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Efficacy of Low Dose Computed Tomography Using Adaptive Statistical Iterative Reconstruction in Lung Cancer Screening

SABRY ALAM EL-DIN M. EL-MOGY, M.D.*; MOHAMMAD Kh. EL-BADRAWY, M.D.*;
NEHAL E. EL-EMAM, M.Sc.** and NEHAL THARWAT, M.D.*

The Departments of Diagnostic Radiology and Chest Disease**, Faculty of Medicine Mansoura University* and Ministry of Health***

Abstract

Background: Lung cancer is the most common malignant tumor and the leading cause of cancer-related deaths all over the world. Early detection and treatment are important to increase survival rate. Therefore, screening of lung cancer should target those individuals at high risk.

Aim of Study: To detect the efficacy of low dose computed tomography (LDCT) of the chest with adaptive statistical iterative reconstruction (ASIR) algorithmas a screening method in diagnosing early stages of lung cancer and thus decrease the disease related morbidity and mortality as itminimizes exposure to ionizing radiation while maintaining sufficient image quality.

Material and Methods: Ninety-six high risk cases (current smokers or ex-smokers), 94 males and 2 females, withage range from 50-78 yearswere included in this study. All cases underwent CT of the chest using low dose protocol with-ASIR algorithm with different blending levels of reconstruction (40%, 60%) for lung cancer screening. All images were interpreted using the International Early Lung Cancer Action Program (I-ELCAP) diagnostic protocol for lung nodule diagnosis and management.

Results: From 96 cases included in the study, 82 cases had normal chest CT and 14 cases showed abnormal findings in chest CT (4 of them showed nodular lung lesions and the other 10 cases showed other findings related to smoking as bullae, bronchial wall thickening, emphysema, honey combing and bronchiectasis). Among the 6 nodules detected in the 4 cases, one nodule was ≥15mm, and 5 nodules were <15mm. According to I-ELCAP diagnostic protocol, one nodule was considered positive and 5 nodules were considered semi-positive. LDCT chest using ASIR algorithm for lung cancer screening revealed high sensitivity and specificity for detecting lesions at cut off point size 6 mm (84.9% and 100% respectively). The area under receiver operating characteristic (ROC) curve for prediction of nodule with cutoff point size 6mm was 0.938 with 95% confidence interval (0.887-0.990).

Conclusion: LDCT of the chest using ASIR algorithm is a promising and efficient tool for lung cancer screening with significant minimization of ionizing radiation exposure as well as preserved optimum image quality.

Key Words: *Lung cancer – Chest CT – Low dose – ASIR.*

Correspondence to: Dr. Sabry Alam El-Din M. El-Mogy, The Department of Diagnostic Radiology, Faculty of Medicine Mansoura University

Introduction

LUNG cancer is the most common malignant tumor and the leading cause of cancer-related deaths all over the world [1-3]. Its prevalence in Egypt is 4.22% in both sexes according to the National Population-Based Cancer Registry Program of Egypt in 2008-2011 [4]. About 75% of patients have advanced disease (stage III/IV) at time of diagnosis. In developed countries, the 5 year survival rate is about 15%-18% in patients with lung cancer. However, patients diagnosed early at (stage I) and underwent surgical resection the survival rate is above 70% that's why early detection and treatment is important [5-7].

Early cancer detection enhances prognosis. As early lung cancer is mostly asymptomatic, screening of lung cancer should target those individuals at risk such ascurrent smokers or former smokers as

Abbreviations:

LDCT	: Low dose computed tomography.
ASIR	: Adaptive statistical iterative reconstruction.
I-ELCAP	: International early lung cancer action program.
ROC	: Receiver operating characteristic.
CXR	: Chest X-ray.
NLST	: National lung screening trial.
IRTs	: Image reconstruction techniques.
GGO	: Ground glass opacity.
FBP	: Filtered back projection.
IR	: Iterative reconstruction.
IRB	: Institutional research board.
HU	: Hounsfield unit.
NCN	: Non calcified nodule.
PET	: Positron emission tomography.
SD	: Standard deviation.
CNR	: Contrast to noise ratio.

well, past radiation therapy to the chest, exposure to radon and asbestos, older age and those with lower socioeconomic status [5,8,9]. Smoking is the leading preventable risk factor for development of lung cancer. In Egypt prevalence of cigarette smoking is about 29% among adults [10,11].

