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Role of Dual Energy CT in the Characterisation of Lung Lesions

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Abstract:

Aim: *To study the clinical utility of Dual energy CT in differentiating benign and malignant lung lesions.* ***Introduction:*** *Dual energy CT is emerging as a problem solving tool with rapid data acquisition. The images are acquired at two energy levels, namely 80 and 140 kVp. Changing the photon energy levels allow us to manipulate the tissue attenuation.* ***Methodology:*** *The study included patients referred to Department of Radio diagnosis at our hospital for evaluation of lung lesions. These patients underwent a plain CT study of thorax, routine contrast enhanced CT and dual energy CT protocols on a dual source dual energy Siemens Somatom Definition CT scanner. Comparison was done using intraclass correlation coefficient between plain and virtual non contrast CT values and between degree of enhancement and iodine overlay values. Lesions were defined as benign or malignant based on histopathological or clinical correlation. The diagnostic accuracy of dual energy CT for differentiating benign and malignant lesions using a 20 HU cut off was calculated using statistical tools. Receiver operating Characteristic analysis was performed to obtain cut off value with appropriate sensitivity and specificity.* ***Results:*** *41 patients were involved in our study. CT numbers on virtual non enhanced and plain CT images showed good agreement. Degree of enhancement from dynamic contrast enhanced CT and iodine overlay showed good agreement. Diagnostic accuracy for malignancy using CT numbers on iodine overlay images showed good significance with a sensitivity of 94.29%, specificity of 68.75%, positive predictive value of 86.84%, negative predictive value of 84.62%. The overall accuracy was calculated to be 86.27. Using ROC analysis, we have proposed a cut off of 22.250 with a sensitivity of 91.4% and specificity of 75%. We concluded that Dual energy CT of thorax can be convincingly used in evaluation of lung pathologies to differentiate benign and malignant lesions with significant accuracy.*

Keywords: ***Dual energy CT, thorax, lung lesions***

1. Introduction

The key attraction of dual energy CT is its ability for material differentiation and a far more objective quantification. Independent attenuation values from two energy sets can be used to create virtual non-contrast images from contrast enhanced imaging thus avoiding the need for multiple phases of imaging.

Dual-energy CT imaging of the thorax simultaneously provides a virtual non-enhanced and an iodine contrast enhanced image from a single scan performed after iodine contrast administration. The advantages of this technique include reducing radiation exposure to patients and reducing measurement error during comparison of multiple scans as well as an objective measurement of the amount of iodine concentration in these lesions which can help with better characterization and delineation of benign and malignant pathologies.

2. Methodology

Based on the inclusion and exclusion criteria, 51 patients referred to the Radiodiagnosis department of AJ Institute of Medical Sciences with clinical history or chest radiograph investigation of pulmonary pathologies were selected for the study.

The imaging reports and patient charts and investigations were utilised to establish a final diagnosis. This was then classified into either a benign or malignant group. Whenever a histopathology proven diagnosis was available, it was used as the reference standard. In conditions without a tissue diagnosis, the final clinical diagnosis, considering treatment and eventual outcomes, were considered as a reference standard. Studies that lacked a confident clinical or pathological diagnosis were excluded. Patients of age less than 18 years, with contraindications for intravenous contrast agent administration, those who were suspected to have interstitial lung diseases or show an interstitial pattern of pathology on routine imaging, Restless or uncooperative patients were excluded from the study.

CT examinations were performed by using the Dual Energy CT mode of the Siemens Somatom Definition dual source dual energy CT scanner. Each patient underwent a full series of routine contrast enhanced CT thorax scan as per the department protocol from lung apices to costophrenic angles which includes a plain Thorax CT at 120 kVp followed by injection of 1 - 1.5 ml/ kg of body weight with a minimum of 60 ml of ultravist (iopromide) contrast containing an iodine concentration of 370mg/ml which was injected at the rate of 3 ml/sec using a power injector. This was followed by a 40ml saline bolus. Venous phase image at 120 kVp was obtained at approximately 60 seconds delay after scan initiation using bolus triggering depending on ROI attaining 100HU threshold at aorta. This was followed by a dual energy CT Thorax protocol at approximately 3 minutes' delay. We have ensured that the area of interest is placed within the dual energy circle and used a dedicated dual energy CT protocol for the thorax, which was recommended by the manufacturer. Tube currents of two x-ray tubes of 80 kV and 140 kV were fixed as ratio of approximately 4:1 (50 mAs [effective] for 80 kV and 210 mAs [effective] for 140 kV). The parameters set for the study are as in Table 1.

