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## ORIGINAL ARTICLE

### Incremental Benefit of Maximum Intensity Projection Images on Detection of Metastatic Small Pulmonary Nodules Revealed by Multi-Detector Ct.

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#### ABSTRACT

**Background:** Difficulty of detecting pulmonary nodules on CT is a common clinical problem in radiology. Lung nodules of less than 10mm in size can be very easily over looked specially when located close to nodules& however Failure of both conventional CT and the radiologist to detect small lesions is well known vessels. CT chest is the imaging modality with the highest sensitivity for detection of pulmonary.

**Aim and objectives:** To prove that multi-detector computed tomography (MDCT) with maximum intensity projections (MIP) is more accurate than conventional MDCT in detection of metastatic small pulmonary nodules.

**Subjects and methods:** This study was a cross sectional study that was performed in Radio-diagnosis Department, Zagazig university hospitals during the period from March to December 2019 and included 24 patients with metastatic cancer to the lung. All patients were subjected to complete history taking, full clinical examination, laboratory examination; kidney function tests and radiological examination including Multi-detector CT, post contrast studies and processing "MIP reconstruction image". All examinations were reviewed by two readers.

**Results:** There was a significant difference between axial CT and MIP in numbers of pulmonary metastatic nodules detected. The diagnostic performance of MIP was statistically highly significant compared with axial CT in detection of small nodules. There was a highly significant difference in detection time of nodules between both reviewers regarding axial CT and MIP images.

**Conclusion:** The use of axial MIP images for small pulmonary nodule detection improves the diagnostic performance when compared with conventional source axial thin-slice MDCT images alone.

**Keywords:** Multi-detector CT, MIP, Radiology.



#### INTRODUCTION

Lung nodule is a rounded or irregular opacity, which may be well or poorly defined, measuring less than 3 cm in diameter, surrounded by aerated lung and not attributable to a pulmonary vessel. (An opacity <3 mm should be defined as a micro nodule). The nodule could be attached to any neighboring structure like the pleura or vessels. [1]

According to current international guidelines, the determination of metastatic lung nodule is very important, size and the growth rate are the main indicators for assessing the nature of a pulmonary nodule. [2]

Difficulty of detecting pulmonary nodules on computed tomography (CT) is a common clinical problem in radiology. Lung nodules of less than 10mm in size can be very easily overlooked specially when located close to vessels. CT chest is the imaging modality with the highest sensitivity for detection of pulmonary nodules, however Failure of both conventional CT and the radiologist to detect small lesions is well known. Overall sensitivity is only 47-69% for detection of small nodules. [4]

Multi-detector computed tomography (MDCT) scanners made it possible to acquire volumetric data of the lung with high spatial resolution. It enables simultaneous increased z-axis coverage

and thinner slice collimation in comparison to single-detector helical CT. Thin sections improve resolution and decrease slice-to-slice volume average resulting in more accurate detection of small nodules. [4]

However, two major factors restrict observer identification of these nodules, large numbers of axial images are produced which lead to reviewer fatigue during analysis, and nodules mimic normal vessels in cross-section, especially in the central lung zones, on individual thin sections. These considerations limit realization of the true potential of MDCT in the detection of nodules in the lung. [4]

New computer-based image processing tools can facilitate the full use of large volumetric MDCT data sets. One example is maximum-intensity-projection (MIP) imaging. This device uses techniques for ray projection across a stack of pre-selected axial images; the highest density point detected by the ray traversing the stack is projected onto the final image. [5]

MIP processing has many advantages, vascular structures appear as distinctly tubular and branching structures rather than as isolated nodules, the MIP slab maintains the quality inherent in the axial images from which it is produced, and the number of images is greatly reduced relative to the axial image collection. [7]

The aim of the study is to prove that multi-detector computed tomography (MDCT) with maximum intensity projections (MIP) is more accurate than conventional MDCT in detection of metastatic small pulmonary nodules.

#### **SUBJECTS AND METHODS**

This study was a cross sectional study performed in Radio diagnosis Department, Zagazig University hospitals during the period from March to December 2019. Twenty four patients were included in the study, they were 13 males and 11 females and their age ranged from 40 to 81 years.

Inclusion criteria: Patients with known extra-pulmonary primary malignancy of any age and sex.

