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Review

A review of lung cancer screening and the role of computer-aided detection

B. Al Mohammad*, P.C. Brennan, C. Mello-Thoms

Faculty of Health Sciences, University of Sydney, Lidcombe, NSW, Australia

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Lung cancer is the leading cause of cancer-related death worldwide; however, early diagnosis of lung cancer leads to higher survival rates. The National Lung Screening Trial (NLST) demonstrated that scanning with low-dose computed tomography (LDCT) led to a 20% reduction in mortality rate in a high-risk population. This paper covers new developments in screening eligibility criteria and the possible benefits and the harm of screening with CT. To make the screening process more feasible and help reduce the rate of missed lung nodules, computer-aided detection (CAD) has been introduced to assist radiologists in lung nodule detection. The aim of this paper is to review how CAD works, its performance in lung nodule detection, and the factors that influence its performance. This paper also aims to investigate the effect of different types of CAD on CT in lung nodule detection and the effect of CAD on radiologists' decision outcomes.

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Introduction

Lung cancer is the leading cause of cancer death worldwide. According to the World Health Organization (WHO), there were 1.8 million new cases and around 1.6 million lung cancer-related deaths in 2012.[1] It is considered one of the most aggressive cancers, with a 5-year survival of only 10–15%[2]; however, outcomes are significantly better if the cancer is detected in an early stage, with a 10-year survival of stage 1 lung cancer up to 75%.[3]

Computed tomography (CT) is considered one of the key methods in imaging and investigation of lung disease.[4] Features such as morphological lesion characterisation, nodule size measurement, follow-up of nodule growth, and attenuation characteristics of a nodule have made it the examination of choice in lung cancer investigation.[5] Furthermore, because of the three-dimensional nature of CT and its ability to visualise the chest in axial sections, it provides assessment of the chest wall, diaphragm, and mediastinum invasion, in addition to staging of the tumour.[5] The drawback from using CT as a screening method is the fact that radiation can be carcinogenic and the probability of developing cancer increases with higher radiation dose. The optimal solution will be to use the lowest radiation dose possible without compromising image quality. Low-dose computed tomography (LDCT) uses significantly lower radiation exposure than standard-dose computed tomography (SDCT; LDCT radiation exposure is approximately 1.5 mSv/scan, SDCT radiation exposure is around 8 mSv/scan[6]) thus reducing the effective dose delivered by the imaging process. Studies comparing the sensitivity of nodule detection rates have shown that there was no significant difference between sensitivities in SDCT and LDCT.[7,8] As suggested by some authors, the dose can be further reduced by means of iterative reconstruction.[8,9] The

*Guarantor and correspondent: B. Al Mohammad, Faculty of Health Sciences, University of Sydney, 75 East St, Lidcombe, NSW 2141, Australia. Tel.: +61410095070.

E-mail address: baal8200@uni.sydney.edu.au (B. Al Mohammad).

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dose in LDCT ranges from four to 12-times the dose of chest radiography depending on the reconstruction method implemented.[9] Furthermore CT has a high rate of false-positive findings that result in additional unnecessary follow-up and investigations.

Higher anatomical detail improves the sensitivity in lung nodule detection, which can be achieved by thinner sections and overlapping reconstruction; however this comes at the expense of large data sets (depending on factors such as section thickness and reconstruction parameters, the number of sections can range from around 100[10] to more than 500 sections/scan[11]). As a result of this high number of images produced by CT and LDCT during a single scan, if implemented as a screening method, radiologists' workload will significantly increase (the average time for an experienced chest radiologist to interpret a single scan ranges from around 2 minutes[12] to 3.5 minutes[13]). This may lead to an increase in diagnostic error.[14] Errors arising in relation to CT form 62% of radiology errors.[15]

