



Challenges in implementation of lung cancer screening – radiology requirements

Gerlig Widmann

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Summary Implementation of lung cancer screening is a challenge for radiology. The present short review summarizes major requirements which are needed to ensure high rates of diagnostic accuracy and appropriate protocols for follow-up and invasive work-up. Standardization of procedures, structured reporting, assessment of quality metrics, close multidisciplinary collaboration, and continuous education are essential. Additional quantification of coronary artery calcium and emphysema may provide synergistic medical benefits for a lung cancer screening programme.

Keywords Computed tomography · Structured reporting · Pulmonary nodules · Risk stratification · Image protocols

Published data from the National Lung Screening Trial (NLST) have shown that lung cancer screening with a low-dose computed tomography (CT) scan can decrease lung cancer deaths by 20% in high-risk individuals (current and former [quit <15 years] cigarette smokers aged 55–74 with at least a 30 pack-years) [1]. It may result in three fewer lung cancer deaths for every 1000 individuals screened and seems to be at least as effective as mammography is in preventing breast cancer deaths and colonoscopy is in preventing colon cancer deaths. Lung cancer screening provides a significant stage shift from 70% of lung cancers detected at stage 1 and 2 with low-dose CT reverted to 37% during follow-up after screening rounds completed. In addition, a 6.7% reduction of all-cause mortality has been demonstrated. Preliminary European

data from the Dutch–Belgian Randomized Lung Cancer Screening Trial (NELSON study) indicates results that are even more promising. Major medical organizations now recommend annual lung cancer screening for high-risk individuals.

Nevertheless, lung cancer screening faces important challenges [2]. According to the NLST, per 1000 individuals, 365 participants will have at least 1 false-positive result and 25 participants a false-positive result leading to an invasive procedure. The risk for a major complication from invasive procedures such as biopsy and surgery is three for every 1000 individuals undergoing such additional testing. One in five individuals screened may have a significant incidental extrapulmonary finding on the scan that is not causing any symptoms but may require evaluation.

Radiology has a key role in lung cancer screening and the following requirements can be considered as crucial for a successful implementation.

Participating radiologists

Lung cancer screening should be in hands of capable radiology facilities, which are an integral part of an interdisciplinary thoracic oncology group. Participating radiologists should fulfil the criteria of board certification, documented training in diagnostic radiology and radiation safety, experience by involvement in supervision and documentation of at least 300 chest CTs in the past three years, and participation in continuing medical education [3]. Familiarity with lung nodule classification and reporting systems is essential to improve reproducibility and accuracy and to reduce false-positive results, which will lead to unnecessary repeat CTs, invasive work-up, and downstream medical costs. [4]. Implementation of a national accreditation program of lung cancer screening facilities is recommended. The facility has to assure that relevant

G. Widmann, MD, PD, MSc, EBIR (✉)
Department of Radiology, Medical University of Innsbruck,
Anichstraße 35, 6020 Innsbruck, Austria
gerlig.widmann@i-med.ac.at

data is documented and submitted to the screening registry so that high quality scientific and epidemiologic data can be obtained. A quality and safety control program with regular review and benchmark of quality metrics should be established and maintained.

Screening images

Screening images may come from different CT manufacturers and different technological generations. Requirements are 16-detector rows and above low-dose CT examinations with a computed tomographic dose index volume (CTDI_{vol}) threshold of 3 mGy for a standard-sized patient [5]. The protocol in the NELSON study used body weight adopted (<50, 50–80 and >80 kg) settings to achieve a CTDI_{vol} of 0.8, 1.6 and 3.2 mGy [6]. The effective radiation dose was <0.4 mSv, <0.8 mSv and <1.6 mSv and is considerably lower than the annual natural background radiation of 2.4 mSv. Continuous improvement of CT technology can provide ultralow-dose images reaching the radiation dose of a posteroanterior and lateral chest radiograph [7]. However, more data are needed to assess the effect of ultralow doses and the many variations of iterative reconstruction algorithms currently implemented by various CT manufacturers on screening results. Intravenous contrast is not required. Section thickness should be ≤2.5 mm, and contiguously reconstructed images with thickness of ≤1.5 mm are recommended for size measurement [4]. Use of a standardized acquisition technique is a prerequisite to ensure identical image quality in longitudinal studies.