Table 1: Study Parameters

	DUAL ENERGY CT	PLAIN CT	CONTRAST CT
Kv	140 kV / 80 kV	120 kV	120 kV
Mas	Automatic (CARE Dose4D)	Automatic (CARE Dose4D)	Automatic (CARE Dose4D)
Rot. Time	0.33 s	0.5 s	0.5 s
Pitch	0.55	1.2	1.2
Scan Duration	10 - 12 s	7-8 s	7-8 s
Scan Direction	Cranial-caudal	Cranial-caudal	Cranial-caudal
Slice Width	5 mm	5 mm	5 mm
Increment	5 mm	5 mm	5 mm
Kernel	B31f medium smooth +	B30f medium smooth	B30f medium smooth

For all patients, data of 80 kV, 140 kV, and weighted average image of nonenhanced and 3-minute-delayed scans were transferred to a workstation (MultiModality Workplace; Siemens Medical Solutions). Reconstructed images of 1.5 mm thickness were generated from 5mm thick images. The weighted average image is the approximate 120-kV image, which is automatically generated from a combination of 140-kV and 80-kV data by using weighting factor 1:4 (140 kV: 80 kV). The plain and venous phase images were transferred to PACS for clinical use and independent generation of an imaging diagnosis.

2.1 Image analysis

Image data was reconstructed using a slice thickness of 1.5 mm. The images were analysed using Lung Nodules Dual Energy Application of Siemens Medical solutions on a dedicated research MultiModality Workplace workstation. Virtual non contrast and iodine enhanced images were generated from the 3 mins delayed scan data. The iodine component can be demonstrated as a color overlay on a background virtual nonenhanced image of 3-minute-delayed scan with semitransparent mode. The mean CT attenuation value on virtual non contrast images and iodine overlay value was generated by drawing Region Of Interest (ROI) circles in the lesions. ROI circles were as centrally placed as possible excluding areas of necrosis or cavitation, if present. The data sets obtained include CT attenuation value on plain routine images, CT attenuation value on venous phase images. The degree of enhancement is determined by calculating the difference between CT value of venous phase images and plain images. The CT attenuation value on virtual non contrast images and overlay value from iodine maps were tabulated. We compared the CT values on plain routine CT images with that of virtual non contrast images and between the CT values generated from iodine overlay values with the degree of enhancement of the lesion. The iodine overlay values were compared in terms of their diagnostic accuracy for distinguishing malignant and benign lesions.

2.2 Statistical analysis

For each case, the patient identification details, age, gender, clinical indication, imaging diagnosis, final (clinical/histopathological) diagnosis, characterisation of final diagnosis into benign and malignant, virtual non contrast CT value, iodine overlay CT value, Plain CT value, Venous phase CT value and degree of enhancement were recorded and data was collected on a Microsoft Excel Spread sheet. The virtual non contrast CT value was compared with the CT value on routine non contrast scans. The overlay CT value obtained from iodine maps were compared with the degree of enhancement. Degree of enhancement on iodine enhanced image as depicted by overlay value was used to assess diagnostic accuracy for malignancy. Receiver Operating Curve analysis was performed to obtain cut off value with appropriate sensitivity and specificity. Collected data was analysed by SSPS software according to frequency, percentage, mean, standard deviation, descriptive statistics and confidence intervals. Comparison of plain CT values and Virtual non contrast values was done by intraclass correlation coefficient. Similarly, comparison of degree of enhancement and iodine overlay values were also performed by intraclass correlation coefficient. Man whitney U test was calculated to analyse statistically significant differences between the CT numbers of benign and malignant nodules.

