Canadian Association of Radiologists
L'Association canadienne des radiologistes

CANADIAN ASSOCIATION OF RADIOLOGISTS:

GUIDE ON CT SCREENING FOR LUNG CANCER

The practice guidelines of the Canadian Association of Radiologists (CAR) are not rules, but are guidelines that attempt to define principles of practice that should generally produce radiological care. The radiologist and medical physicist may modify an existing practice guideline as determined by the individual patient and available resources. Adherence to CAR practice guidelines will not assure a successful outcome in every situation. The practice guidelines should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The practice guidelines are not intended to establish a legal standard of care or conduct, and deviation from a practice guideline does not, in and of itself, indicate or imply that such medical practice is below an acceptable level of care. The ultimate judgment regarding the propriety of any specific procedure or course of conduct must be made by the physician and medical physicist in light of all circumstances presented by the individual situation.

Approved on April 14, 2016

Chair, Jana Taylor, MDcM; Daria Manos, MD; Heidi Schmidt, MD; Marie-Hélène Lévesque, MD; Michael C. McInnis, MD

TABLE OF CONTENTS

INTRODUCTION

The past several years have seen the publication of the results of several major studies, evaluating the use of low dose CT (LDCT) scanning in the screening of high risk individuals for lung cancer. Many major US organizations have issued guidelines in support of performing lung cancer screening in appropriate populations, and organized screening programs are becoming well established in the United States. In Canada, however, there are currently very few documents outlining screening recommendations. Cancer Care Ontario issued a statement on lung cancer screening in 2013[1] and the Canadian Task Force on Preventive Health Care has just published new guidelines for lung cancer screening.[2] There are pilot projects underway in some provinces, as well as smaller regional centres. There is also growing concern about opportunistic screening being performed outside of organized screening programs. Although this discussion is outside the scope of the document, the CAR does recommend that individual provinces undertake a provincial screening program with a provincial registry, respecting the limitations and constraints of provincial budgets.

There are currently a number of guidelines in circulation. While most guidelines agree that LDCT screening only be provided for individuals at high risk for lung cancer, there are slight differences among these guidelines as to the definition of high risk individuals. Recognizing that we are in early stages of lung cancer screening in North America, data is still accumulating and there is currently no one definitive guideline. This guide was prepared by a working group of expert advisory members of the CAR, without whom this document would not have been possible. The CAR would also like to acknowledge the many CAR members and external reviewers who contributed to this document. We also received valuable comments from a number of specialty organizations including:

- Canadian Association of Medical Radiation Technologists (CAMRT)
- Canadian Respiratory Health Professionals/ Canadian Thoracic Society
- Canadian Task Force on Preventative Health Care (CTFPHC)
- Cancer Care Ontario
- College of Family Physicians of Canada (CFPC)

In the absence of any unifying guidelines, the CAR has provided recommendations based on the current literature and evidence-informed expert opinion.

As LDCT scanning is the central tool for lung cancer screening, the radiologist has a crucial role to play in the screening process. This document is intended mainly for use by radiology departments or clinics that intend to undertake a screening program. This involves radiologists, technologists, and support staff who would participate in the enrollment, scanning, interpretation and follow up of patients eligible for screening.

Although the primary target of this document is radiologists, it is recognized that screening is a multidisciplinary process. As such, family physicians, respirologists and thoracic surgeons all have roles to play in the screening process and can potentially be impacted by the recommendations of this document. This document may also be useful in assisting administrators and policy makers responsible for making decisions about appropriate use of diagnostic imaging.

These guidelines are meant to be recommendations based on the literature currently available, regarding the best practice to carry out lung cancer screening. The management of patients once a diagnosis of lung cancer has been established is outside the scope of this document. It is important to recognize as well that different provinces and regions will have variable resources to dedicate to the purpose of lung cancer screening, and may need to modify their screening practices to reflect this reality.

LDCT for lung cancer screening is still a relatively new field and best screening practices are still being established. This guide is meant to reflect the best evidence currently available. Recognizing that this is a rapidly evolving area of medicine, the guide will be revised as needed.

POPULATION/STATISTICS

In Canada, lung cancer is the leading cause of cancer-related death in both genders.3 Although the incidence of lung cancers in men has been decreasing since the mid-1980's, and the incidence in women is no longer increasing, it is estimated that there were 26 600 new cases of lung cancer in Canada in 2015, and 20 900 deaths due to lung cancer.[3]

The two most common risk factors for lung cancer are exposure to cigarette smoke and increasing age. Smoking is associated with approximately 85% of all lung cancer cases.[4] Although the prevalence of smoking has decreased, 18.1% of Canadians (approximately 5.4 million people) were current smokers in 2014. 20.2% of Canadians age 45 to 64, and 9.4% of people age 65 and over are still smoking.[5] The highest incidence of new cases of lung cancer is seen in age groups 60 and older, although there are also a significant number of cases in the 50-59 year-old age group.[3]

