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RESEARCH ARTICLE

COMPARISON OF SUBMILLIMETRESWITH MILLIMETRESSLICE THICKNESS OF LUNG 16 SLICE MDCT IN METASTATIC PULMONARY NODULE DIAGNOSIS

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ABSTRACT

Background and Objective: The most common radiographic abnormalities related to lung metastasis are pulmonary nodules .The CT scan in most circumstances are the best modality for lung metastasis evaluation..In this study we aimed to investigate the diagnostic accuracy of lung CT scan with slice thickness less than 1 mm (0.625 mm) compared with the usual slice thickness for detection of tiny metastatic pulmonary nodules.

Materials and Methods: This study was a diagnostic study performed on 110 patients with malignant diagnosis who were referred to the Radiology Department of Hospital. At first, following performance of routine CT scan with millimetres slice thickness (2mm) from the patients' lung, extra images were taken by sub millimetres slice thickness to assess either presence or not of nodules by two radiologists simultaneously. Data were analysed using Chi2, Fisher Extract, one way ANOVA, SPSS version 18 and Independent t statistical tests. In all cases, $p < 0.05$ was considered statistically significant.

Results: Radiologists reported nodules in 40 (36.36%) of cases using millimetres slice thickness of the images and in the submillimetreslice thickness images, nodules were found in 58 (52.70%) cases (P=0.001). There were significant differences between images with different thickness in visibility, resolution and the number of nodules observation.

Conclusion: With reducing thickness, pulmonary nodule detection is increased and the use of submillimetric slice thickness (0.625mm) in comparing to conventional millimetres slice thickness has a significant difference in detection, and the number of pulmonary nodules. Environmental factor as an independent factor non-related to the modality and the observer can be also effective.

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INTRODUCTION

Pulmonary nodules are discrete spherical radiographic opacities that are less than 3cm in diameter, and surrounded by lung parenchyma. The lung is a common site for metastasis from primary tumours of other organs. Lung nodules are the most common form of the metastatic disease (Ginsberg *et al.,* 1999). Pulmonary opacities are divided into the miliary type of less than 2mm, micronodules 2-7mm, macronodules 7-30 mm, and lung masses more than 30mm. Depending on the pulmonary nodule growth pattern, imaging pattern are different from a miliary like diffused micro-nodular (snowstorm of thyroid carcinoma), to a numerous large - defined masses (cannon balls), as in choriocarcinoma. (Boitsios *et al.,* 2010). Absence of metastatic in malignancies nodules is a good sign of the treatment response (Herold, 1996). The CT scan in most situations is the best modality for lung metastasis evaluation. CT scan imaging is the choice method for evaluation of pulmonary nodules and sequential follow-up of patients with extra-pulmonary malignancies (Diederich, 2004). For routine examination of the lungs, a CT scan will be done with 1-1.5 and 2mm(In our center) slice thickness to diagnose metastatic lung nodules with complete overlap of sections (Diederich *et al.,* 1999). On the other hand, as pulmonary nodules are important findings in patients with primary malignancies, it is important to determine whether the cancer has metastasized to the lungs or not? Moreover, this issue is important in cancer staging. Previous study showed that a thin slice thickness improved small nodule detection (Fishbach *et al.,* 2003).

With MDCT, submillimetric slice thickness can be acquired. This should optimize lung nodule detect though no study has yet confirmed these data (Knollmann and Coakley, 2006).In this diagnostic study, the ability of pulmonary multi-slice CT scan of 0.625 mm slice thickness with 2 mm slice thickness were compared in pulmonary metastatic nodular diagnosis . To our knowledge, this is a first study at the level of submillimetric slice thickness.