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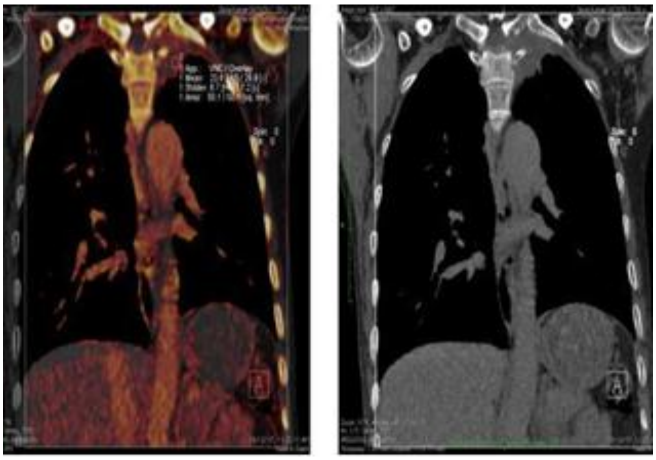

Figure 1 (a,b): Iodine overlay image and coronal virtual non contrast image of a pancoast tumour in a 59 year old male patient showing overlay value > 20 HU (26.8)

3. Ethics

The study was performed after review and clearance by the Institute's ethical committee. Informed consent was taken from every participant in the study. The authors whose names are listed above certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter.

4. Statistics and Results

In this study, a total of 41 (80%) male patients and 10 (20%) female patients were involved. Our study subjects ranged in ages from 17 to 71 years. Of these, 5 (10%) were below 40 years of age, 8 (16%) between 41 to 50, 16 (31%) between 51 to 60 and 22 (43%) above 60 yrs of age.

The 51 cases included in this study included both benign and malignant etiologies. 35 (68.6%) of the cases were malignant and 16 (31.4%) were benign. The benign spectrum included cases of tuberculosis (n =7, 13.7%), aspergilloma (n = 1, 2%), sarcoidosis (n = 1, 2%), infective (n = 3, 5.9%), inflammatory nodule (n = 1, 2%) and consolidation (n = 4, 7.8%). The malignant etiologies included cases of metastases (n = 14, 27.5%), mesothelioma (n = 1, 2%), small cell carcinoma (n = 3, 5.9%), adenocarcinoma (n = 6, 11.7 %) and squamous cell carcinoma (n = 11, 21.5%).

Agreement of CT numbers of the image series was analysed by calculating the intraclass correlation coefficient between plain and virtual non contrast images with a 95% confidence interval. The mean CT value on plain and virtual non contrast images were 30 and 28.5 respectively. Comparison of CT numbers on plain CT images and virtual non contrast images showed excellent agreement (ICC 0.96; $p < 0.001$).

Agreement of enhancement of the lesions were analysed by calculating the intraclass correlation coefficient between degree of enhancement and iodine overlay with a 95% confidence interval. Comparison of degree of enhancement and iodine overlay values showed good agreement (ICC 0.83; $p < 0.001$). The mean value of degree of enhancement and iodine overlay were 32 and 39 respectively.

The Mann Whitney U test was used to analyse statistically significant differences between the CT numbers of benign and malignant nodules. In our study, the test yielded a p value of 0.002 for degree of enhancement and 0.001 for iodine overlay values which are highly significant.

Between the degree of enhancement and iodine overlay values, the diagnostic accuracy was compared by calculating sensitivity, specificity and accuracy. By comparing the diagnostic accuracy for differentiating benign and malignant nodules with a 20 HU enhancement cutoff for malignant nodules, the iodine overlay values had a sensitivity of 94.29 (Confidence interval 86.6 - 101.98), specificity of 68.75 (Confidence interval 46.04 - 91.46), positive predictive value of 86.84 (confidence interval 76.09 - 97.59), negative predictive value of 84.62 (confidence interval 65 - 104.2). The overall accuracy was calculated to be 86.27 (confidence interval 76.83 - 95.72).

We performed Receiver Operating Characteristics (ROC) analysis to determine the accuracy of a cut off of 20 HU overlay value in differentiating benign and malignant thoracic lesions. The area under the curve was 0.785 with a p value of 0.001 indicating it is acceptable for differentiating malignant lesions from benign. Based on the coordinate assessment of the curve, we propose a cut off of 22.250 with a sensitivity of 91.4% and specificity of 75%.