Lung cancer has a poor prognosis, and more than 90% of persons with lung cancer die of the disease.[6] However, early-stage lung cancer has a better prognosis and is potentially curable. The five-year survival for stage I lung cancer is 66 to 82%.[7] Unfortunately, the majority of lung cancers are only detected at an advanced stage where the five-year mortality rate is much higher than for earlier stage cancers. From 2006-2008, the overall five-year relative survival ratio for people diagnosed with lung cancer was 17%.[3]

SUMMARY OF CURRENT EVIDENCE

In recent years, the results of several European and North American randomized control trials evaluating the utility of annual LDCT for the detection of lung cancer have been published. The largest and most robust of these studies is the National Lung Screening Trial (NLST), which enrolled more than 50 000 patients. It evaluated participants aged 55 to 74 years, with a smoking history of at least 30 pack-years, and who were either current smokers or had quit within the past 15 years. The result of the NLST, published in 2011, showed that screening CT, when compared to screening chest radiograph, resulted in a 20% decrease in lung cancer specific mortality and a 7% decrease in overall mortality.[8]

Other smaller European trials failed to show any benefit of LDCT for lung cancer screening. For example, two small fair-quality trials, the DANTE (Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays) trial (n = 2472) and the DLCST (Danish Lung Cancer Screening Trial) (n=4104) did not show any benefit associated with LDCT compared with no LDCT.[9,10,11] A recent update of the DLST study with longer term follow-up did show a stage shift in the highest stage screening group as compared to the control group.[12]

The smaller sample size of these studies may have had limited power to detect a true benefit. In addition, the DLCST included lower risk (younger and healthier) participants than in other trials such as the NLST. A third study, the MILD (Multicentric Italian Lung Detection) study, was rated as poor quality because of concerns about the adequacy of randomization.[13] The Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) study is a trial of lung cancer screening comparing LDCT with no screening. The NELSON trial is currently ongoing.[14] When the results of the NLST, DANTE, and DLCST trials were combined in a meta-analysis, the combined relative risk for lung cancer mortality was 0.81 (95% CI, 0.72 to 0.91).[15]

QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

TRAINING REQUIREMENTS FOR RADIOLOGISTS INTERPRETING SCREENING EXAMINATIONS

There are currently no recommendations in the literature to indicate specific qualifications for radiologists reporting lung cancer screening studies, unlike other screening examinations such as mammography, where specific training requirements and a minimum number of studies are recommended.[16,17] The American College of Radiology (ACR) currently recommends only that radiologists reporting lung cancer screening CTs meet the general requirements for reporting CT scans.[18] As screening becomes more widely established, training criteria for the radiologist may become part of the process to demonstrate adequacy as a screening site. Double reading and expert reading have been found to improve sensitivity and specificity for nodule detection and characterization,[19] suggesting there is likely a role to play in radiologists needing at least some initial training or supervision when beginning to read lung cancer screening studies.

Best practice guidelines for radiologists reporting lung cancer screening studies are recommended below:

1. CT screening for lung cancer should be reported by radiologists who are committed to maintaining up to date knowledge and who participate in a quality assurance program.
2. Radiologists involved in CT screening should complete a Continuing Professional Development (CPD) program prior to reporting screening CTs. This could include either didactic education or active learning (e.g., case banks, self-assessment modules).
3. We recommend the first 25 to 50 screens be supervised by an experienced reader. These initial studies could include cases read in a CPD setting.

SCREENING REFERRAL REQUIREMENTS

Lung cancer screening CT should only be performed following a shared decision making visit including discussion of the risks, benefits and limitations of screening to the individual. In the absence of a provincially-organised approach to screening (with infrastructure for informed consent and risk/benefit discussion), CT screening should only be performed by referral (as prescribed by primary health provider or specialist). Lung cancer risk calculators can help individuals and their primary care providers estimate risk.[20] Either the referring practitioner or the screening centre may be responsible to assess that the patient meets the eligibility criteria for lung cancer screening and that his or her medical condition does not substantially limit life expectancy or ability to undergo curative treatment. A validated risk model is available to the public at **www.brocku.ca/cancerpredictionresearch** (validated Tammemagi model). In addition to the risk prediction model, there are other tools that can be used in the shared decision making visit. These tools include:

- **http://canadiantaskforce.ca/tools-resources/lung-cancer-2/**
- **www.shouldiscreen.com**

The written prescription for lung cancer screening CT should include sufficient information to demonstrate that the patient meets the inclusion criteria. It is strongly recommended that when a patient is referred for screening, the referring physician should also provide smoking-cessation counselling to the patient or referral to an evidence-based smoking cessation program.

