aspects of the lung masses allowing us to know central/peripheral location, bone/mediastinal extension and destruction, associated lymphadenopathy, calcification and metastasis. The size of the lung masses cannot predict malignancy specifically since benign lesions may increase in size due to inflammation or haemorrhage as was seen in the index study. On histopathological comparison, it

was found that these parameters were significantly different among benign and malignant lung masses; however, the usage of these parameters as a benchmark to classify the masses into benign and malignant is not suggested.

On the other hand, the perfusion parameters assist in understanding the tumour biology and ongoing angiogenenesis which forms the basis of lung masses characterisation, prognostication and a tool for newer anti-angiogenic tumour therapies in lung cancer [8]. The current study found all perfusion parameters, that is, BV, BF, MTT and FEP, to be significantly higher in malignant lesions as compared to benign ones (p<0.001). The findings were in line with previous studies who determined the perfusion CT parameters to be higher among malignant lung nodules as compared to benign [Table/Fig-10] [9,18-20].

Study	Benign	Malignant	p-value			
Present study						
Blood volume	6.43±1.67	61.39±9.82	p<0.001			
Blood flow	14.97±2.24	61.39±9.82	p<0.001			
Mean transit time	5.2±0.58	8.95±1.32	p<0.001			
Flow extraction product	11.39±1.3	16.74±3.46	p<0.001			
Li Y et al., (2010)[18]			,			
Perfusion (ml min-1 ml-1)	13.1	61.5	p=0.000			
Peak enhancement intensity (HU)	11.3	60.2	p=0.000			
Blood volume	33.1	3.4	p=0.000			
Time to peak	28	32.5	p=0.087			
Yi CA et al., (2004) [7]						
Peak enhancement (HU)	78	98	p<0.001			
Net enhancement (HU)	35	53	p<0.001			
Preenhancement value (HU)	44	46	p=0.303			
Maximum relative enhancement ratio	0.848	1.267	p<0.001			
Time to peak enhancement (sec)	119	103	p=0.033			
Slope of enhancement (sec)	0.009	0.015	p<0.001			
Swensen SJ et al., (2000) [20]						
Enhancement (HU)	10	38.1	- 0.044			
Peak enhancement attenuation (HU)	17	15	p=0.244			
Swensen SJ et al., (1996) [19]						
Enhancement (HU)	8.0	46.5	p<0.001			
Diameter (mm)	13	16	p<0.005			

[Table/Fig-10]: Comparison of perfusion CT parameters between the present study and other studies.

HU: Hounsfield units

Barring few previous studies on lung masses (malignant) [16,17], most of the studies have focused on the characterisation of Solitary Pulmonary Nodules (SPN). A SPN is different from lung mass in terms of size (<3 cm) and absence of atelectasis or lymphadenopathy [21]. In addition, the use of the DCE-CT technology which is one of the strengths of the current study, has been for research purposes rather than being routinely used in the current scenario. It is unfortunate that despite the distinguishing features of DCE-CT, its role as primary non invasive investigation for diagnosis of lung cancer has not been explored to its fullest. The present study was an attempt in that direction.

The main advantage of DCE-CT is that it provides the functional data about the masses in addition to the anatomical details from the conventional CT. The problems in data collection with DCE-CT persists in only upto 6% cases [22], which is due to small lesion size (<8 mm), contrast allergy, voluntary refusal for cannulation, panic attacks or breathing difficulties during the procedure [23].

Among the two approaches of DCE-CT examination, we used the first pass technique to assess the contrast enhanced vascular perfusion parameters of the lung masses; which is mainly a research approach [10,24]. The other approach is established and more validated which determines the enhancement by Hounsfield Unit (HU) with sensitivity, specificity and area under the ROC curve of 93%, 76% and 0.93, respectively [20,25,26].

In the current study, the overall, sensitivity, specificity, PPV, NPV and diagnostic accuracy was 96.90%, 86.70%, 88.60%, 96.30%, and 91.90%, respectively which was comparable to the other approach. Before performing DCE-CT, we made sure to assess the masses through conventional CT to know the morphological details among which central location, less calcification, more mediastinal extension, bone involvement were significantly associated with malignancy, whereas spiculated margins, angiogram sign, size and volume showed no association with histopathological findings.