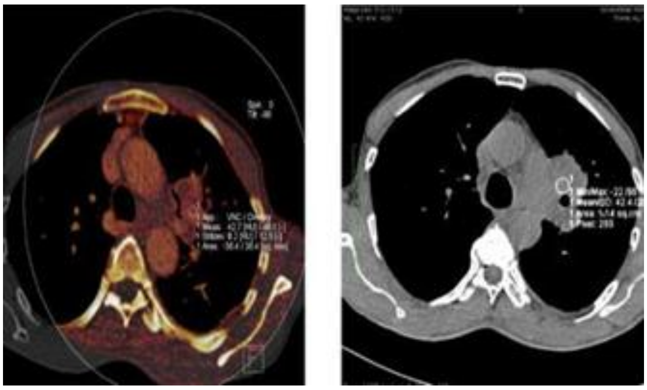

Figure 2 (a,b): Iodine overlay image and plain CT image of a malignant lung lesion in a 63year old male patient showing overlay value > 20 HU and similar values of CT attenuation of VNC and plain CT images

5. Discussion

Dual energy CT is gaining popularity due to the spectrum of unprecedented applications it provides as added diagnostic gain in a variety of pathologies. Its attraction lies not only in the incremental diagnostic value but also the added advantage of shorter scan time, reduction of artifacts and radiation dose.

The Characteristics of malignant lesions as confirmed by previous studies by Swensen et al,[1] Zwirevich et al,[2] Ogawa et al,[3] Chae et al,[4],[5] Wei Shu Hou et al[6] and Kawai et al[7] indicated that malignant lesions show increased uptake on iodine enhanced images.

Our study indicated that benign and malignant lesions can be distinguished with a threshold of 20 HU on dual energy CT with a sensitivity and specificity of 94.29% and 68.75% compared to Wei Shu Hou et al[6] who used Normalised iodine concentration value of 0.34 as a cut off to distinguish \benign and malignant lesions on dual energy spectral CT with a sensitivity and specificity of 86% and 100 %. Hence dual energy CT has a better role in identifying malignant lesions but the accuracy of dual energy spectral CT seems to be better.

Ogawa et al[3] performed the dual energy CT scan at 60 seconds delay and late contrast enhanced image 120 kVp CT at 100 seconds. They observed that peak enhancement of the lesion was seen at 60 seconds dual energy images. However, our study has employed the use of delayed dual energy CT images at 3 minutes' delay to quantify iodine values for successful differentiation of benign and malignant lung lesions.

Our study results were very similar to Chae et al[4],[5] who studied pulmonary nodules on dual energy CT using a protocol similar to ours. They showed an intraclass correlation coefficient of 0.83 between CT numbers on virtual non enhanced images and non enhanced weighted average images as compared to 0.96 on our study and an intraclass correlation coefficient of 0.91 between CT values on iodine overlay images and degree of enhancement as compared to 0.83 on our study. They found that when they compared the accuracy of differentiating malignant and benign nodules on iodine-enhanced image, it showed a sensitivity of 92.0%, specificity of 70.0% and high diagnostic accuracy of 82.2%. In comparison, our study had a sensitivity of 94.29%, specificity of 68.75 %, and an overall accuracy of 86.27% which indicates very similar results. However, Receiver operating curve analysis of our data yielded a cut off of 22.250 as a better indicator for differentiating benign and malignant lesions with higher sensitivity and specificity.

Long Jiang Zhang et al studied dual-energy CT imaging of thoracic malignancies and concluded that Dual Energy CT can provide helpful information for the characterization and staging of thoracic malignancy by quantitatively measuring iodine enhancement on iodine maps or monochromatic imaging.[8] This can be an adjunctive to our present study

Hence, our findings generally concur with other studies which used dual energy CT to characterise benign and malignant lesions such as Chae et al and Wei Shu Hou et al as described earlier.

Study by Shingo Iwano et al[9] on lung cancer patients with dual energy CT to correlate degree of histopathological

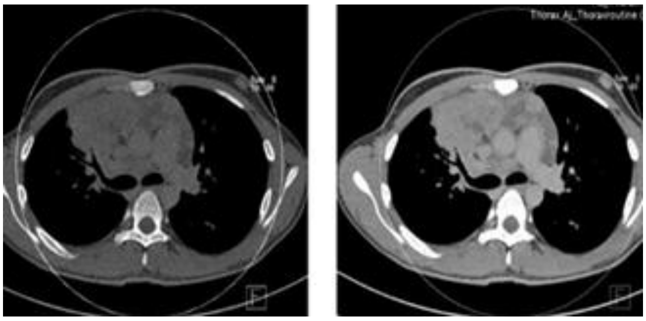

Figure 3 (a,b): Virtual non contrast image and dual energy enhanced weighted average image of the same lesion

differentiation and iodine concentration indicated that high-grade tumours tended to have lower iodine volumes than low-grade tumours, particularly at the delayed phase.