Structured reporting

The goal of structured reporting is to categorize results and recommend follow-up based on malignancy probabilities taking into account size, appearance (benign characteristics such as certain calcifications or fat contain, or malign characteristics such as spiculation), and growth (Table 1). Using Lung-RADS (Lung Reporting and Data System) developed by the American College of Radiology may reduce 26.6% false-positive rates at baseline scan to 12.8% in a retrospective assessment of the NLST data [8]. To avoid significant variations of two-dimensional size measurements, volume measurement and calculation of volume doubling times (VDT) have been proposed in the NELSON management protocol [9]. Growth is defined as a percentage volume change of ≥25% and VDTs are classified as A—VDT >600 days (negative), B—VDT 400–600 days (indeterminate), and C—VDT <400 days (positive: required work-up). Dedicated software may assist radiologists by semi-automated size and volume estimations. Follow-up images can be synchronized for image comparison on a nodule-by-nodule basis and an automated reporting of volume changes and VDT is provided.

Biopsy

Positive findings should be discussed in an interdisciplinary board before invasive diagnostic procedures. Recently published results from nonprotocol-driven community practices show 13.6% minor, 13.9% intermediate and 4.0% major incremental complication rates from cytology and needle biopsy [2]. However, in an experienced centre use of safety protocols such as published by the Medical University of Innsbruck may substantially reduce complication rates in CT-guided transthoracic biopsy with systemic air embolism in 0.16%, pneumothorax in 5.99%, and overall rates of major complications C (require therapy, minor hospitalisation <48 h) and major complications D (major therapy, unplanned increase in level of care, prolonged hospitalisation >48 h) of 0.55% and 1.84% [10].

Relevant co-findings

Approximately 60% of screened subjects may have extrapulmonary co-findings of which about 20% may be potentially significant, with the highest prevalence for cardiovascular findings in up to 8–9% [11]. Evaluation of coronary artery calcium (CAC) has proven to be the most robust predictor of coronary artery disease events in the asymptomatic primary prevention population, particularly in those with an intermediate-risk [12]. As a gold standard, CT calcium score (Agatston score) is evaluated on ECG-gated acquisitions using structured reporting (CAC-RDS) [13]. However, CT calcium scores can also be obtained from non-gated lung cancer screening CTs and higher numbers of calcified lesions and scores of more than 400 may predict the likelihood of cardiovascular events in screening subjects with high confidence [14–16]. Smoking cessation interventions and modification of heart disease risk by using statins in those with high CAC scores may improve long-term improvements to quality of life for participants without lung cancer [17].

Lung cancer screening subjects have a high prevalence of chronic obstructive pulmonary disease (COPD) which accounts for significant morbidity and mortality and is an independent risk factor for lung cancer [18]. Imaging biomarkers for emphysema may be quantified using the density mask technique with CT attenuation values (Hounsfield Units [HU]) threshold –950 HU in inspiratory images (%LAA-950ins) and a percentile method using the 15th percentile cut-off of the HU attenuation distribution curve (Perc15). Bronchial wall thickness quantified as the square root of wall area for a theoretical bronchus with 10 mm lumen perimeter (Pi10) may serve as a separate marker of airway disease indicating the chronic bronchitis phenotype of COPD, independent of emphysema. In the absence of lung function testing, lung cancer screening CTs allow identifying COPD with sensitivity 73.2%, specificity 88.8%, PPV 80.8% and NPV 84.2% [19]. In male asymptomatic lung cancer screening

Table 1 Comparison of the Fleischner Society guidelines for a single incidentally detected pulmonary nodule in high-risk adults and the Lung-RADS and Nelson criteria proposed for lung cancer screening