Among the perfusion parameters, BV, BF and MTT were able to differentiate malignant lesions as seen in another study [16,27,28]. The index study showed that the BV, BF and MTT were significantly higher for adenocarcinoma and Squamous Cell Carcinoma (SCC) and low for sarcomatoid and metastasis. Compared to the present study, in Mondal A et al., study, the difference was significant only for BF and permeability among adenocarcinoma and SCC (p=0.001 and p=0.049) [16]. Shi J et al., found significantly higher permeability in adenocarcinoma than SCC (p<0.05) Ovali GY et al., found significantly higher BF in SCC than adenocarcinoma as was seen in the current study [27,28]. The statistical associations but differences stress on the need to standardise the dye dosage, calculations software and analysis methods since it becomes difficult to compare the cross-sectional studies with different used techniques.

Limitation(s)

The DCE-CT demonstrates high sensitivity in differentiation of malignant and benign lesions; however, one of the limitations related to it is its relatively poor specificity. This might be due to increased vascular flow in benign processes due to infection, inflammation. The false negatives may also increase among lesions such as pneumonic consolidation, hypervascular benign tumours, and masses with less vascular stroma [23]. Another limitation of the technique is the high cost of the machine and the procedure, which has restricted the routine use of DCE-CT. In addition, the lack of standardised cut-offs for malignancy also restricts the conclusive prediction of lung masses without histopathological correlation.

CONCLUSION(S)

The findings of present study showed that DCE-CT has a high diagnostic value in differentiation of malignant from benign lung masses. With proper exploration of dynamic contrast enhanced parameters such as BF and MTT and their skillful use in combination with other parameters, diagnostic efficacy of DCE-CT can be increased further. Future studies on a larger sample size with focus on increasing the accuracy of DCE-CT are recommended to promote its use as a non invasive method for lung cancer diagnosis and characterisation.

REFERENCES

[1] Li CR, Li YZ, Li YM, Zheng YS. Dynamic and contrast enhanced CT imaging of lung carcinoma, pulmonary tuberculoma, and inflammatory pseudotumour. Eur Rev Med Pharmacol Sci. 2017;21(7):1588-92.