QUALITY STANDARDS

SCREENING CENTRE REQUIREMENTS

Screening must be performed in a centre with experience and expertise in thoracic imaging. Studies should be interpreted in a setting with access to a multidisciplinary team. All members involved in diagnostic work up and management of screening

patients should be able to communicate quickly and easily with each other. Established communication and collaborative expertise can reduce unnecessary work up and diagnostic procedures. Management decisions of complex cases will often require a multidisciplinary discussion involving radiology, respirology, pathology, thoracic surgery, nuclear medicine and oncology. There should be access to rapid investigation programs such as Cancer Care Ontario's Diagnostic Assessment Program (DAP).

The Canadian Partnership Against Cancer is in the process of developing quality metrics for monitoring data in lung cancer screening centres. Once these metrics are published, screening centres should monitor these metrics on a routine basis.

PATIENT ASSESSMENT AT SCREENING CENTRE

Prior to the examination, every effort should be made by the referring physician and the patient to obtain prior chest CT studies. The patient should be instructed to bring these to the appointment, if not already available to the radiologist. The ability to compare with prior imaging substantially improves the specificity and sensitivity of CT screening, reduces risk and reduces false positive rates.

To allow proper interpretation, the patient should be questioned, with the help of a standardized check list[21] regarding recent symptoms of a lower respiratory tract infection that may lead to false positive results and unnecessary investigation. In the presence of acute respiratory symptoms, the appointment should be rescheduled for several weeks (4-6) after the patient's symptoms have resolved.

TECHNICAL REQUIREMENTS

LDCT screening exams are similar in technique to routine non-infused CT scans of the chest and do not require any additional training if performed by a qualified CT technologist, as licensed by provincial regulators.

Radiation dose to screening participants must be minimized while still providing diagnostic quality examinations.

Scan parameters will differ depending on the equipment available at a given centre but should include:

- Scan performed in a single breath hold.
- Scan performed without IV or oral contrast.
- Scan to include the entire circumference of the lungs and extend from the lung apices to the costophrenic sulci (the adrenals do not need to be included in the field and the field should not be enlarged to include them).

Dosimetry measurements with phantoms should be performed at least annually and after every x-ray tube change. CT facilities should participate in regular ongoing dose monitoring (annual patient dose survey; sample of at least 20 patients).

CT screening for lung cancer must be performed in facilities that participate in a CT quality assurance program. Water phantom to assess for uniformity should be performed daily. Acceptance testing should be performed on any newly installed CT scanner, and annual inspection should be performed as part of the routine QC program.

Technical lung cancer screening protocols should be established, reviewed and updated annually by a radiologist with the assistance of a medical physicist to obtain diagnostic quality images with the lowest possible patient radiation exposure. The technique should be set to yield a CT Dose Index (CTDIvol) of 3.0 mGy or less for a standard-sized patient (70 kg), as measured using the 32-cm diameter CTDIvol phantom. The average effective dose should be below 1 to 1.5 mSv, as estimated in thoracic CT by calculating the Dose Length Product (DLP) multiplied by a conversion factor of 0.014 mSv/(mGy*cm). The dose should be reduced for smaller-sized patients and increased for larger-sized patients. This is accomplished through either the use of automatic dose modulation methods, such as automatic exposure control (AEC) and/or automatic kV selection, or through manual adjustment, for example with the use of a chart that prescribes different tube current (mAs) and/or peak kilovoltage (kVp) values according to patient size. According to body habitus, the dose parameters should be 120 to 140 kVp and 20 to 60 mAs. Collimation is 3 mm or less and the gantry rotation time is 0.5 sec or less. A multi-detector CT scanner is required to meet these standards, at minimum 4-detector row and preferably 16-detector row or greater.[22]

Examples of low-dose screening protocols for different manufacturers and models are provided by The American Association of Physicists in Medicine.[23]

TECHNICAL PARAMETERS FOR LOW-DOSE CT LUNG CANCER SCREENING

Peak kilovoltage	120 to 140 kVp
Tube current	20 to 60 mAs
Collimation	≤ 2.5 mm
Gantry rotation time	≤ 0.5 sec
$CTDI_{vol}$	≤ 3.0 mGy
Average effective dose	≤ 1 to 1.5 mSv
Multidetector CT	≥ 4-detector row, preferably ≥ 16-detector row
Image slice thickness	≤ 3 mm

Images should be read at 3 mm slice thickness or less. Thin slices of 1 mm or less may be useful for analysis of certain small or subsolid nodules. Coronal and sagittal reformations should be available for review. Axial maximum intensity projection (MIP) reconstruction or computer-aided detection (CAD) software may be valuable adjuncts to improve the detection of nodules.[24]

DOCUMENTATION

STANDARDIZED/ STRUCTURED REPORTING

Lung cancer screening should be reported efficiently according to **CAR Practice Guidelines for Communication of Diagnostic Imaging Findings**.[25]