Exclusion criteria: - Patients with nodules larger than 10 mm in diameter, any pleural or parenchymal disease that could interfere with optimal nodule identification or presence of calcified nodules. Also, patients with allergic reaction to contrast media, with renal dysfunction (serum creatinine = 1.6mg/dl) not on dialysis or pregnant females were excluded.

Methods:

All the studied groups were subjected to the following:

a. Complete history taking as (age, sex, chest symptoms, history of extra-pulmonary primary malignancy). Full clinical examination including

general examination for pulse, blood pressure, temperature and respiratory rate and local chest examination, laboratory examination; kidney function tests and radiological examination including Multi-detector CT examination.

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board IRB). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Technique of CT examination: All examinations were performed on Philips ingenuity 128 multi-detector CT as the following:

- Setting up the scan: All patients underwent contrast study. (1ml/kg) non-ionic contrast material was injected via ante-cubital vein following by rapid acquisition of constructive thin sections through the chest.

- Scanning parameters were: during examination the patients hold breathing in full inspiration, scout was from clavicular head through both costophrenic angles, 120 kv/150-280mA, slice thickness is 10 mm, exposure time nearly (4-6 sec), section collimation of 2.5-0.5 mm, table speed of 2.5-10 mm/rotation during a single breath hold, the acquired volumetric data was used to reconstruct multi-planner reformatted (MPR), volume rendering (VR) and Maximum intensity projections (MIP) and finally CT acquisition was done in cranio-caudal direction with standard scan delay of 3sec.

- Data Processing: was done using Intellispace ISP workstation unit. The raw data obtained ranges about 100-200 images per examination. The axial images, multi-planner reformatted images (MPR), maximum intensity projection (MIP), virtual 3D(VRT), were examined through the final reporting.

- Image Interpretation: all examinations were reviewed by two readers; a senior resident and a consultant radiologist to read axial or MIP images independently. Each reader reviewed all datasets across multiple separate sessions with a gap of at least 1 week to minimize familiarity and practice performance.

**Statistical Analysis:** The collected data were analyzed by computer using Statistical Package of Social Services version 24 (SPSS), Data were represented in tables and graphs, Continuous Quantitative variables e.g. age were expressed as the mean  $\pm$  SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number)& relative frequencies (percentage). Suitable statistical tests of significance were used after checked for normality.

The results were considered statistically significant when the significant probability was less than 0.05 (P <0.05). P-value < 0.001 was considered highly statistically significant (HS), and P-value ≥ 0.05 was considered statistically insignificant (NS).

**RESULTS:**

Table (1) shows the demographic data of the included patients. The patients were 13 (54.2%) males and 11(45.8%) females and their age ranged from 40 to 81 years with a median of 56 and mean of 56.17 ± 11.01 years.

The mean of number of pulmonary metastatic nodules using axial CT is 0.55 ± 1.43 nodule, it ranged from zero to 6 nodules while mean of number of nodules using MIP is 1.85 ± 1.66 nodules with a range from 1 to 8 nodules, these difference between axial CT and MIP in detection of nodules was statistically highly significant (P value = 0.000) (table 2).

The mean size of the detected nodules was 4.05 ± 1.95 mm with a range from 2 to 10 mm (table 3).

Table (4) shows that the most of detected metastatic pulmonary nodules was small in size followed by medium size nodules and large nodules between both reviewers (54%, 24.3%, 2.7%) by MIP and (45.9% , 18.9% , 67.5%) by axial CT for reviewer A respectively and (70.3%, 27.0% , 2.7 %) by MIP and (59.4% , 27% , 2.7%) by axial CT for reviewer B respectively. There is

significant difference between the two reviewers (P= 0.01) regarding the number of detected small nodules, while the difference in medium sized and large nodules were statistically non-significant. Also there was a significant difference between reviewers regarding total numbers of nodules detected using axial CT and MIP where No. of nodules detected by axial CT was 25(67.5%) nodules by reviewer A, Vs 33 (89.1%) nodules by reviewer B, while No. of nodules detected by MIP was 30(81%) nodules by reviewer A vs 37 (100%) nodules by reviewer B.

We found that the diagnostic performance of MIP was statistically highly significant compared with axial CT in detection of small nodules (100%, vs 84.6%) respectively and p-value (< 0.001) (table 5).

In this study the most predominant site of detected metastatic pulmonary nodules was peripheral (78.4% ) when compared to the centrally located ( 21.6%) (table 6).

