# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Diagnostics Assessment Programme

# Software with artificial intelligence derived algorithms for automated detection and analysis of lung nodules from CT scan images

## Final scope

December 2021

## *1 Introduction*

The topic selection oversight panel identified software with automated analysis of CT scan images as potentially suitable for evaluation by the Diagnostics Assessment Programme based on a NICE medtech innovation briefing on artificial intelligence for analysing chest CT images published in January 2021. The scope of this diagnostics assessment focuses on the use of these software to assist radiologists in detecting and analysing lung nodules.

Any functionality of the included software to provide alternative, or updated, estimates of risk of malignancy for newly detected nodules to the currently used Brock model will not be assessed. An ongoing NICE assessment of EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules has highlighted a lack of data in several areas needed for a health technology assessment of technologies with this function. This includes uncertainty about how decisions about further assessment or treatment are made based on risk of malignancy estimates. The draft diagnostics guidance document sets out several areas for further research and data collection that need to be addressed for such an assessment. In addition, any functionality to assess malignancy risk of previously detected lung nodules during CT surveillance, beyond helping to assess the speed of nodule growth as per British Thoracic Society guidelines for the investigation and management of pulmonary nodules (described in section 3.2.3), will not be included in this assessment.

The software identified for this assessment use algorithms that have been produced using artificial intelligence. The algorithms are fixed but updated periodically.

The revised scope was informed by discussions at the scoping workshop held on 3 November 2021 and the assessment subgroup meeting held on 18

November 2021. A glossary of terms and a list of abbreviations are provided in appendices A and B.

# 2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE by manufacturers and experts, and information available in the public domain. NICE has not carried out an independent evaluation of this description.

## 2.1 Purpose of the medical technology

Detecting lung nodules, small growths inside the lung, may help to find and treat lung cancer early. Lung nodules may be challenging to detect because of their small size, varying shape, and depending on where and how close to other structures in the lung they are.

Lung nodules are found when people are referred for a CT scan that includes the chest because of signs and symptoms suggestive of lung cancer, to investigate other conditions unrelated to lung cancer, or as part of lung cancer screening programmes. People with previously identified lung nodules can also have CT scans done as part of surveillance to assess whether the growth of the nodules indicates malignancy (lung cancer) and if further assessment or treatment is needed.

Software capable of automatically detecting and analysing lung nodules on chest CT scan images could be used to assist radiologists or other healthcare professionals when reviewing scan images. This could increase detection of lung nodules that need further investigation or surveillance. The same software could also help in assessing the growth of previously identified nodules in CT surveillance. Use of the software may improve the reporting of those lung nodule characteristics that are important for decisions on appropriate follow up. It may also reduce the time it takes to review and report the CT scan images. However, the healthcare professional reporting the scan is still expected to review the findings of the software.

## 2.2 Product properties

Software is included in this assessment if it has automated nodule detection and volume measurement capability.

Some of the software can also compare subsequent scans to automatically measure the volume-doubling time. In some of the software, parameters can

be changed to adjust the nodule detection performance. Some include an integrated Brock model calculator.

Some of the software may only be able to analyse images of CT scans that include the entire lung. Some may be indicated for use only with a specific type of CT scan (for example scans without contrast or low-dose CT) or in specified populations (for example people without symptoms suggestive of lung cancer or people aged 18 or older).

The specific technologies included in this assessment are described below. Some of the descriptions contain less information because less detail or only information in the public domain was available. A summary of the included technologies is provided in table 1.

### *2.2.1 AI-Rad Companion Chest CT (Siemens Healthineers)*

AI-Rad Companion Chest CT is a CE-marked (class IIa medical device) software. It includes Lung-CAD, a tool that can detect and measure solid lung nodules in CT scans that cover the entire lung, with and without contrast. The algorithms are optimised for nodules between 3mm and 30mm. Lung-CAD is compatible with slice thickness of up to 2.5mm. It is indicated for use in both screening and diagnostic protocols in people without diffuse interstitial or airway diseases, severe pneumonia, extensive granulomatous diseases, prior thoracotomy or history of radiation therapy involving the lung parenchyma who are aged 22 and over. The software integrates with the Picture Archiving and Communication System (PACS).