Systems to optimize communication are necessary, such as the use of structured/standardized reporting and the use of Lung-RADS[26] or LU-RADS systems.[27] Structured/standardized reporting provides consistent organization of the report to facilitate communication of results and improve adherence of radiologist to screening guidelines. Lung-RADS, LU-RADS, and the British Thoracic Society Guidelines for the Investigation and Management of Pulmonary Nodules[28] provide standard definitions of negative, indeterminate and positive CT screen results with risk stratification and specific recommendations for the management of detected lung nodules. Both the Lung-RADS or LU-RADS category and its corresponding management recommendation should be clearly stated in the report. It is important to understand that nodule management of screen-detected nodules differs from the Fleischner guidelines, which remains standard for non-screening patients.[29, 30]

At minimum, reports must include:

1. Date of most recent and most remote prior comparative CT.
2. All concerning nodules should be listed. Size criteria and number of the nodules to be reported will depend on the lung screening algorithm in use at the centre.*
3. Rather than simply relying on positive or negative criteria, a degree of concern (likelihood of malignancy) should also be expressed. Many positive screens are of very low suspicion for malignancy.
4. Recommendations regarding whether or not referral is indicated. Many positive scans will not require referral.
5. Specific recommendations regarding timing of next CT.
6. Incidental findings such as presence and severity of coronary artery calcification and relevant recommendations when possible.
7. Evidence of smoking-related lung disease including emphysema.
8. Statement that inclusion in a screening program does not preclude the need for work up should clinical signs and symptoms of lung cancer develop prior to the next screen.

* A guide regarding nodule management is being developed and is considered out of scope for the current document.

Technical parameters of the study may also be included in the report (mAs, kVp, DLP).

All studies should be read in a timely manner. The referring practitioner is responsible for communication of the results to the patient and referral of patients with suspicious findings.

NODULE EVALUATION

The challenge of nodule evaluation stems not only from the identification of pulmonary nodules but also from their characterization and management. Lung nodules are a common finding in lung cancer screening. In order to avoid costly and potentially harmful workup of benign screen-detected nodules, non-invasive, pragmatic nodule evaluation strategies must be employed.

The first step in evaluation of a lung nodule is to identify its attenuation on lung windows as solid or subsolid. Subsolid nodules are further classified as part solid part ground glass nodules or pure ground glass nodules depending on the presence or absence of a solid component.

The second step is measuring size. Pulmonary nodules are most commonly measured in the axial plane in two perpendicular dimensions with the average of the two measurements determining overall size in millimeters, rounded to the nearest millimeter. Evaluation of part solid nodules includes reporting both the size of the ground glass component as well as the size of the solid component.

Overall, nodule size and change over time, both in size and attenuation, are the most important characteristics in evaluation of a pulmonary nodule. This is the primary basis for determining follow up in lung cancer screening. There are multiple other nodule characteristics which play a role in determining follow up and risk of malignancy. For nodules detected on a baseline screen, a probability prediction model may be useful.[31]

Finally, attention must be paid to clinically significant incidental findings. Early identification of severe coronary artery calcification and other clinically significant findings such as emphysema are promising for improving the cost effectiveness of lung cancer screening, though this has yet to be proven.

Two additional documents, one outlining a recommended standardised report for lung cancer screening, the other detailing recommendations for nodule evaluation and work up, are currently in development by the working group and will provide more detailed information regarding the requirements of screening examination reporting and nodule characterization.

INCLUSION/ EXCLUSION CRITERIA FOR SCREENING

CURRENT SCREENING RECOMMENDATIONS

Several major organizations to date have evaluated the data on lung cancer screening and have issued recommendations in favor of lung cancer screening in selected high risk populations. In some cases, following the NLST enrollment criteria is recommended; in others there have been modification of the NLST criteria based on additional data from modeling studies.

The Canadian Task Force on Preventative Healthcare recently issued a recommendation in favour of LDCT screening for lung cancer for individuals at high risk. The grade of the recommendation is labelled as weak. The Task Force uses this definition to recognise that although the research shows that screening reduces deaths from lung cancer, there are harms associated with CT screening and some high risk patients will reasonably choose not to participate in screening. The task force recommends that patients should discuss screening with their health care provider. Cancer Care Ontario will be implementing a multicentre pilot but the specific details of the screening recommendations have not yet been published.

The US Preventative Services Task Force (USPSTF) has assigned a grade of B (high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial) to annual screening for lung cancer with LDCT. Their screening recommendations include annual screening of adults aged 55 to 80 years with at least a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.[4]

Cancer Care Ontario[32] American College of Chest Physicians, the American Society of Clinical Oncology, the American Thoracic Society[33] and the American Cancer Society[34] all recommend screening for lung cancer with LDCT, using eligibility criteria that closely follow those of the NLST.