Currently, no definitive biomarker or genetic factor has been identified for the prediction or the early diagnosis of lung cancer [12,13]. Computerized tomography (CT) is more useful for diagnosing cancer than chest X-ray (CXR) but its radiation dose is nearly 100 times more than CXR [14,15]. Therefore, it has more risks than its benefits of early diagnosis due to high radiation exposure. Low dose computed tomography (LDCT) is a chest CT scan done at settings to reduceradiation exposure compared to a standard chest CT. The radiation dose of LDCT is 22% of a standard CT [16]. LDCT has been applied as a promising approach for lung cancer screening according to the National Lung Screening Trial (NLST) [17,18]. The United States NLST has informed 20% decrease in lung cancer mortality rate with LDCT screening than that with CXR screening [19,20].

The image reconstruction techniques (IRTs) such as adaptive statistical iterative reconstruction (ASIR) in conjunction with lowering tube current will minimize radiation doses, while maintaining ground glass opacity (GGO) definition and overall image quality [21,22]. Quantitative image analysis using ASIR allows a decrease of about 40% in the tube current and the radiation dose with the same result in image noise magnitude and contrast-to-noise ratio compared with the conventional filtered back projection (FBP) [23-26]. To date, many types of iterative reconstruction (IR) algorithms have been introduced according to the CT machines or vendors, and widely used in clinical practice. Recently, application of the artificial intelligence showed a great promise for improving image quality of the reconstructed CT [27-29].

Aim of study:

The aim of this study is to detect the efficacy of LDCT of the chest with ASIR algorithmas a screening method in diagnosing early stages of lung cancer and thus decrease the disease related morbidity and mortality as it minimizes exposure to ionizingradiation while maintaining sufficient image quality.

Material and Methods

This is a prospective observational study that was conducted in the duration from December 2018 to December 2020. Study protocol was approved by our Institutional Research Board (IRB). Study cases were chosen from vulnerable population and written informed consents from all participants were taken. Personal privacy and confidentiality of all collected dataare guaranteed and respected in all levels of this study. Ninety-six cases were included in the study and subjected to detailed history taking and full clinical examination.

Inclusion criteria:

1- Age 50 years or more.
2- Smoking history ≥ 15 pack-years, being a current cigarette smoker or a former smoker who quit within the past 15 years.
3- Normal chest X-ray.

Exclusion criteria:

1- Patients with chest CT within the past 18 months.
2- Patients with previous lung cancer diagnosis.
3- Patients who have other previous cancer.
4- Patients with hemoptysis, unexplained weight loss >6.8kg in the past year.
5- Metallic implants or devices in chest or back.
6- Patients need for home oxygen supplementation or acute respiratory tract infection treated with antibiotics in the past 12 weeks.

CT scan image acquisition:

All cases underwent CT screening of the chest using low dose protocol [80-100 kilovolt (kVp) according to patient weight and 50 milli Ampere/second (mA/s)] using ASIR techniquewith different blending levels of reconstruction (40%, 60%) using multidetector CT scanner (Revolution EVO, GE Medical Systems). All the participants were asked to hold their breath at the end of inspiration as long as possible. Non contrast enhanced images were acquired with scan range from the costophrenic angle to the thoracic inlet. Other imaging parameters used were as follows: Matrix 512 X 512, field of view 500mm X 500mm, collimation 64 X 0.625mm, rotation time 0.5s, pitch2, slice thickness 2mm and scan duration 3-10s. Images were transferred to workstation supplied by the vendor and were evaluated with lung window settings (Level-450HU, Width 1500HU) and mediastinal window settings (Level 60HU, Width 400HU) by two radiologists with 15 years and 20 years of experience, respectively. Lung nodules were classified according to their density into calcified, solid, part-solid, and nonsolid nodules. The size and density classification of each nodule were recorded.

Lung nodule diagnosis and management:

The International Early Lung Cancer Action Program (I-ELCAP) diagnostic protocol was followed for image interpretation **[30]**:

1- *The CT scan was considered negative if:*

There are no non calcified nodules (NCNs).