There was highly significant difference in detection time of nodules between both reviewers regarding axial CT and MIP images where mean of axial CT time is 108.9 ± 40.52 sec in reviewer A, Vs 52.9 ± 27.5 sec in reviewer B with (p-value < 0.001) while mean MIP time is 80.5 ± 36.8 sec in reviewer A vs 37.8 ± 17.5 sec in reviewer B. (with p- value < 0.001) (Table 7).

**Table (1): Demographic data of the included patients**

Demographic data	patients(N=24)	
	No.	%
<b>Sex</b>		
Male	13	54.2%
Female	11	45.8 %

The mean ± SD & median (range)

**Table (2): Number of detected metastatic pulmonary nodules using axial CT and MIP among the studied group(N=24)**

pulmonary metastatic nodules	Studied patients(N=24)	Test	p-value
<b>Number of nodules using Axial CT</b>			
Mean ± SD	0.55 ± 1.43	-3.841	0.000* (HS)
Median (Range)	0(0-6)		
<b>Number of nodules using MIP</b>			
Mean ± SD	1.85 ± 1.66		
Median (Range)	1(1-8)		

Test: Wilcoxon signed rank test

\*highly significant

**Table (3): Size of detected metastatic pulmonary nodules among the studied group**

pulmonary metastatic nodules (N=37)	
Size of nodules (mm)	
Mean ± SD	4.05 ± 1.95
Median (Range)	4(2-10)

The mean ± SD & median (range)

**Table (4): Detection of metastatic pulmonary nodules according to size**

Size	Metastatic nodules (N=37)				P
	Reviewer A		Reviewer B		
		MIP		MIP	
• Small( $\geq 4$ mm)	17(45.9%)	20(54%)	22(59.4%)	26 (70.3%)	0.01*
• Medium(>4-8mm)	7(18.9%)	9(24.3%)	10(27%)	10 (27%)	0.3 <sup>NS</sup>
• Large(>8-10mm)	1 (2.7%)	1 (2.7%)	1 (2.7%)	1 (2.7%)	0.0 <sup>NS</sup>
Total	25(67.5%)	30(81%)	33(89.1%)	37(100%)	0.01*

- NS non-significant, \* significant

**Table (5): Diagnostic performance of detection of small pulmonary nodules.**

Detection of small pulmonary nodules (N=26)	Diagnostic technique				p-value
	Axial CT		MIP		
	A	B	A	B	
• Detected	17 (65%)	22 (84.6%)	20 (76%)	26 (100%)	<0.001** (HS)
• Undetected	9 (34%)	4 (15.3%)	6 (23%)	0.0	

\*\*highly significant

**Table (6): Site of detected metastatic pulmonary nodules using MIP among the studied group**

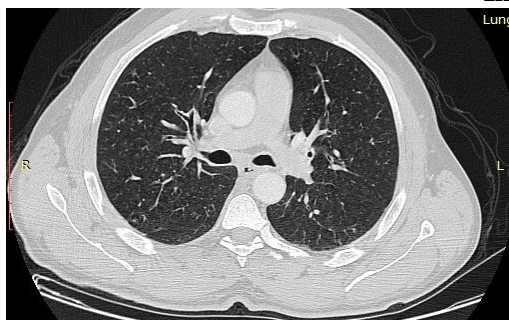
Item	Metastatic nodules (N=37)	
	No.	%
• Peripheral	29	78.4
• Central	8	21.6

**Table (7): Time of detection of metastatic pulmonary nodules by reviewers using axial CT and MIP among the studied group**

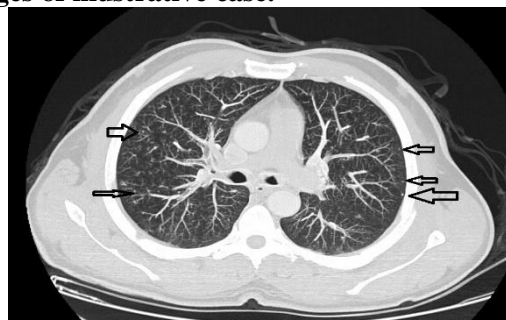
time	Reviewer A	Reviewer B	Test	p-value
<b>Axial CT time (S)</b>				
Mean $\pm$ SD	108.9 $\pm$ 40.52	52.9 $\pm$ 27.5	-5.74	<0.001** (HS)
Median (Range)	92.8(60-120)	50(30-78)		
<b>MIP time (S)</b>				
Mean $\pm$ SD	80.5 $\pm$ 36.8	37.8 $\pm$ 17.5	-4.82	<0.001** (HS)
Median (Range)	75(50-90)	36(25-45)		