- [2] International Agency for Research in Cancer. Latest Global Cancer Data: Cancer Burden Rises to 18.1 Million New Cases and 9.6 Million Cancer Deaths in 2018. Geneva: World Health Organization; 2018.
- [3] National Center for Disease Informatics and Research. Annual Report 2016– 2017. India: Indian Council for Medical Research; 2017.
- [4] Pauls S, Mottaghy FM, Schmidt SA, Kruger S, Moller P, Brambs HJ, et al. Evaluation of lung tumour perfusion by dynamic contrast-enhanced MRI. Magn Reson Imaging. 2008;26(10):1334-41.
- [5] Sharma A, Eisen JE, Shepard JAO, Bernheim A, Little BP. Case 25-2020: A 47-year-old woman with a lung mass. N Engl J Med. 2020;383(7):665-74.
- [6] Mazzone PJ, Gould MK, Arenberg DA, Chen AC, Choi HK, Detterbeck FC, et al. Management of lung nodules and lung cancer screening during the COVID-19 pandemic: CHEST Expert Panel Report. Radiology: Imaging Cancer 2020;158(1):406-15.
- [7] Cui S, Ming S, Lin Y, Chen F, Shen Q, Li H, et al. Development and clinical application of deep learning model for lung nodules screening on CT images. Sci Rep. 2020;10(1):01-10.
- [8] Ng QS, Goh V, Fichte H, Klotz E, Fernie P, Saunders MI, et al. Lung cancer perfusion at multi-detector row CT: reproducibility of whole tumour quantitative measurements. Radiology. 2006;239(2):547-53.
- [9] Yi CA, Lee KS, Kim EA, Han J, Kim H, Kwon OJ, et al. Solitary pulmonary nodules: dynamic enhanced multi-detector row CT study and comparison with vascular endothelial growth factor and microvessel density. Radiology. 2004;233(1):191-99.
- [10] Ohno Y, Nishio M, Koyama H, Seki S, Tsubakimoto M, Fujisawa Y, et al. Solitary pulmonary nodules: Comparison of dynamic first-pass contrast-enhanced perfusion area-detector CT, dynamic first-pass contrast-enhanced MR imaging, and FDG PET/CT. Radiology. 2015;274(2):563-75.
- [11] Miles KA, Lee TY, Goh V, Klotz E, Cuenod C, Bisdas S, et al. Current status and guidelines for the assessment of tumour vascular support with dynamic contrast-enhanced computed tomography. Eur Radiol. 2012;22(7):1430-41.
- [12] Spira D, Adam P, Linder C, Spira SM, Pintoffl J, Claussen CD, et al. Perfusion and flow extraction product as potential discriminators in untreated follicular and diffuse large B cell lymphomas using volume perfusion CT with attempt at histopathologic explanation. AJR Am J Roentgenol. 2012;198(6):1239-46.
- [13] Kiessling F, Boese J, Corvinus C, Ederle JR, Zuna I, Schoenberg SO, et al. Perfusion CT in patients with advanced bronchial carcinomas: A novel chance for characterisation and treatment monitoring? Eur Radiol. 2004:14(7):1226-33.
- [14] Swensen SJ, Morin RL, Schueler BA, Brown LR, Cortese DA, Pairolero PC, et al. Solitary pulmonary nodule: CT evaluation of enhancement with iodinated contrast material- A preliminary report. Radiology. 1992;182(2):343-47.
- [15] Zhang M, Kono M. Solitary pulmonary nodules: Evaluation of blood flow patterns with dynamic CT. Radiology. 1997;205(2):471-78.
- [16] Mondal A, Pradhan G, Manchanda A, Garg A, Daga MK, Jain SL. Role of perfusion computed tomography in the characterisation of lung cancers. JMSCR. 2018;6(7):662-69.
- [17] Khanduri S, Bhagat S, Shokeen P, Kumar G, Khanduri S, Singh B. Rationale of using dynamic imaging for characterisation of suspicious lung masses into benign or malignant on contrast enhanced multi detector computed tomography. J Clin Imaging Sci. 2017;7:24.
- [18] Li Y, Yang ZG, Chen TW, Yu JQ, Sun JY, Chen HJ. First-pass perfusion imaging of solitary pulmonary nodules with 64-detector row CT: Comparison of perfusion parameters of malignant and benign lesions. Br J Radiol. 2010;83(993):785-90.
- [19] Swensen SJ, Brown LR, Colby TV, Weaver AL. Lung nodule enhancement at CT: Prospective findings. Radiology. 1996;201(2):447-55.
- [20] Swensen SJ, Viggiano RW, Midthun DE, Müller NL, Sherrick A, Yamashita K, et al. Lung nodule enhancement at CT: Multicenter study. Radiology. 2000;214(1):73-80.
- [21] Khan AN, Al-Jahdali HH, Irion KL, Arabi M, Koteyar SS. Solitary pulmonary nodule: A diagnostic algorithm in the light of current imaging technique. Avicenna J Med. 2011;1(2):39-51.
- [22] Institute of Health Research (NIHR) Health Technology Assessment funded multicentre SPUtNik trial which should report in 2018 (ISRCTN 30784948).
- [23] Qureshi NR, Shah A, Eaton RJ, Miles K, Gilbert FJ; Sputnik investigators. Dynamic contrast enhanced CT in nodule characterisation: How we review and report. Cancer Imaging. 2016;16(1):16.
- [24] Jeong YJ, Lee KS, Jeong SY, Chung MJ, Shim SS, Kim H, et al. Solitary pulmonary nodule: characterisation with combined wash-in and washout features at dynamic multi-detector row CT. Radiology. 2005;237(2):675-83.
- [25] O'Connor JPB, Tofts PS, Miles KA, Parkes LM, Thompson G, Jackson A. Dynamic contrast-enhanced imaging techniques: CT and MRI. Br J Radiol. 2011;84(Spec Iss 2):S112-20.
- [26] Cronin P, Dwamena BA, Kelly AM, Carlos RC. Solitary pulmonary nodules: Meta-analytic comparison of cross-sectional imaging modalities for diagnosis of malignancy. Radiology. 2008;246:772-82.
- [27] Shi J, Schmid-Bindert G, Fink C, Sudarski S, Apfaltrer P, Pilz LR, et al. Dynamic volume perfusion CT in patients with lung cancer: Baseline perfusion characteristics

of different histological subtypes. Eur J Radiol. 2013;82(12):e894-900.

[28] Ovali GY, Sakar A, Goktan C, Celik P, Yorgancioglu A, Nese N, et al. Thorax

perfusion CT in non-small cell lung cancer. Comput Med Imaging Graph. 2007;31:686-91.

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