The American Association for Thoracic Surgery[35] recommends annual screening with LDCT in patients aged 55 to 79 years with a 30 pack year smoking history, as well as screening starting at age 50 to 79 years in patients who have a 20 pack-year smoking history and any additional comorbid conditions that produce a cumulative risk for cancer of at least 5% over the next 5 years. It also recommends annual screening in long-term lung cancer survivors aged 55 to 79 years.

The National Comprehensive Cancer Network[36] recommends LDCT screening in patients aged 55 to 74 years who have at least a 30 pack year smoking history or persons aged 50 years or older who have at least a 20 pack-year smoking history and 1 additional risk factor (personal history of smoking related cancer, first degree relative with lung cancer, chronic lung disease [emphysema/fibrosis], or pulmonary carcinogen exposure).

RISK MODELING

In addition to considering the multiple RCT studies, several organizations have also looked at modeling data to best determine the benefits and harms in lung cancer screening.

The US Preventative Services Task Force (USPSTF) evaluated data from modeling studies over different screening intervals, age ranges, smoking histories, and time since quitting in the assessment of the benefits and harms of lung cancer screening in order to reach their current screening recommendations.

The Canadian Partnership Against Cancer's Cancer Risk Management Model (CRMM)[37] developed with Statistics Canada, simulates the risk of developing lung cancer using an established risk equation.[38] The model incorporates the risk of developing cancer, disease screening and clinical management with cost and labor data to assess health outcomes and economic impact. Multiple scenarios have been evaluated for different target populations with varying rates of participation, compliance, and frequency of LDCT screening. When the NLST data was simulated using the CRMM-LC, the mortality reduction from LDCT screening was found to be 23%, showing reproducibility similar to the actual results of the NLST. The CRMM-LC is a potentially useful tool which can be utilized to evaluate a variety of population-based screening strategies.

Another lung cancer risk prediction model developed and validated from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial has incorporated additional risk factors in selecting patients for screening and was found to be more sensitive than the NLST criteria in detecting lung cancer on screening studies.[20,39] The use of an accurate lung-cancer risk prediction model may in fact identify persons at highest risk, enabling an increased number of lung cancers identified per given sample size. Such a model could reduce the number of persons needed to be screened per fixed number of lung cancers detected. This in turn could contribute to a decrease in harms of screening, a decreased in false positive exam results and improved cost-effectiveness of screening.

POTENTIAL IMPACT OF LUNG CANCER SCREENING

Modeling evidence from the USPTF suggests that an annual screening program starting at age 55 years and ending after age 80 years (in persons who have a 30 pack-year smoking history and currently smoke or have quit in the past 15 years) resulted in approximately 50% of lung cancer cases detected at an early stage.[40] This screening protocol would result in a 14% reduction in lung cancer mortality, or an estimated 521 lung cancer deaths prevented per 100 000 persons in the population.

Using NLST data for modelling, the CRMM calculated the incremental cost-effectiveness ratios (ICERs) for lung cancer screening as $52 000 CaD per health-related quality-adjusted life-year (QALY) for annual screening.[41] When an adjunct smoking cessation program with a quit rate of 22.5% was evaluated, the ICERs improved to $24 000/QALY (Canadian dollars).[42]

Analysis using data from actual NLST participants, rather than modelling, resulted in an estimated $81 000/QALY (USD), although the authors of that study noted that only modest changes in the assumptions used in this estimation would result in significant alterations of this figure. There was a wide variation in ICERs in various subgroup and sensitivity analyses.[43]

A prospective study of resource utilization in the Pan-Canadian Early Detection of Lung Cancer Study found that the mean per person cost of screening was $453 CnD (includes cost of screening and investigation) for participants who were not diagnosed with malignancy.

HARMS AND LIMITATIONS SCREENING FOR INDIVIDUAL PARTICIPANTS

The harms associated with LDCT screening include false-negative and false-positive results, incidental findings that result in unnecessary investigations, over diagnosis, and radiation exposure. Aggressive interval cancers may appear before the patient is re-evaluated at annual screening. Central tumors are difficult to detect on LDCT and may be missed. The USPSTF found insufficient evidence on the harms associated with incidental findings.[4]

False-positive LDCT results occur in a substantial proportion of screened persons; up to 95% of all positive results do not lead to a diagnosis of cancer. However, the definition of what constitutes a true "false positive" scan is evolving at a rapid rate. In a high-quality screening program, surveillance LDCT can resolve most false-positive results; however, some patients may require additional imaging or invasive procedures. There are known risks and potential complications with these invasive procedures. With improved experience, the number of true false positives can potentially be dramatically reduced, and most false-positive results should be resolved without the need for invasive procedures. Use of nodule classification systems such as Lung-RADS have shown a dramatic reduction in the false-positive rates and are promising for reducing morbidity and improving cost effectiveness of lung cancer screening.[44]

As with any screening modality, the use of LDCT could potentially lead to over-diagnosis (detecting cancers that would not have been diagnosed in the person's lifetime in the absence of screening). The CRMM projects an increased number of new cases detected in the first several years of screening and a higher than expected number of new cases while screening continues. Modeling studies estimated an over diagnosis of 10-18% of screen-detected cases.[45]

Radiation harms, including potential cancer resulting from cumulative exposure to radiation, vary depending on the age at the start of screening; patient size; the number of scans received; and the person's exposure to other sources of radiation, particularly other medical imaging.