### *2.2.2 AVIEW LCS+ (Coreline Soft)*

AVIEW LCS+ is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose chest CT scans. AVIEW LCS+ is indicated for use in adults. Other indications for use include detection of emphysema (damage to the air sacs in the lung) and coronary artery calcification. The software integrates with PACS. The software is commercially available to the NHS.

### *2.2.3 ClearRead CT (Riverain Technologies)*

ClearRead CT is a CE-marked (class IIa medical device) software. It consists of ClearRead CT Vessel Suppress, ClearRead CT Detect and ClearRead CT Compare features. Using these features, the software can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose and regular dose CT scans where both lungs are visible, with and without contrast. The software is compatible with slice thickness of up to 5mm. ClearRead CT

is indicated for use in people aged 18 and over who are asymptomatic. The software is updated frequently but none of the functionality is expected to be removed in future updates. The software integrates with, and the findings of the software are visible within, PACS. The company expects that training of radiologists on how to use ClearRead CT is usually done within a day. The software is commercially available to the NHS directly from the manufacturer and through partner organisations.

### *2.2.4 contextflow SEARCH Lung CT (contextflow)*

contextflow SEARCH Lung CT is a CE-marked (class IIa medical device) software. It can detect and measure solid and sub-solid lung nodules in chest CT scans with or without contrast. It is intended for use in clinically stable-symptomatic patients. Other indications for use include identification of lung-specific image patterns related to diseases such as airway wall thickening, bronchiectasis, emphysema and pneumothorax. contextflow SEARCH Lung CT integrates with PACS. The company expects users to attend a training presentation before using the software. The software is commercially available to the NHS.

### *2.2.5 InferRead CT Lung (Infervision)*

InferRead CT Lung is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose or regular dose CT scans with or without contrast. The company advises that InferRead CT Lung is intended for use in asymptomatic population. The company also states that the use is recommended in people aged 18 and over. Users can dismiss nodules found by the automated analysis but editing the findings is not possible. Users can add nodules but the software will not measure the volume of user added nodules. A new version of InferRead CT Lung is expected to be released within 18 months. The current version will continue to be supported and available to the NHS. InferRead CT Lung includes rules for reporting that follow the British Thoracic Society (BTS) guidelines for the investigation and management of pulmonary nodules. The software integrates with, and the findings of the software are visible within, PACS. The company expects radiologists to complete a 1-hour training session before using the technology. The software is commercially available to the NHS.

### *2.2.6 JLD-01K (JLK Inc.)*

JLD-01K is a CE-marked (class I medical device) software. It can detect and measure solid and sub-solid lung nodules in chest CT scans without contrast.

The software was trained in CT scans where nodules were at least 3mm in diameter. JLK-01K integrates with PACS.

### *2.2.7 Lung AI (Arterys)*

Lung AI is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in chest CT scans. The nodule detection and segmentation algorithms are optimised for low dose chest CT scan but the software will analyse any chest CT scan including regular dose CT scans with contrast without generating an error. Users can add, edit, or dismiss detected nodules with automatic updates to quantitative nodule information. Lung AI integrates with PACS.

### *2.2.8 Lung Nodule AI (Fujifilm)*

Lung Nodule AI is a software that can detect, measure and assess the growth of lung nodules in chest CT scans. The software is currently approved for use in Japan. The company plans to introduce the technology in Europe once required regulatory clearances are obtained.

### *2.2.9 qCT-Lung (Qure.ai)*

qCT-Lung is a CE-marked (class I medical device) software. It can detect lung nodules at least 3mm in diameter in chest CT scans without contrast. The software can also measure the volume and assess the growth of lung nodules but these features are currently available for research purposes only. Other indications for use include detection of emphysema. qCT-Lung is intended for use in people aged 18 and over. The software is compatible with slice thickness of up to 6mm. qCT-Lung integrates with PACS.

### *2.2.10 SenseCare-Lung Pro (SenseTime)*

SenseCare-Lung Pro is a CE-marked (class IIb medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in chest CT scans without contrast. Other indications for use include detection of pneumonia (including COVID-19) lesions. The software is compatible with slice thickness of up to 5mm but the preferred slice thickness is up to 1.5mm. SenseCare-Lung Pro integrates with PACS.