2- *The CT scan was considered semi -positive if:*

a- Only nonsolid nodules of any size.

b- Largest solid (soft tissue density) NCN <6.0mm or largest solid component of part-solid NCNs <6.0mm.

c- Largest solid NCN or solid component of part-solid NCN 6.0 to 14.9mm with growth at non-malignant rate on CT scan 3 months later.

3- *The CT scan was considered positive if:*

a- Largest NCN ≥15.0mm.

b- Largest solid NCN or solid component of part-solid NCN 6.0 to 14.9mm with growth at malignant rate on CT scan 3 months later.

c- Solid endo bronchial nodule.

For negative and semi-positive results annual screening 12 months later is highly recommended. Positive results will need further investigations such as biopsy, positron emission tomography (PET) scan (if NCN ≥1 0mm), or if likely an infection, follow-up CT one month after antibiotics.

Malignant rate of growth in bronchogenic carcinoma corresponds to doubling time of nodule volume in about 1-18 months with average (4-8 months). Doubling time more than 18 months makes bronchogenic carcinoma unlikely except with broncho-alveolar carcinoma which need 2 years to double its size. While, benign nodules grow slowly or might even stop growing or shrink.

Statistical analysis of data:

The collected data were statistically analyzed using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 22 for Microsoft Windows (10). The normality of data was tested with one-sample Kolmogorov-Smirnov test. Data was statistically described as Mean ± standard deviation (SD), or frequencies (number of cases) and percentages (%). Sensitivity and specificity at different cut off points will be determined by receiver operator characteristic (ROC) curve to calculate the diagnostic performance.

Results

Ninety-six cases fitting the criteria of case selection were included in the study. Socio-demographic characteristics of studied cases are shown in Table (1).

Table (1): Socio-demographic characteristicsin the studied cases.

	Study group (n=96)	
Age/years:		
Mean ± SD	58.76±7.29	
Min-Max	50-78	
Age group:		
50-59	55.2%	
60-69	35.4%	
≥70	9.4%	
Sex:		
Male	94	97.9%
Female	2	2.1%
Smoking:		
Current smoker	88	91.7%
Ex-smoker	8	8.3%

Data are expressed as Mean ± SD or number (%).

All cases underwent LDCT chest screening using ASIR algorithm with different blending levels of reconstruction (40%, 60%). Among the 96 cases included in the study, 82 cases (85.4%) had normal chest CT while 14 cases (14.6%) showed abnormal findings in chest CT (4 of them showed nodular lung lesions and the other 10 cases showed other findings related to smoking as bullae, bronchial wall thickening, emphysema, honey combing and bronchiectasis).

The size of the 6 nodules detected in the 4 cases are shown in Table (2). According to theI-ELCAP diagnostic protocol, only one nodule was considered positive(16.7%) (Fig. 1) and the other 5 nodules (83.3%) were considered semi-positive (confirmed on follow-up CT after 3 months) (Fig. 2). As regards the site of the lesions, 5 nodules (83.3%) were peripheral while 1 nodule (16.7%) was central.

Table (2): Size of nodules in the studied cases.

Size of lesion (mm)	Nodules (n=6)	
	No.	%
<15 mm	5	83.3
≥15 mm	1	16.7
Mean ± SD	8.67±3.82	
Min-Max	6-15	

Data are expressed as Mean ± SD or number (%).