All of these potential harms only further underscore the need for screening to be done in an appropriate and organized manner, with only high risk individuals who could benefit from screening being enrolled in a screening program. Appropriate training of radiologists who will be reporting screening studies in the interpretation of these cases is crucial. A multidisciplinary team to discuss and resolve challenging management cases is the key to any successful screening program.

FREQUENCY AND DURATION OF SCREENING

The optimal frequency and duration of screening have yet to be established, and these are areas that require further research. It is important to note that all screening trials are done over a limited time frame, with the NLST evaluating the effect of three annual screenings. These studies were concluded once their end point was met, and this is not meant to imply that only three rounds of screening were thought to be of benefit to patients. Although the Canadian Task Force on Preventative Healthcare recommends three rounds of screening no other major organization has suggested a similar approach. Data from the COSMOS model, which is designed to estimate screen-detected cancers, showed that neither cancer frequency nor proportion at stage I decreased over 10 years, indicating that screening should continue beyond 3 years.[46] The USPSTF report recommends discontinuing screening once a person has stopped smoking for more than 15 years or has developed health problems that substantially limit life expectancy or would preclude curative lung treatment.[4]

All of the large randomized controlled trials evaluated the benefit of annual screening. To date, there is no data to support a screening frequency other than annual screening. Modeling studies from the USPSTF conclude that annual screening with LDCT provides the greatest benefit in decreasing lung cancer mortality compared with biennial or triennial screening.[44]

SCREENING RECOMMENDATIONS OF THE CANADIAN ASSOCIATION OF RADIOLOGISTS

INCLUSION CRITERIA

These recommendations are based on a review of best available literature and stakeholder consultation outreach and consultation, according to the CAR process. Various medical societies have issued similar but slightly different recommendations for inclusion criteria for screening. What is clear is that only patients that can be defined as "high risk" are likely to benefit from lung cancer screening with LDCT. Patients who do not meet criteria for high risk have the potential to be harmed by screening and should not be included in a screening program.

Recognizing that provinces, regions, and institutions may differ in how they chose to define a high-risk population, the recommendation of this working group is that only high risk patients be considered for screening.

The use of validated risk prediction models currently appears to be the best method of selecting those patients who would most benefit from screening. We recommend screening patients who have a 1.5% or higher risk of developing lung cancer over the next six years. If a risk prediction model is not implemented as part of a screening program, patients should at a minimum meet the same smoking history criteria as those enrolled in the NLST.

Based on the current data available, we recommend routine annual screening for high risk patients until such time as they no longer meet eligibility criteria. In addition, screening should be discontinued in those who develop health problems that substantially limit life expectancy or would preclude curative treatment.

EXCLUSION CRITERIA

Screening may not be appropriate for all patients; those with serious comorbid conditions may experience net harm or no/decreased net benefit. Similarly, persons who are unwilling to undergo curative treatment are unlikely to benefit from a screening program. The baseline characteristics of the NLST showed a relatively healthy sample and excluded persons who were unlikely to complete curative treatment and those with medical conditions that posed a substantial risk of death during the 8-year trial.[8]

Screening should also not be performed on individuals with symptoms requiring clinical evaluation, i.e., who are already presenting with symptoms that could be due to lung cancer. These symptoms would include hemoptysis or unexplained weight loss of more than 6.8 kg (15lb) in the preceding year. These patients should proceed directly to diagnostic evaluation rather than a screening examination.

Participants should not begin a screening program if currently undergoing workup or surveillance CT for any clinically or incidentally detected abnormalities in the thorax. Participants who have had a CT of the chest within the past year should wait to begin screening until 12 months after the last CT of the chest.

Patients with a previous history of lung cancer diagnosed and treated within the last five years should not be included in the routine screening population, because presumably they are already undergoing regular clinical imaging surveillance for lung cancer recurrence.

Individuals who are unable to undergo CT scanning due to inability to lie flat, unmanageable claustrophobia, inability to breath-hold, or weight over CT scanner limit should also be excluded from screening.