### *2.2.11 Veolity (MeVis)*

Veolity is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of lung nodules in low-dose and regular dose

CT scans that include complete chest, with and without contrast. The software is compatible with slice thickness of up to 3mm. Veolity is indicated for use in asymptomatic populations. Users can interact with the software by adding and dismissing nodules in the analysis and editing the findings of the software. With input from the user, the software also calculates the malignancy risk of the nodules using Brock model. Veolity's current detection algorithm only detects solid nodules. A new version of the software (Veolity 2.0) is planned for the beginning of 2022. This version will detect solid and sub-solid nodules. Usually, 2 updates or functional upgrades per year are planned. Existing versions will continue to be supported. Veolity includes rules for reporting following the British Thoracic Society (BTS) guidelines for the investigation and management of pulmonary nodules and integrates with PACS. The company states that usually 4 to 6 hours of training are needed for radiologists to learn how to use Veolity. The software is commercially available to the NHS, distributed in the UK by SynApps Solutions.

### *2.2.12 Veye Lung Nodules (Aidence)*

Veye Lung Nodules is a CE-marked (class IIb medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose or standard dose CT scans where both lungs are visible, with and without contrast. The software is compatible with slice thickness of up to 3mm. Veye Lung Nodules is intended for use in people aged 18 and over. Users can dismiss nodules found by the automated analysis but editing the findings is not possible. Users can add nodules but the software will not measure the volume of user added nodules. The software is updated frequently. Veye Lung Nodules includes rules for reporting following the British Thoracic Society (BTS) guidelines for the investigation and management of pulmonary nodules. The software integrates with, and the findings of the software are visible within, PACS. The company expects radiologists to attend a 1-hour training session before using the technology. The software is commercially available to the NHS.

### *2.2.13 VUNO Med-LungCT AI (VUNO)*

VUNO Med-LungCT AI is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose chest CT scans. It is intended for use in lung cancer screening populations. The software integrates with PACS.

**Table 1. Summary of the included technologies**

| Product name (manufacturer) | CE mark | Available to the NHS | CT scan types | Detection | Volumetry |
|---|---|---|---|---|---|
| AI-Rad Companion Chest CT (Siemens) | Class IIa * | To be confirmed | Low dose, regular dose with and without contrast * | Yes * | Yes * |
| AVIEW LCS+ (Coreline Soft) | Class IIa * | Yes | Low dose * | Yes | Yes |
| ClearRead CT (Riverain Technologies) | Class IIa | Yes | Low dose, regular dose with and without contrast | Yes | Yes |
| contextflow SEARCH Lung CT (contextflow) | Class IIa | Yes | With and without contrast | Yes | Yes |
| InferRead CT Lung (Infervision) | Class IIa | Yes | Low dose, regular dose with and without contrast | Yes | Yes |
| JLD-01K (JLK Inc.) | Class I | To be confirmed | Without contrast | Yes | Yes |
| Lung AI (Arterys) | Class IIa * | To be confirmed | Low dose, regular dose with and without contrast * | Yes * | Yes * |
| Lung Nodule AI (Fujifilm) | To be confirmed | To be confirmed | To be confirmed | Yes | Yes |
| qCT-Lung (Qure.ai) | Class I * | To be confirmed | Without contrast * | Yes * | Research only * |
| SenseCare-Lung Pro (SenseTime) | Class IIb * | To be confirmed | Without contrast * | Yes * | Yes * |
| Veolity (MeVis) | Class IIa | Yes | Low dose, regular dose with and without contrast | Yes | Yes |
| Veye Lung Nodules (Aidence) | Class IIb | Yes | Low dose, regular dose with and without contrast | Yes | Yes |
| VUNO Med-LungCT AI (VUNO) | Class IIa * | To be confirmed | Low dose * | Yes * | Yes * |

* information only from public domain.

# 3 Target condition

## 3.1 Lung cancer

Lung nodules are small growths found inside the lung. Most lung nodules on a CT scan appear as solid structures, but some are sub-solid. Sub-solid nodules have either a solid part surrounded by a non-solid, cloud-like structure (part-solid nodules) or they appear entirely non-solid (pure ground-glass nodules).