MATERIALS AND METHODS

This study was classified as a diagnostic study to determine the accuracy of multi-slice CT scan in metastatic lung nodule detection performed on the submillimetric slice thickness. The patients were selected from patients attending a university hospital clinic in Sari. Inclusion criteria were all patients who were diagnosed with a primary malignant tumour, suspected to lung metastasis which was influential on the primary tumour staging, treatment plan and patient follow up. Exclusion criteria were history of chronic disease such as tuberculosis, occupational pulmonary diseases, other pulmonary nodular diseases, more than six pulmonary nodules and history of chemotherapy or radiotherapy for any malignancies. Based on the similar previous studies, 110 patients with primary neoplasms were included in this study for rule out of lung metastasis. Consecutive attendances of the CT scan of the hospital were enrolled into this study. Demographic variables (age and gender), clinical and laboratory history of each patients were recorded. Primary tumour location, pathologic type and number and diameters of pulmonary nodules also demonstrated. A nodule was defined as opacity with less than 3 cm diameter. For the aim of staging, all patients were studied by a 16-slice MDCT GE with 2mm slices. Then thin submillimetric slice thickness (0.625 mm) were studied and saved on the PACS. All CT scans were seen and reported by two board-certified radiologists simultaneously the radiologists undertook consensus review. At first all CT scan of 2mm slice thickness (routine), latter submillimeter slice thickness to assess pulmonary nodules. Not more than 10 patients per day were investigated, to avoid a negative effect of the reviewer's fatigue during interpretation. Scans were offered in randomized order. If inconsistencies existed, a second opinion of third observer was obtained to resolve unclear cases. Diameter sizes were measured by software after finding a nodule visually. The biggest and smallest diameters were recorded. The data is then extracted and analysed by conventional statistical methods and equations by using SPSS version 18. Chi-Square and Fisher Extract tests were used for qualitative variables. Independent t-test and one way ANOVA was used for analysing quantitative variables. Sensitivity, specificity, positive and negative predictive values were estimated for imaging methods. In all cases $P < 0.05$ was considered statistically significant. to the method and implementation, no change or any negative inappropriate intervention in the treatment of patients were imposed. No injection of contrast medium and radiation above the standard limits were used. Informed consent was obtained from patients to collaborate on projects.

Imaging Methods

Pulmonary nodules may be identified and followed through a chest radiograph, CT scan, MRI and PET scan (Chandarana *et al.,* 2013). Spiral CT scanning is the technique of choice in the

Table 1. Parameters of lung 16 MDCT acquisition

1.Slice thickness	2mm	0.625mm
2.Reconstruction interval (mm)	0.6	0.6
3.Pitch(collimation/table displacement)	1.375	1.375
4.Table speed(mm per rotation)	27.5	13.75
5.Acqusition time(sec)	5.5 to 9	11to 18
6.Rotation time(sec)	0.5 to 0.8	0.5 to 0.8
7.Reconstruction thickness(mm)	2.5- 5	1.25-2.5
8.FOV(cm)	25-35	25-35
9.MAS	50-100	50-100
10.KV	120	120

Table 2. Comparsion of the results of 2mm with submillimetricslice thicknessin patients

	Negative	Positive	2mm submm
58	19	39	Positive
52	51	1	Negative
110	70	40	

the importance of CT scans with multiple and thinner slices in diagnosis of pulmonary nodules are shown. By changing the parameters, detection of lung nodules increased. In other words, creating a gap will miss small pulmonary nodules. On the other hand, in the thin slice thickness, the detection of pulmonary nodules is higher. Therefore, slice thickness is the most significant factor for pulmonary nodule detection. By reducing the slice thickness from 10 to 5 and then to 2mm, the sensitivity or proportion of lesions detection increases dramatically (Schoepf *et al.,* 1999). The multi-detector systems would lead to better detection of small nodules (Schoepf *et al.,* 1999; Hanamiya *et al.,* 2012; Retico *et al.,* 2008) In addition, the pitch standard must be limited to a maximum of 1.5 to prevent the under-staging of pulmonary metastatic disease (Wright *et al.,* 1996). The CT images were obtained from the entire lung in a single breath hold at 120 kv, 100 mAs, and with a collimation of 1 mm. In order to increase resolution in all planes, thin-slice sections were reconstructed with a high-resolution reconstruction algorithm with window and center settings appropriate for lung parenchyma (level 600 HU, width level 1600 HU).The MDCT protocols are presented in Table1. The CT was scored as positive when at least one nodule was detected. Readout was performed simultaneously for the different slice thickness, starting with 2 mm for all patients, followed by submillimeter .Instances of more than six nodules were classified as diffuse disease and were excluded from the study.