REFERENCE LIST

1. Robert H, Walker-Dilks C, Sivjee K, et al. Screening High-Risk Populations for Lung Cancer: Guideline Recommendation. *JTO*. 2013; 8: 1232-1237.
2. Canadian Task Force on Preventative Health Care. Recommendations on Screening for Lung Cancer. *Can Med Assoc J.* 2016; 188(6): 425-432.
3. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2015. Toronto, ON: Canadian Cancer Society; 2015.
4. Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med*. 2014; 160: 330-338.
5. Reid JL, Hammond D, Rynard VL, Burkhalter R. Tobacco *Use in Canada: Patterns and Trends*, 2014 Edition. Waterloo, ON: Propel Centre for Population HealthImpact, University of Waterloo.
6. Jett J. Current treatment of unresectable lung cancer. *Mayo Clinic Proc*. 1993; 68(6): 603-11.
7. Goldstraw P, Chansky K, Crowley J et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. JTO. 2016; 11(1): 39-51.
8. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al; National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011; 365: 395-409.
9. Infante M, Lutman FR, Cavuto S, Brambilla G, Chiesa G, Passera E, et al; DANTE Study Group. Lung cancer screening with spiral CT: baseline results of the randomized DANTE trial. *Lung Cancer*. 2008; 59: 355-63.
10. Infante M, Cavuto S, Lutman FR, Brambilla G, Chiesa G, Ceresoli G, et al; DANTE Study Group. A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial. *Am J Respir Crit Care Med*. 2009; 180: 445-53.
11. Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, et al. CT screening for lung cancer brings forward early disease. The randomized Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. *Thorax*. 2012; 67: 296-301.
12. Mathilde MW, Dirksen A, Ashraf H, et al. Results of the Randomized Danish Lung Cancer Screening Trial with Focus on High-Risk Profiling. *Am J Respir Crit Care Med*, Vol. 193, No. 5 (2016), pp. 542-551.
13. Pastorino U, Rossi M, Rosato V, Marchiano A, Sverzellati N, Morosi C, et al. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. *Eur J Cancer Prev*. 2012; 21: 308-15.
14. van Klaveren RJ, Oudkerk M, Prokop M, et al. Management of lung nodules detected by volume CT scanning. *N Engl J Med*. 2009; 361(23): 2221-9.
15. Humphrey L, Deffebach M, Pappas M, Baumann C, Artis K, Priest Mitchell JP, et al. Screening for Lung Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation Statement. Evidence Synthesis No. 105. AHRQ Publication No. 13-05196-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

16. Canadian Association of Radiologists. CAR Practice Guidelines and Technical Standards for Breast Imaging and Intervention. Ottawa, ON: Canadian Association of Radiologists, 2013. **http://www.car.ca/uploads/standards%20guidelines/20131024_en_breast_imaging_practice_guidelines.pdf**

17. American College of Radiology. Mammography Program Accreditation Requirements. Reston, VA: American College of Radiology, December 2015. **http://www.acraccreditation.org/~/media/ACRAccreditation/Documents/Mammography/Forms/FULL-APPLICATION--SECT-G.pdf?la=en**

18. American College of Radiology. ACR-STR Practice Parameter for the Performance and Reeporting of Lung Cancer Screening Thoracic Computed Tomography (CT). Reston, VA: American College of Radiology, 2014. **http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/LungScreening.pdf**

19. Xu DM, Lee IJ, Zhao S, et al. CT Screening for Lung Cancer: Value of Expert Review of Initial Baseline Screenings. *AJR*. 2015; 204(2): 281-286.

20. Tammemagi MC, Katki HA, Hocking WG, Church TR, Caporaso N, Kvale PA, Chaturvedi AK, Silvestri GA, Riley TL, Commins J, Berg CD. Selection Criteria for Lung-Cancer Screening. *N Engl J Med*. 2013; 368(8):728-36.

21. Canadian Association of Medical Radiation Technologists. Best Practice Guidelines: Patient History. CAMRT: Ottawa, 2011. **https://ww2.camrt.ca/bpg/qualityofcare/appropriatecare/patienthistory/**

22. Murugan VA, Kalra MK, Rehani M, Digumarthy SR. Lung Cancer Screening: Computed Tomography Radiation and Protocols. *J Throac Imaging*. 2015; 30(5): 283-9.

23. American Association of Physics in Medicine. Lung Cancer Screening Protocols. Accessed September 9, 2016. **http://www.aapm.org/pubs/CTProtocols/documents/LungCancerScreeningCT.pdf**

24. Ritchis AJ, Sanghera C, Jacobs C et al. Compuer Vision Tool and Technician as First Reader of Lung Cancer Screening CT Scans. *JTO* 2016; 11(5): 709-717.