Lung nodules can be detected from chest CT scans. These may be done because of signs and symptoms suggestive of lung cancer or potentially if CT scans are used as part of lung cancer screening (for people who have a higher risk of lung cancer but have no symptoms suggestive of lung cancer). Lung nodules can also be detected from CT scans done for reasons unrelated to lung cancer (incidental detection). For example because of trauma (this may mean younger people at low risk of lung cancer) or heart problems (this may mean people with risk factors similar to risk factors for lung cancer). While most lung nodules are benign, some may be cancerous and develop into lung cancer.

Lung cancer is one of the most common types of cancer in the UK. It causes symptoms such as persistent cough, coughing up blood, and feeling short of breath. People in the early stages of the disease may not have symptoms and so lung cancer is often diagnosed late. In 2018, more than 65% of lung cancers were diagnosed at stage 3 or 4 (Cancer Research UK). The NHS Long Term Plan (section 3.52) sets out NHS's ambition to diagnose 75% of all cancers at an earlier stage, stages 1 or 2, by 2028.

## 3.2 Diagnostic and care pathway

### *3.2.1 Pathway to CT scan due to signs and symptoms suggestive of lung cancer*

The identification of people with signs and symptoms suggestive of lung cancer often happens in primary care. NICE guideline on recognition and referral for suspected cancer recommends that people aged 40 and over are offered an urgent chest X-ray (within 2 weeks of referral) if they have 2 or more, or if they have ever smoked and have 1 or more, of the following unexplained symptoms:

- cough

- fatigue
- shortness of breath
- chest pain
- weight loss
- appetite loss.

An urgent chest X-ray should also be considered for people aged 40 or over if they have persistent or recurrent chest infection, finger clubbing, enlarged lymph nodes near the collarbone or in the neck (supraclavicular lymphadenopathy or persistent cervical lymphadenopathy), chest signs consistent with lung cancer or increased platelet count (thrombocytosis).

If the chest X-ray findings suggest lung cancer, referral to secondary care should be made using a suspected cancer pathway referral for an appointment within 2 weeks. Clinical experts noted if the X-ray findings do not show abnormalities but an ongoing suspicion of lung cancer remains, referral to secondary care for a CT scan may also be made. People aged 40 or over who present with unexplained coughing up of blood (haemoptysis) should be referred directly to secondary care without a chest X-ray using the suspected cancer pathway referral.

In secondary care, people with known or suspected lung cancer should be offered a contrast-enhanced chest CT scan to further the diagnosis and stage the disease (NICE guideline on diagnosis and management of lung cancer).

### *3.2.2 Lung cancer screening*

The National Screening Committee does not currently recommend screening for lung cancer. This recommendation is currently under review, expected to be completed in 2022. The Targeted Lung Health Check programme (TLHC) is NHS England's targeted lung cancer screening programme that is currently being evaluated in some areas of England. In this programme, people aged over 55 but less than 75 who have ever smoked are invited to a free lung health check. The lung health check involves collecting information about lung health, lifestyle and family and medical history, and measuring height and weight. Following the lung health check, people assessed as at high risk of lung cancer are offered a low-dose CT scan (Targeted screening for lung cancer with low radiation dose CT: standard protocol prepared for the Targeted Lung Health Checks Programme). The use of computer aided detection systems is not a requirement under this protocol, but software is being used as part of the TLHC programme.