Test: Wilcoxon signed rank test \*\*highly significant

**Images of illustrative case.**



(Axial CT)



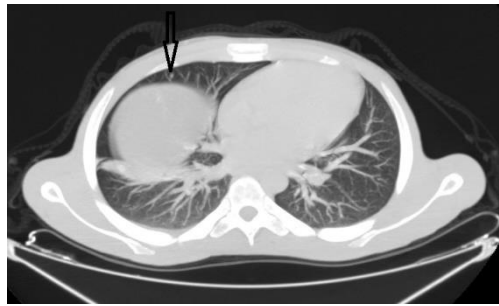
(MIP Image)  
CT Images of cases;



**Case 1)**



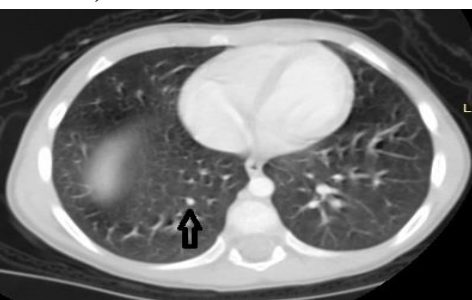
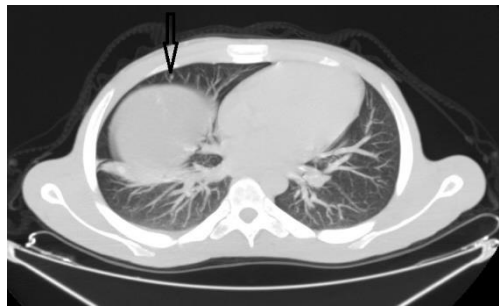
**A**