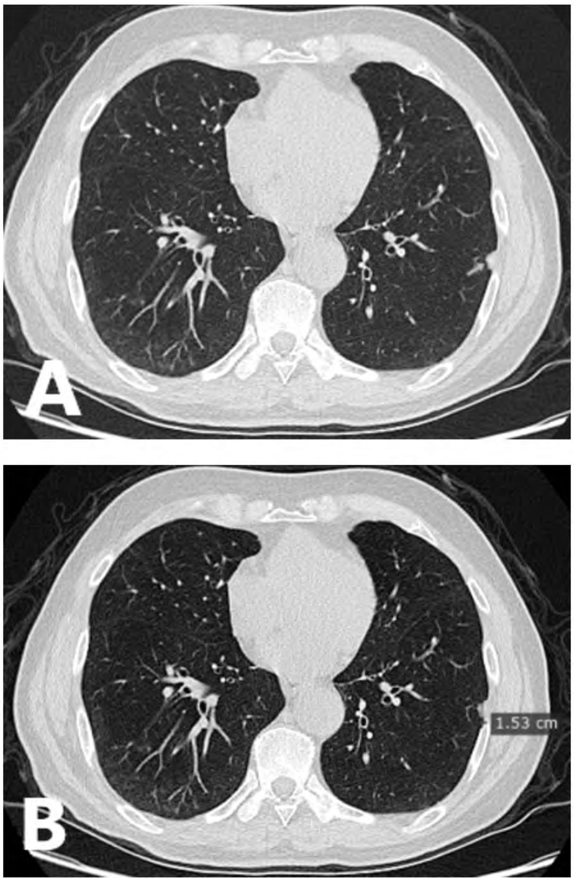

Fig. (1): Male patient aged 78 years old, current smoker with normal chest X-ray. (A) axial pulmonary window LDCT chest screening with ASIR algorithm revealed pleural based soft tissue nodule seen in the lateral basal segment of the left lower lung lobe (green arrow). (B) Itmeasures about 15mm. According to the I-ELCAP diagnostic protocol, this nodule considered positive.

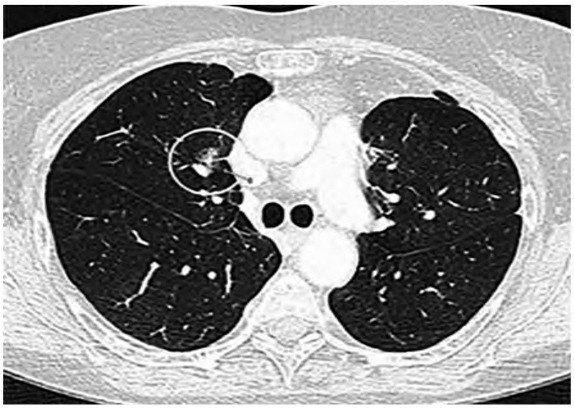

Fig. (2): Male patient aged 55 years old, current smoker with normal chest X-ray. Axial pulmonary window LDCT chest screening with ASIR algorithm revealed centrally located soft tissue nodule seen in anterior segment of right upper lung lobe surrounded with area of ground glass density (green arrow), the solid part measures about 9mm with fixed size on follow-up CT. According to the I-ELCAP diagnostic protocol, this nodule considered semi-positive.

By using LDCT and ASIR algorism with different blending levels of reconstruction (40%, 60%) in lung cancer screening in our study, there was no difference in image clarity and degree of image sharpness compared to standard dose CT. By using ROC curve, the sensitivity and specificity of LDCT chest with ASIR algorithm with different blending levels of reconstruction (40%, 60%) in detecting lesions at cut off point 6mm size were 84.9% and 100% respectively with area under curve 0.938 and 95% confidence interval (0.887-0.990) (Fig. 3, Table 3).

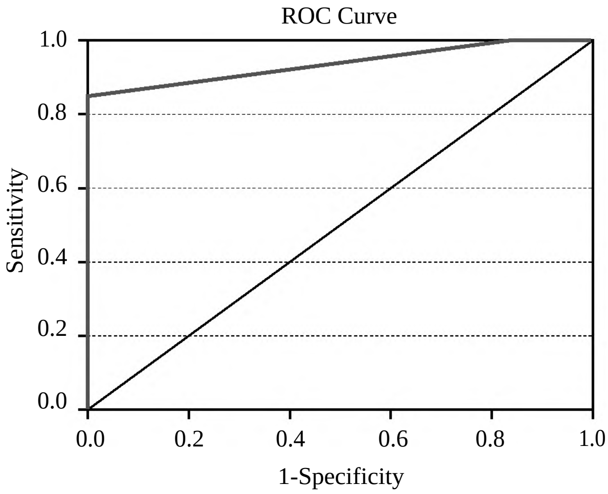

Fig. (3): ROC curve for the diagnostic performance of LDCT with ASIR algorithm in lesion detection.