RESULTS

Of the 110 patients studied, 61 were male, 55.45%, and 49 patients, 44.54%, were female. The age range was 17-88 years old, and the mean age was 60.79 ± 14.63. The average age of men was 58.32 ± 15.46 and 63.87 ± 13.57 for women. The most commonly reported cancer in patients was ductal cell carcinoma of breast (21.78%), B cell lymphoma (10.89%) and Hodgkin lymphoma (9.90%), respectively (Fig.1). In the performed CT scans by radiologists, the patients images with 2mm slice thickness, in 36.36% (40 cases) nodules were found and in the remaining patients (63.64% or 70 cases), nodules were not seen. The images with submillimetricslice thickness were examined, in which 52.70% (58 cases) nodules were found and in 47.30% (52 cases) nodules were not seen (Table2). The largest nodule (a mass) measured by radiologists in 2mm slice thickness andsubmillimetricslice thickness was

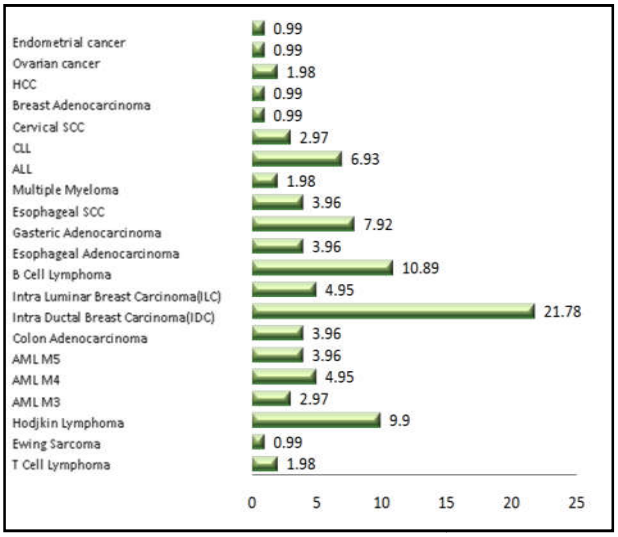

Figure 1. The frequency of primary malignancies in patients

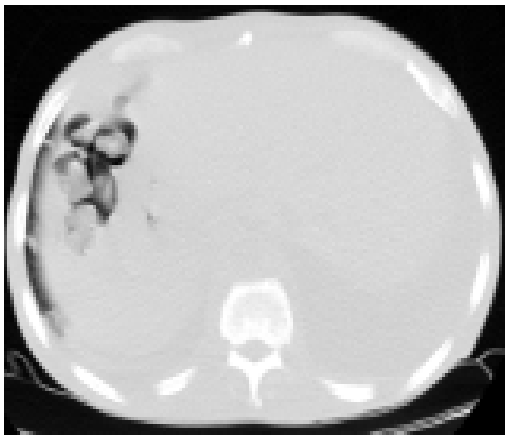

Fig. 2A. The 2mm slice thickness of lung CT of 77 years man with oesophageal carcinoma show one nodule at sub pleural of lower right lung lobe

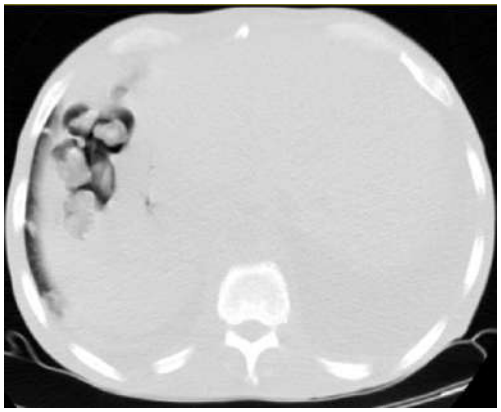

Fig. 2B. The 0.625mm slice thickness show two nodules with better delineation

59mm and 57mm, respectively and the smallest nodule was 2mm in both images. Radiologists confirmed more than 215 nodules in images with 2mm slice thickness and more than 288 nodules in submillimetricslice thickness. Based on the results, the maximum sighting of nodules in the submillimetricslice thickness that radiologists have reported that in 58 patients (52.70%) nodules were found, of which in 42 cases (72.4%) the number of nodules were from 1 to 6 and 16 cases (27.6%) had more than 6 and uncountable nodules. In addition, sensitivity, specificity, negative predictive value and positive predictive value were calculated using the 0.625 mm sections as the gold standard Sensitivity.