Lu GM, Zhao Y, Zhang LJ and Schoepf UJ[10] studied dual energy CT of lung and advocated the usefulness of DECT-based selective iodine uptake measurements in the diagnosis and surveillance of thoracic malignancies. They suggest that the diagnostic accuracy of Dual Energy CT for malignancy using CT numbers on iodine-enhanced images obtained with a cutoff of 20 HU was comparable to that using the degree of enhancement.

Dual energy CT in clinical practice by Thorsten Johnson, Christian Fink, Stefan O[11] describes the application of dual energy CT to differentiate between malignant and benign lesions on dual energy CT and its application in characterisation of pulmonary nodules and response assessment in lung cancer. The differentiation of iodinated contrast media by DECT is a potential surrogate marker for regional blood volume and thus angiogenesis, which can be used for non-invasive characterization of pulmonary lesions.

Based on our assessment, we can conclude that dual energy CT of thorax provides incremental diagnostic gain in differentiating benign and malignant lung lesions with a single post contrast scan. CT numbers of virtual non contrast images and plain CT images showed reliable agreement. In routine contrast enhanced CT, there can be errors in measurement due to different positioning of ROIs. Effect of such measurement errors might be more significant in the smaller lesions. This is eliminated in Dual energy CT protocols as the same ROI generates both virtual non contrast CT value and iodine overlay values.

The significant correlation between CT numbers on plain 120 kVp images and virtual non contrast images indicates that the virtual non contrast images provide similar diagnostic detail as routine plain CT images. There is also the additional advantage of reducing beam hardening artifacts and better characterisation of the margins of the lesion.

However, we have observed that cases that were concluded as of tubercular in etiology seemed to show variation between their agreement between overlay values and degree of enhancement. This requires further evaluation.The use of dual energy CT in morbidly obese patients is limited due to the limited FOV and also because of

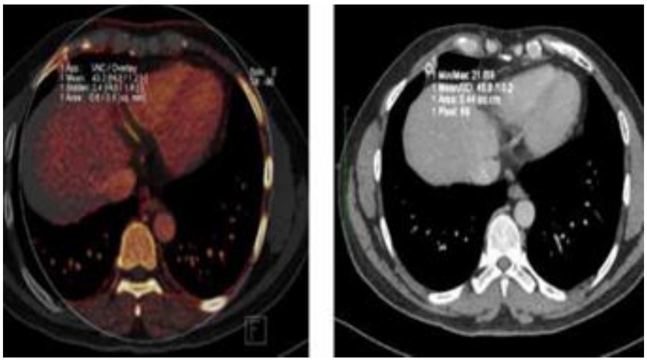

Figure 4 (a,b): Iodine overlay image and routine contrast CT image of a benign lesion in a 45 year old male patient showing overlay value < 20 HU and similar values of CT attenuation.

high image noise often interfering with structural and functional image analysis. We observed that there was more image noise in virtual non contrast images as compared to plain CT images. This provides a challenge to the radiologists interpreting these images and tiny details such as small calcifications may be missed.

There are several limitations of this study such as single reader analysis of the regions of interest, small number of cases of benign pathologies. Many of the final diagnosis were not supported by histopathological analyses which is a challenge faced in a clinical scenario.

Despite the well-established evidence in favour of dual energy CT being capable of delineating lesion characteristics and characterising benign and malignant lesions with acceptable accuracy, some limitations of this technique needs to be accepted in order to exhaust the full potential of this modality for routine clinical applications. Further efforts are encouraged to firmly establish Dual Energy CT as the default technique for CT image acquisition.

6. Conclusion

Dual energy CT of thorax can be convincingly used in evaluation of lung pathologies to differentiate benign and malignant lesions with significant accuracy. Virtual non contrast images generated from dual energy CT is at par with routine plain CT images in terms of CT values of the lesions. The iodine overlay values generated from dual energy CT images is similar to degree of enhancement of lesions obtained from routine dynamic contrast enhanced images. The degree of enhancement of a pulmonary lesion after iodine injection aids in distinguishing benign from malignant lesions, a test that Dual Energy CT can now perform in a single scan, and using the same Region of interest thus decreasing measurement error and radiation dosage that subjects are exposed to.

We propose a cut off of 22.250 with a sensitivity of 91.4% and specificity of 75% to differentiate benign and malignant lung lesions. However, this should be considered in addition to other standard imaging characteristics of the lesion.

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