Table (3): ROC curve analysis for detection of lung nodules using LDCT with ASIR algorithm.

Item	AUC	95% Confidene interval		Cut off point	Sensitivity	Specificity
		Lower	Upper			
	0.938	0.887	0.990	6mm size	84.9%	100%

AUC: Area under curve.

Discussion

Chest CT is one of the most frequently done examinations. Because chest CT is accompanied by radiation exposure to the thyroid and breasts, the radiation dose for chest CT examinations should be kept as low as reasonably achievable. Unlike the abdomen, the air-filled lungs in the chest allow a considerable reduction in the overall attenuation of X-ray beam, and the existence of high inherent soft-tissue contrast (air filled lungs versus fluid or soft tissue or higher-attenuation lesions) in the chest can permit a substantial decrease in radiation dose for chest CT [31]. The radiation dose is directly proportional to the tube current-time product at a fixed peak tube kilovoltage and slice thickness. Consequently, decreasing tube current is simple and achievable means to reduce the radiation exposure [32].

This study was carried out on ninety-six cases fitting the criteria of case selection with age range 50-78 years using LDCT chest with ASIR algorithm with different blending levels of reconstruction (40%, 60%). The age had no significant effect on our results as regarding nodule detection or image clarity. A previous study reported that the age of examined subjects was between 40 and 58 years, and also there was no significant effect on the image clarity or diagnosis [33]. In similar study, the mean age was about 60 years, which also did not affect the results which agreed to our results [34].

Most of the subjects enrolled in this study (97.9%) were males. The sex of the patients had no significant effect on the image quality or results. In previous study, the percent of males in the study was 52.6% with no significant effect on the results [34].

In our study, the size of the nodules varied from 6-15mm (mean 8.67±3.82mm). We classified the nodules to ≥15mm (1 nodule, 16.7%) and <15mm (5 nodules, 83.3%) following the I-ELCAP diagnostic protocol.

In the study done by Ono et al., the size of the lesions was varying from 13 to 16mm, and this was associated with no significant effect on the diagnosis of the lesions [34].

In our study we investigate potential strength of LDCT chest with ASIR algorithm with different blending levels of reconstruction (40%, 60%) as regard to image quality that could be of an applicable interest at low and very low radiation exposure levels. The analysis performed to characterize the quality of images acquired through ASIR technique in (Revolution EVO, GE Medical systems). In our study, at LDCT with tube current time less than 100mAs, there was no difference in image clarity and degree of image sharpness compared to standard dose CT. In our study, the least current time that can be used was 50mAs (below which decrease in the image quality occurred).Previous studies had evaluated the role of LDCT chest in comparison with standard dose in assessment of pulmonary neoplasms [31,32,34,35].

In a previous study, Barca et al., evaluated the image quality performance of a CT equipment (optima. CT 660 GE healthcare, Waukesha, USA) which implants the ASIR algorithm and performed a systematic analysis of noise and contrast to noise ratio (CNR) by changing the main exposure parameter in a wide range of values and testing the ASIR's performance of different images contrasts. The study showed that a relevant noise decreased and CNR increased in CT images obtained by ASIR algorithm compared to conventional FBP reconstruction. Also, noise decreased and CNR increased with the increase of ASIR blending level of reconstruction (20%,40%,60%,80%,100%) as well as with increasing tube potential [36].

In our study lowering the current time below 50mAs produced significant blurring of images, and above this there were no significant differences in the image quality. This came in accordance with the study done by Zhu et al., [32]. On the other hand, previous study reported that the tube current-time settings of 10mAs and greater were not associated with significant difference in the image quality [37].

In our study the sensitivity of LDCT chest in detection of pulmonary nodules was about 84.9%. Ono et al., demonstrated higher sensitivity of LDCT chest in detecting pulmonary neoplastic lesions (about 94%) [34]. On the other hand, Zhu et al., demonstrated 74% sensitivity of LDCT chest in detection of pulmonary neoplastic lesions [32]. Also, Christeet al., found thatthe sensitivity of LDCT chest in detecting pulmonary neoplastic lesions was about 77% [37].