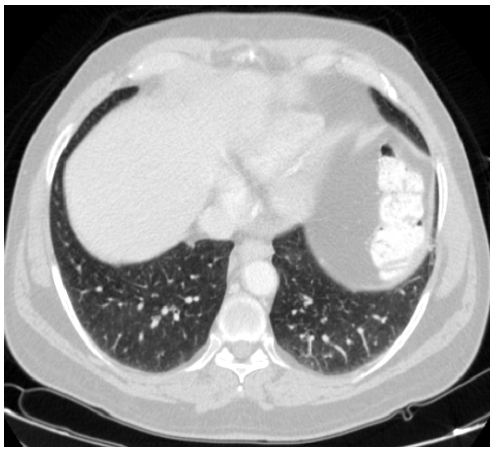

Fig. 3A. The 2mm slice thickness of lung CT of 57 years man with colon carcinoma show subtle right juxtadiaphragmatic thickening (scar?)

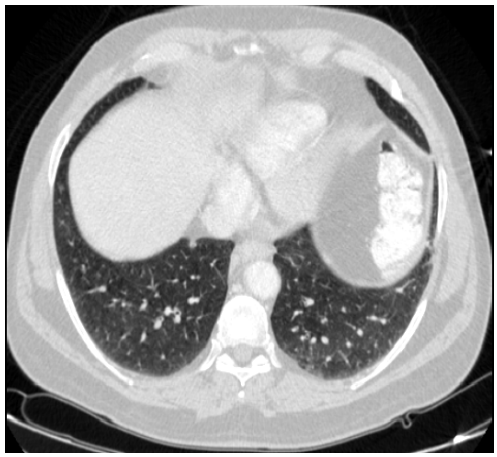

Fig. 3B. The 0.625mm slice thickness show improved visualization of nodule

Specificity, positive and negative predictive value and positive predictive value of 2mm sections were 97.5(87.1-99.5) ,72.8(61.4-81.8) ,72(61.3-82.7) and 98(94.3-100) respectively. False positive findings were reported%2.5(1 case) for 2-mm section for radiologists meaning all reported nodules were confirmed with 0.625 mm slice thickness. As an index for concordance the Kappa value was used. Nodules detection determined for 2 and 0.625mm reconstruction intervals showed a k value of 0.64, indicating a good agreement (Fig.2, 3). In terms of the type of cancer associated with the presence of nodules in the lungs, most were associated with B cell lymphomas, adenocarcinomas of the stomach and the breast ductal cell carcinoma (DCC); the lowest is lobular cell carcinoma of breast (LCC), and secondly is ALL. Also observed with increasing age, is the number of nodules in the lungs of patients with pulmonary nodule increases; this increase is in ages above 50 years old, with a greater slope. In women, the most common type of cancer was ductal cell carcinoma (DCC) and lobular cell carcinoma of breast (LCC), and B cell lymphoma and Hodgkin's disease was more common in men.

DISCUSSION

Application of submillimetricslice thickness of multi-slice CT scan compared with 2 mmslice thickness showed a higher of pulmonary nodule detection for the submillimetricslice thickness. The most important results of our study was the importance of searching for lung metastases in patients with malignancy using submillimetric CT scans and the complete overlap of the lung. In this study 110 patients were evaluated for pulmonary nodules using multi-detector CT scan of thorax. In this study 55.45% of patients were men and 46.54% were women, which were expected because of higher prevalence rate of lung cancer in men. In 36.36% of 2mm slice thickness CT scan, pulmonary nodules were reported compared to 51.81% of submillimetric slice thickness CT scan. The chest CT scan resolution can be improved by reducing the thickness of the slices. Hence, a CT scan with thin slices is preferred for evaluation of pulmonary nodules. Early detection of pulmonary metastases of extra-pulmonary cancers at the beginning of the treatment is crucial. Small peripheral pulmonary nodules, most of which are metastatic, are difficult to be diagnosed by radiography because of being overshadowed by vessels or ribs (Hanamiya *et al.,* 2012; Retico *et al.,* 2008). If single nodules were found in CXR, the risk of lung nodules in CT scans should be considered. It is important to know whether the number of pulmonary metastases is rising, unchanged or declining.