The need for a tool that will assist the radiologist in nodule detection, such as detecting missed nodules, reduce reading time so that the screening process is made possible and helps differentiate between benign and malignant lesions, has led to the development of computer-aided detection (CAD) systems. A CAD system is a computer technology used to assist physicians to decrease observational oversights when examining digital medical images, and as a result, reduce diagnostic errors.[16] The primary goal of CAD is to increase the nodule-detection rate in a way that is more efficient than double reading, will cost less, and will not require employing additional radiologists for the screening procedures; however, researchers have reported a wide span of nodule-detection sensitivity by CAD in LDCT ranging from 38%[17] to 100%,[18] with false-positive rates from one per scan[19] to 8.2 per scan.[20] The range reported was probably due to the use of different CAD systems and different data sets in each of these studies, which makes it difficult to compare the performance of the CAD systems used. Therefore, it is important to examine whether CAD as an adjunct in LDCT can be helpful in the future of lung cancer screening.

The main aim of this paper is to review the performance of CAD systems in lung nodule detection, explore the effect of different types of CAD systems on LDCT for lung nodule detection, the factors that influence the performance of a CAD system, and its effect of CAD on radiologists' decision outcomes. In addition, this paper will briefly discuss updates in the field of lung cancer screening.

Screening for lung cancer

Randomised controlled trials (RCT) using chest radiography, with or without sputum cytology, have been used to screen high-risk populations for lung cancer.[21–26] The results of these studies demonstrated that screening led to earlier lung cancer detection and improved survival rates; however, none of them showed a reduction in lung cancer mortality.

Advances in CT development have produced high-resolution, volumetric imaging and have made CT a more sensitive imaging method than chest radiography in lung-cancer screening. Several studies have demonstrated that screening a high-risk population with LDCT detects more lung nodules and lung cancers at an early stage than chest radiography; however, they did not prove a reduction in mortality.[3,27–34]

In 2011, the results of the largest randomised controlled trial, the National Lung Screening Trial (NLST), were published. The high-risk current or former smokers, mid-50- to mid-70-year-old participants were randomised to an annual LDCT screening group compared to chest radiography group for 3 years. The average ratio of lung cancer incidence between the LDCT group and the radiography group was 13:1. A significant reduction of 20% was demonstrated in lung-cancer-specific mortality.[31]

Lung cancer screening guidelines in the United States are mainly based on the same criteria for which participants in the NLST study were chosen. Expanding the screening eligibility criteria to include individuals >50-years of age, current or former smokers with a ≥20 pack-year smoking history, in addition to at least one risk factor for developing lung cancer will have the potential to save thousands of additional lives annually.[35]

Although the possible benefit of LDCT screening is reduction in mortality rate, probable harms are a high number of false positives (accompanied by unnecessary workup and invasive evaluation), over-diagnosis, and radiation exposure. Furthermore, due to inconsistencies in nodule characterisation and the reporting manner of the screening studies, comparing results is difficult, leading to a common limitation of the LDCT screening studies: the lack of a standard reference. For example, there is a substantial variation in lung nodule definition among radiologists.[36] In consequence, the American College of Radiology has developed a quality-assurance tool, the Lung Imaging Reporting and Data System (Lung-RADS), with the aim of standardising the reporting of LDCT screening results. Lung-RADS focuses on defining a positive finding on lung-cancer screening CT, attempting to decrease the false-positive rate, with a minimum effect on test sensitivity, and suggesting management recommendations.[37] Applying Lung-RADS retrospectively has shown to substantially reduce the false-positive rate; however, there was also a decrease in detection sensitivity.[38]

Although LDCT is currently being implemented for lung cancer screening, the large number of images produced by a single scan and its complexity makes it prone to different types of diagnostic errors.

Errors in lung nodule detection

Around 4% of daily radiological reporting contains diagnostic errors.[39] As a consequence, 30% of abnormal radiological studies are missed.[40] Diagnostic error has been defined as a miss (no diagnosis made), a false diagnosis (a diagnosis that is different from the correct one), or a

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