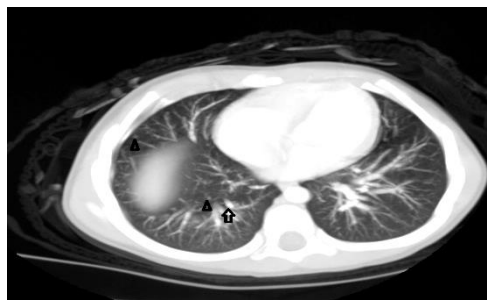
**B**



**Case 2)**

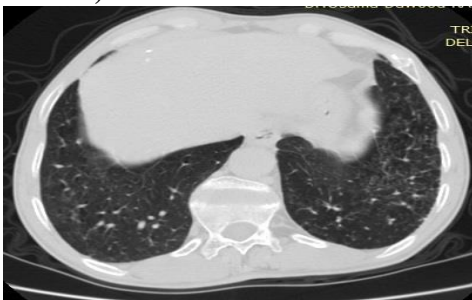


**A**

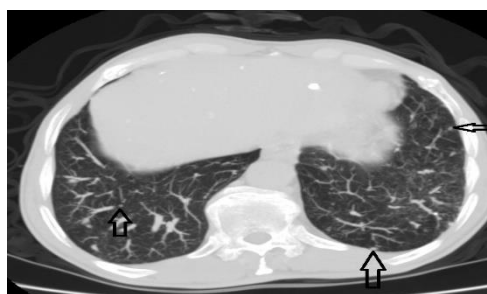


**B**

**Case 3)**

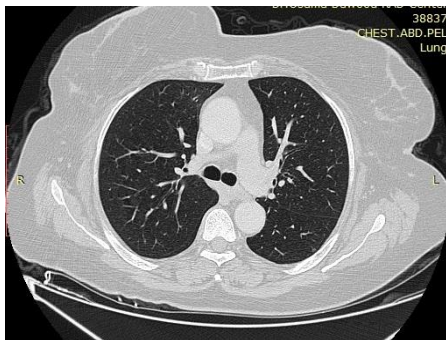


**A**

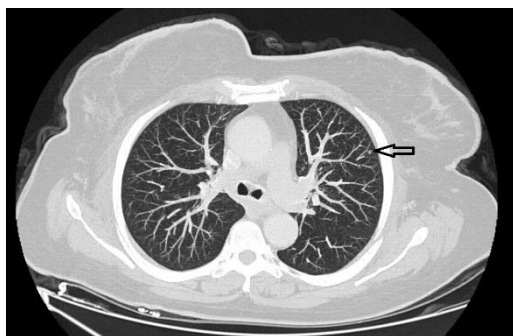


**B**

**Case 4)**

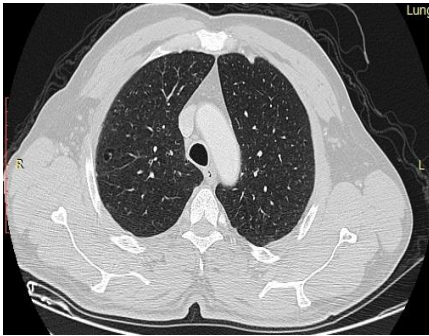


**A**

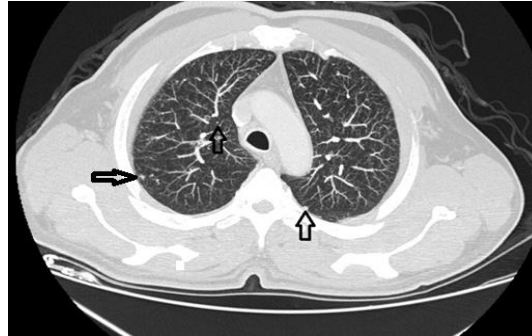


**B**

**Case 5)**



**A**



**B**

**DISCUSSION**

The identification of small pulmonary nodules is a crucial feature of thoracic radiology, and with the increasing use of multi-detector CT (MDCT) has become much more important. High-resolution axial MDCT allows thin collimation for spatial accuracy and eliminates partial-volume effects, thereby enhancing the accuracy of identification of small nodules. [8]

Several additional methods and display modes such as multi-planar reformats, maximum intensity projection (MIP) reformats and computer-aided detection (CAD) can be used to enhance radiologist's performance. [9, 10]

MIP imaging has many theoretical benefits over traditional axial images in the identification of small nodules: the size of the entire sample is smaller and the vascular structures represented in a stack behave as tubular branching structures rather than as isolated nodules. [11]

The aim of this work was to prove that the maximum intensity projection images (MIP) is more accurate than conventional thin slice multi-detector CT (MDCT) in detection of metastatic small pulmonary nodules.

We included 24 patients presented with pulmonary nodules of extra pulmonary origin. They were 11 females (45.8%) and 13 males (54.2%). Their ages ranged from 40 to 81 years and mean age was  $56.17 \pm 11.01$  years. All patients were subjected to Multi-detector CT of the chest first the normal 1-mm lung window images were performed for all the patients, followed by MIP reconstruction of all images on the workstation at slice thickness 7-10mm.

Silva and colleagues have assessed the effect of different MIP thickness on nodule detection, as a balance is required between overall number of images in a dataset and high diagnostic accuracy, as loss of information becoming problematic at greater MIP thicknesses, and they chose 10-mm MIPs for comparison to standard axial images. In accordance to the previous study we use a MIP thickness of 7-10 mm in all patients. [12]

Nodule size has different implications because even small nodules (less than 1 mm) can represent disseminated malignancy in the context of oncology staging. Detection of small nodules is important, leading to the so-called CT-only pulmonary nodule (not present on a conventional chest radiograph), and this increasing mismatch between higher sensitivity and unaltered specificity for lung nodules has become a huge problem in oncology. [13]

In our study we found that, there was a significant difference between Axial CT and MIP in number of detected pulmonary metastatic nodules where mean of number of nodules using Axial CT is  $0.55 \pm 1.43$  nodule, it ranged from (zero to 6) nodules while mean of number of nodules using MIP is  $1.85 \pm 1.66$  nodules with a range from (1 to 8) nodules.

The differences mainly related to more detection of small nodules using axial MIP image in both reviewer A and B (20 and 26 nodules compared to 17 and 22 small nodules using the axial source image respectively) and this difference was statistically highly significant ( $P < 0.001$ ).

Our results agreed with Kilburn-Toppi and colleagues [6] who reported in their study that significantly more nodules were found on MIP images than on axial images (total 228 vs. 174;  $P < 0.05$ ; mean  $1.68 \pm 1.46$  vs.  $1.27 \pm 1.30$  nodules). Also, Valencia and colleagues in their study showed that smaller nodules ( $< 5$  mm) are best detected on axial MIP images, regardless of location. [11]

We found that MIP images did not show an improvement in the detection of large nodules, either because they are sufficiently easy to be detected on axial images or because there were relatively few moderate and large nodules in our dataset.