Multi-detector CT scan, depending on the need, has the ability to obtain images with a slice thickness of 0.5 mm to 10 mm; and on this basis, it has the ability to reconstruct the sagittal and coronal plane according to the conditions and clinical needs. Mostly circular shaped nodules in the peripheral regions of the lower lobes of the lungs (due to the greater volume of blood flow in these areas) can be seen. For routine examination, a CT scan of the lungs is performed in 2mm of slice thickness. The use of multi-detector systems allows images of the entire lung to be obtained during a deep breath (Retico *et al.,* 2008) which its images with increased spatial resolution and thinner slices reduce errors. In thin slices thickness (1mm) comparing with thick slices, metastatic pulmonary nodule can be demonstrated in multiple sections, therefore, mostly to be visible for radiologists. With the technologic progress from single detector to multi-detector spiral CT scans it is possible to produce thinner sections and overlapping the whole lung that helps for better detection. Metastatic pulmonary nodules can be missed by thick slices CT scan. Despite the increase of pulmonary metastatic nodal detection rate by the MDCT in the Ellis *et al.,* (2011), other nodules were found in thoracoscopy and thoracotomy which were not mentioned in the lung CT scan (Ellis *et al.,* 2011). Parson and colleagues (2007) were reported 46% of pulmonary metastases in manual lung palpation and pulmonary metastasectomy that were not reported by the previous CT scan (Parsons *et al.,* 2007). In a retrospective study conducted by Hanamiya and co-workers (2012), 75% of patients with extra-pulmonary malignancies had nodules in thin slices (2mm) CT scan. Nodules with the diameter greater than 10 mm were malignant and less than this threshold were benign (Hanamiya, 2012). Fishbach and colleagues (2003) compared 1.25 mm CT scans with the 5 mm slice thickness visually. The agreement for finding nodules between two radiologists for 1.25 mm scans were more than 5 mm scans, k.value=0.753 versus 0.562. Sensitivity, specificity, positive and negative predictive values of 5 mm sections were 88, 100, 100, and 100% respectively. They were 86, 100, 100, and 93% for 1.25 mm sections (Fishbach *et al.,* 2003). Their results show significant increase of diagnostic rate of nodules in accordance with reducing of slice thickness which were similar to our results. In this study an increase of sensitivity and decrease of specificity were seen by reducing in the slice thickness. Sensitivity or proportion of lesion detection was increased dramatically by decreasing the slice thickness. On the other hand, false positives (specificity) were increased which is an important factor in disease confirmation. In addition to the increased chance of missing small nodules during the movement of heart, mediastinum and diaphragm in thin slices. High numbers of scans, received X-Ray dosage, consumed time are some disadvantages of using thinner slices that increase the interpretation workload of radiologists and physicians. In general, decreasing slices thickness in any conventional or spiral CT scanning system decreases the specificity alongside with increased sensitivity. Histopathology evaluation was not aimed in this study and we suggest it in future works to increase the diagnosis precision. Other limitation is this study, is being the first research in this regard. The most resembling study is the fischbach that allowed a reconstruction of 1.25-mm slice thickness in addition to the standard of 5-mm slices were included in a prospective study. In addition, large number of scans (150-200 scans of 2mm section and 300-600 sections of sub-mm) needs to be checked and interpreted that was time-consuming and tiring.

Conclusion

Sensitivity of diagnosis of metastatic pulmonary nodules increases with submillimetric slices thickness. Submillimetric slice thickness (0.625mm) had significantly higher detection ability compared to the 2 mm slice thickness. Due to the importance of treatment plan and follow-up of patients with metastatic pulmonary nodules, it can be recommended to perform a submillimetricslice thickness CT scan as the gold standard for diagnosis and staging of patients. The MDCT in submillimetricslices increases image quality efficiency and patients' acceptance.

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