Nodule Type	Fleischner Society			Lung-RADS			Nelson		
	Finding	Recommendation	Finding	Category	Recommendation	Finding	Category	Recommendation	
Solid	—	—	No nodule, nodules with specific calcifications: complete, central, popcorn, concentric rings and fat containing nodules	1 (negative; malignancy probability <1%)	CT at 12 months	Benign nodule (with fat/benign calcification) or other benign abnormalities	1 (negative)	CT at 12 months	
	<6 mm (<100 mm ³)	CT at 12 months	<6 mm	2 (benign appearance; malignancy probability <1%)	CT at 12 months	Nodule smaller than category 3, not belonging to category 1	2 (negative)	CT at 12 months	
	6–8 mm (100–250 mm ³)	CT at 6–12 months	6–8 mm	3 (probably benign; malignancy probability 1–2%)	CT at 6 months	50 ≤ V ≤ 500 mm ³ Pleural based: 5 ≤ dmin ≤ 10 mm	3 (indeterminate)	CT at 3 months	
	>8 mm (>250 mm ³)	CT at 3 months, PET/CT, or biopsy	≥8–15 mm	4A (suspicious; malignancy probability 5–15%)	CT at 3 months, PET/CT	V > 500 mm ³ Pleural based: dmin > 10 mm	4 (positive)	Refer to pulmonologist for work-up and diagnosis	
	—	—	≥15 mm	4B (suspicious; malignancy probability >15%)	PET/CT, biopsy	—	—	—	
Part Solid	<6 mm (<100 mm ³)	No routine follow-up	<6 mm in total diameter	2 (benign appearance; malignancy probability <1%)	CT at 12 months	Nodule smaller than category 3, not belonging to category 1	2 (negative)	CT at 12 months	
	≥6 mm (>100 mm ³)	CT at 3–6 month	≥6 mm in total diameter with solid component <6 mm	3 (probably benign; malignancy probability 1–2%)	CT at 6 months	Solid component: 50 ≤ V ≤ 500 mm ³ Non-solid component: dmean ≥ 8 mm	3 (indeterminate)	CT at 3 months	
	—	—	≥6 mm with solid component ≥6–8 mm	4A (suspicious; malignancy probability 5–15%)	CT at 3 months, PET/CT	Solid component: V > 500 mm ³	4 (positive)	Refer to pulmonologist for work-up and diagnosis	
Non Solid (ground glass)	—	—	Solid component ≥8 mm	4B (suspicious; malignancy probability >15%)	PET/CT, biopsy	—	—	—	
	<6 mm (<100 mm ³)	No routine follow-up	<20 mm	2 (benign appearance; malignancy probability <1%)	CT at 12 months	Nodule smaller than category 3, not belonging to category 1	2 (negative)	CT at 12 months	
	≥6 mm (>100 mm ³)	CT at 6–12 month	≥20 mm	3 (probably benign; malignancy probability 1–2%)	CT at 6 months	Dmean ≥ 8 mm	3 (indeterminate)	CT at 3 months	
CT computed tomography, PET/CT positron emission tomography/computed tomography, V volume, dmin minimal diameter, dmean mean diameter									

patients pulmonary CT measurements are significantly associated with cardiovascular events but may not improve cardiovascular event risk stratification [16]. However, the main beneficial role of emphysema quantification in lung cancer screening patients is an earlier diagnosis and therapy of COPD with smoking cessation strategies, inhaled bronchodilators with or without inhaled corticosteroids potentially leading to less exacerbations and hospitalizations for COPD.

Conclusion

Participating radiology facilities involved in a lung cancer screening programme require appropriate technical infrastructure and trained personnel to ensure high rates of diagnostic accuracy, appropriate follow-up protocols for indeterminate results and high rates of diagnostic accuracy and safety during work-up. Standardization of procedures, structured reporting, proper screening registries, regular assessment of quality metrics, close interdisciplinary collaboration, and continuous education are demanded. Additional coronary artery calcium evaluation and emphysema quantification in low-dose lung CTs may improve medical benefits and cost-effectiveness.

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Conflict of interest G. Widmann declares that he has no competing interests.

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