25. Canadian Association of Radiologists. CAR Practice Guidelines for Communication of Diagnostic Imaging Findings. Ottawa: Canadian Association of Radiologists, 2010. Accessed September 29, 2016. **http://www.car.ca/uploads/standards%20guidelines/20101125_en_standard_communication_di_findings.pdf**

26. American College of Radiology. LungRADS Assessment Categories 2014. Accessed January 3, 2016. **http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/LungRADS/AssessmentCategories.pdf**.

27. Manos D, Seely JM, Taylor J, Borgaonkar J, Roberts HC, Mayo JR. The Lung Reporting and Data System (LU-RADS): a proposal for computed tomography screening. *Can Assoc Radiol J.* 2014; 65(2): 121-34.

28. Callister ME, Baldwin DR, Akram AR et al. British Thoracic Society guidelines for the investigation and management of pulmonary nodules. *Thorax*. 2015;70 (Suppl 2): ii1-ii54.

29. Naidich DP, Bankier AA, MacMahon H, et al. Recommendations for the Management of Subsolid Pulmonary Nodules Detected at CT: A statement from the Fleischner Society. *Radiology*. 2013; 266(1): 304-17.

30. MacMahon H, Austin JH, Gamsu G, Herold CJ, Jett JR, Naidich DP, Patz EF Jr, Swensen SJ; Fleischner Society. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. *Radiology*. 2005 Nov; 237(2): 395-400.

31. McWilliams A, Tammemagi MC, Mayo JR, Roberts H, Liu G, Soghrati K, et al. Probability of cancer in pulmonary nodules detected on first screening CT. *N Engl J Med*. 2013; 369(10): 910-9.

32. Roberts H, Walker-Dilks C, Sivjee K, et al. Screening high-risk populations for lung cancer. Toronto (ON): Cancer Care Ontario; 2013 April 18. Program in Evidence-based Care Evidence-based Series No. 15-10.

33. Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA*. 2012; 307: 2418-29.

34. Wender R, Fontham ET, Barrera E Jr, Colditz GA, Church TR, Ettinger DS, et al. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin*. 2013; 63: 107-17.

35. Jaklitsch MT, Jacobson FL, Austin JH, Field JK, Jett JR, Keshavjee S, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *J Thorac Cardiovasc Surg*. 2012; 144: 33-8.

36. National Comprehensive Cancer Network. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Lung Cancer Screening. Fort Washington, PA: National Comprehensive Cancer Network; 2014. 8. Medicare Improvements for Patients and Providers Act, 42 U.S.C.

37. FlanaganWM, Evans WK, Fitzgerald NR, et al. Performance of the Cancer Risk Management Model Lung Cancer Screening Module. Statistics Canada. *Health Reports* May 2015; 26(5): 11-18.

38. Bray I. Application of Markov chain Monte Carlo methods to projecting cancer incidence and mortality. *J R Stat Soc Ser C, Appl Stat*. 2002; 51: 151–64.

39. Tammemagi MC, Church TR, Hocking WG, Silvestri GA, Kvale PA, Riley TL, et al. Evaluation of the Lung Cancer Risks at Which to Screen Ever- and Never-Smokers: Screening Rules Applied to the PLCO and NLST Cohorts. *PLoS medicine*. 2014; 11(12): e1001764.

40. de Koning HJ, Plevritis S, Hazelton WD, ten Haaf K, Munshi V, Jeon J, et al. Benefits and Harms of Computed Tomography Lung Cancer Screening Programs for High-Risk Populations. AHRQ publication no. 13-05196-EF-2. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

41. Goffin JR, Flanagan WM, Miller AB, et al. Cost-effectiveness of lung cancer screening in Canada. *JAMA Oncol*. 2015 Sep; 1(6): 807-13.

42. Cressman S, Lam S, Tammemagi MC et al. Resource utilization and costs during the initial years of lung cancer screening with computed tomography in Canada. *J Thorac Oncol* 2014 Oct; 9(10): 1449-58.

43. Black WC, Gareen IF, Soneji SS et al. Cost effectiveness of CT Screening in the National Lung Screening Trial. *N Engl J Med* 2014; 371: 1793-1802.

44. Pinsky PF, Gierada DS, BlackW, Munden R, Nath H, Aberle D, Kazerooni E. Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. *Ann Internal Med*. 2015:162 (7): 485-91.

45. Patz EF, Jr., Pinsky P, Gatsonis C, et al. Overdiagnosis in low-dose computed tomography creening for lung cancer. JAMA internal medicine. 2014; 174 (2):269-74.

46. Veronesi, G., Maisonneuve, P., Rampinelli, C. et al. Computed tomography screening for lung cancer: results of ten years of annual screening and validation of cosmos prediction model. *Lung Cancer*. 2013; 82: 426–430.

Canadian Association of Radiologists
L'Association canadienne des radiologistes

600 – 294 Albert Street
Ottawa, Ontario K1P 6E6
Tel.: 613 860-3111
Fax: 613 860-3112
www.car.ca