This was similar to the findings reported by Özkan and colleagues in which they claimed that literature examination of the nodules detection reviews found that the largest variation was observed in the small group while the frequencies of the nodules

detected in the medium size and the larger group were almost identical. [7]

Another field where MIP images shows no noticeable improvement in the overall sensitivity to identification of the central nodules. It is logical that peripheral nodules are easier to differentiate from vessels than central nodules, because vessel size generally declines toward the periphery of the lungs. Some experiments have shown a advantage of using MIP images in central nodule identification. Another reason is that central crowding of the vessels may be much more troublesome, reducing the visibility of the central nodule on MIP images. [4]

In accordance to previous studies, we found that the most predominant site of detected metastatic pulmonary nodules using MIP was peripheral as compared to central site (78.4% vs 21.6%) respectively.

In our study there was a significant difference between reviewers regarding the time needed for detection of nodules regarding axial CT and MIP where mean of axial CT time was  $108.9 \pm 40.52$  sec in reviewer A, Vs  $52.9 \pm 27.5$  sec in reviewer B while mean MIP time is  $80.5 \pm 36.8$  sec in reviewer A vs  $37.8 \pm 17.5$  sec in reviewer B (P value<0.05).

In accordance to our results, Kilburn-Toppi and colleagues [6] found in their study that MIP images took significantly less time to read(mean  $71.6 \pm SD 43.7$  s) than axial images ( $92.9 \pm 48.7$  s; P <0.005). Jankowski and colleagues had attributed the increased reading speed of the MIP datasets is likely account for the reduction in total images within a MIP dataset in comparison with axial images. [14]

#### CONCLUSION:

From our study we concluded that the use of axial MIP images for small pulmonary nodule detection improves diagnostic performance when compared with conventional source axial thin-slice MDCT images alone.

#### RECOMMENDATIONS:

We recommended the combined use of axial MIP image and axial source images to complement each other in thoracic metastatic nodule detection.

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#### COMMENTS OF CASES;

##### **Illustrative case;**

CT chest examination of a male patient, 68 years with known brain cancer. Axial CT cut shows clear lung field, no detected pulmonary nodules while MIP image (10 mm thick) shows multiple peripheral bilateral small size nodules ranging between 2 and 4 mm (arrows). Seen at the lateral segment of the right middle lobe and at the anterior and apico-posterior segments of the left upper lobe.

##### **Case 1)**

CT Chest examination of a male patient, 40 years old with known colorectal carcinoma. Axial CT cut shows clear lung field with no detected nodules while MIP image (10 mm thick) shows small (3mm) nodule (arrow) at anterior segment of the right lower lobe.

##### **Case 2)**

CT chest examination of a female patient 50 years old with known breast cancer. Axial CT cut reveals central rounded opacity (suspecting pulmonary nodule) at the posterior segment of the right lower lobe (Arrow) while MIP image (10 mm thick) revealed that the previously described suspected opacity in axial image corresponds to a part of pulmonary vessel while there is another two newly detected small size (3 mm) pulmonary nodules (arrow head) seen at the posterior (central) and

lateral(peripheral) segments of the lower lobe of the right lung respectively not seen at the axial image.

##### **Case 3)**

CT chest examination of a male patient, 69 years old with known HCC. Axial CT cut shows emphysematous lung field, clear of pulmonary nodules while MIP image (10 mm thick) shows multiple bilateral small sized (1-4 mm) nodules (arrows) seen sub pleural peripheral and central scattered at both lower lung lobes.

##### **Case 4)**

CT chest examination shows a female patient, 51 years old with known brain cancer. Axial CT cut shows clear lung field, no detected pulmonary nodules while MIP image (10 mm thick) shows small (3 mm) nodule seen at the apico- anterior segment of the left upper lobe. (Arrow)

##### **Case 5)**

CT chest examination shows a male patient, 65 years with known colorectal carcinoma. Axial CT cut shows clear lung field, no detected pulmonary nodules while MIP image (10 mm thick) shows multiple bilateral pulmonary nodules of small size (arrows). Right side nodules are 2 and 4 mm size seen at the anterior (central) and posterior segment of the upper right lobe respectively while the left side nodule is 4 mm size seen sub pleural at the apico-posterior segment of the upper left lobe.

#### **How to cite**

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