In our study the reduction in the radiation dose was about 66%. However, in thestudy done by Zhu et al., the dose reduction was about 78% [32]. Also, in the study done by Weng et al., the dose reduction was about 72% [38].

In our study, 16.7% of the lesions were central, while 83.3% of the lesions were peripheral. This may affect image clarity as the peripheral lesions had good image quality (sharp) than the central (perihilar) lesions. In similar study, 73.9% of the peripherally located nodules had better image quality [39].

The present study indicated that LDCT provided diagnoses similar to that of standard dose CT. The image quality of LDCT may be high enough to be used for the screening of lung cancer andas a method of repeated follow-up. The dose in LDCT is approximately 33% of that in standard CT. It is important to consider both radiation dose and image quality when creating an effective LDCT protocol for screening of pulmonary malignant lesions.

Conclusion:

Low dose CT of the chest with ASIR algorithm is effective in detecting small lesions which cannot be detected by chest X-ray with high sensitivity and specificity (84.9% and 100% respectively). Therefore, LDCT chest using ASIR algorithmis recommended in screening and follow-up of pulmonary masses and nodules with satisfactory image quality and decreased radiation risk compared to standard dose CT specially in patients who will undergo frequent CT chest examination.

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فعالية التصوير بالأشعة المقطعية ذات الجرعة المنخفضة بخاصية إعادة البناء التكرارى الإحصائى التكيفى فى الإكتشاف المبكر لسرطان الرئة

مقدمة: يعد سرطان الرئة أحد أكثر الأورام الخبيثة شيوعاً و أكثر مسبب للوفيات المرتبطة بالسرطان فى العالم. مما يدل على أهمية الكشف والعلاج المبكر لسرطان الرئة فى المجموعات الأكثر عرضه لحدوث سرطان الرئة.

الهدف من الدراسة: الكشف عن فعالية التصوير بالأشعة المقطعية ذات الجرعات المنخفضة بخاصية إعادة البناء التكرارى الإحصائى التكيفى فى تشخيص المراحل المبكر من سرطان الرئة وبالتالى يقلل من معدلات الاعتلال والوفيات المرتبطة بالمرض مع التقليل من خطر التعرض للإشعاع المؤين والحفاظ على جودة صورة كافية.

المرضى وطرق البحث: تم إدراج ستة وتسعين حالة فى عمر ٥٠ سنة أو أكثر من المدخنين الحالين أو المدخنين السابقين الذين اقلعوا عن التدخين خلال ١٥ سنة الماضية. خضعت جميع الحالات لتصوير الصدر باستخدام بروتوكول الأشعة المقطعية ذات الجرعات المنخفضة بخاصية إعادة البناء التكرارى الإحصائى التكيفى للكشف المبكر عن سرطان الرئة. تم تفسير جميع الصور باستخدام بروتوكول التشخيص الدولى لبرنامج العمل المبكر لسرطان الرئة.

نتائج البحث: من ٩٦ حالة شملتها الدراسة، أظهرت ٤ حالات نتائج غير طبيعية فى الصدر (آفات الرئة العقدية). ومن بين العقيدات الـ٦ التى أكتشفت فى ٤ حالات، ووفقاً لبروتوكول التشخيص الدولى لبرنامج العمل المبكر لسرطان الرئة، اعتبرت عقيدة واحدة إيجابية واعتبرت ٥ عقيدات شبه إيجابية. كشف تصوير الصدر باستخدام الأشعة المقطعية ذات الجرعات المنخفضة بخاصية إعادة البناء التكرارى الإحصائى التكيفى للكشف المبكر عن سرطان الرئة حساسية وخصوصية عالية للكشف عن الآفات فى حجم ٦ ملم (٨٤.٩٪ و ١٠٠٪ على التوالى).

الإستنتاج: إن تصوير الصدر باستخدام الأشعة المقطعية ذات الجرعات المنخفضة بخاصية إعادة البناء التكرارى الإحصائى التكيفى هو أداة واعدة و فعالة للكشف المبكر عن سرطان الرئة مع تقليل كبير من خطر التعرض للإشعاعات المؤينة، فضلا عن الحفاظ على جودة الصورة المثلى.