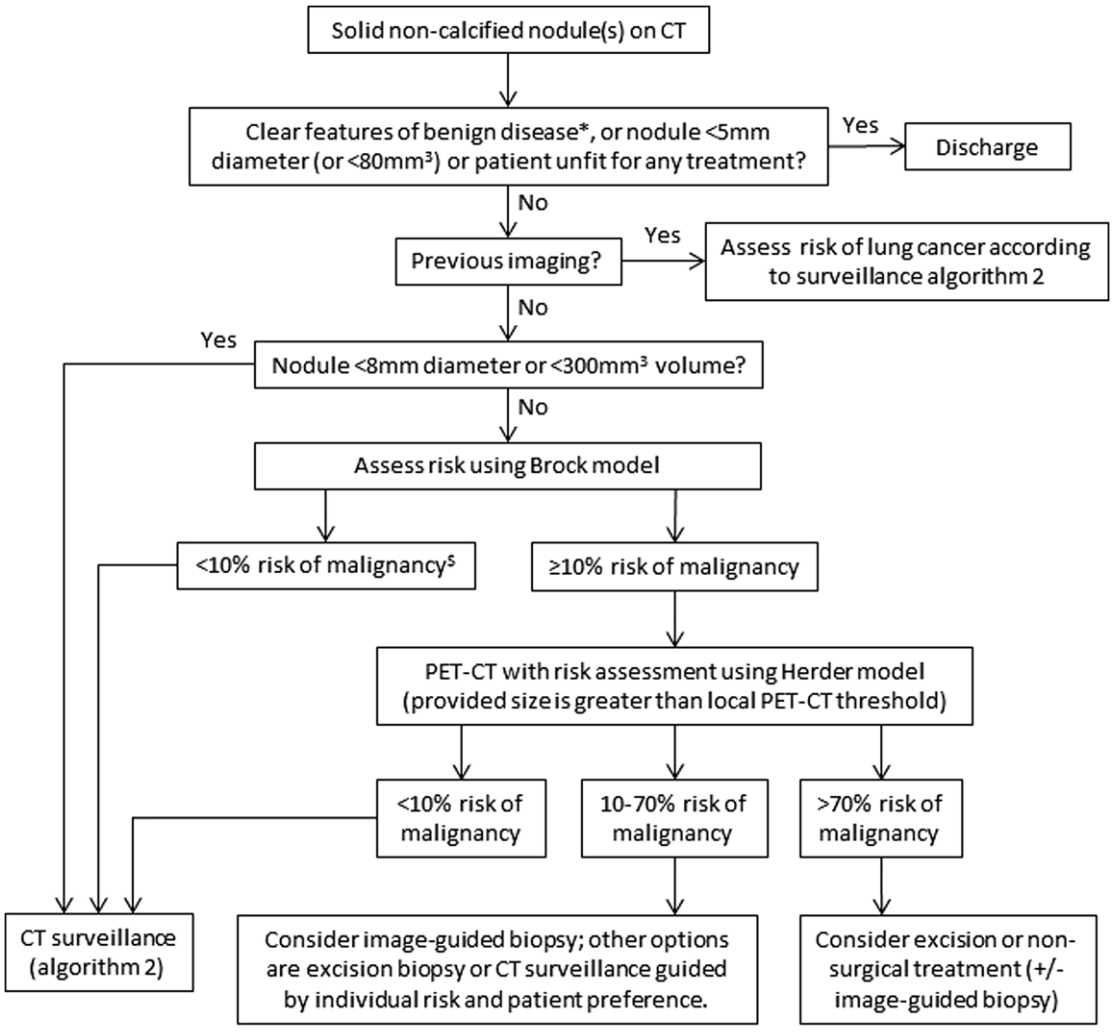
*3.2.3 Initial assessment and CT surveillance of lung nodules*

In the NHS, the investigation of identified lung nodules follows the British Thoracic Society (BTS) guidelines for the investigation and management of pulmonary nodules. The guideline recommends the same diagnostic approach for nodules detected incidentally, due to symptomatic presentation, or through screening (the TLHC Programme also follows the BTS guideline). The guideline recommendations are for lung nodules in adults. Clinical experts explained that lung nodules in children are very rarely malignant and so lung nodules in children are not currently routinely investigated to avoid unnecessary CT scans.

Figure 1 shows the recommended pathway for the initial assessment of solid lung nodules. When there are multiple nodules, the size of the largest nodule should be considered. For newly identified nodules above a specified size, malignancy risk is estimated using Brock model. The nodule size (in diameter) and the number of nodules detected are among the inputs to this multivariable prediction model.

The initial assessment of sub-solid nodules (part-solid and ground-glass) follows a similar pathway. But because these nodules can sometimes disappear on their own, the pathway involves a repeat CT scan at 3 months before the use of the Brock malignancy risk model. The Herder malignancy risk model is not used for sub-solid nodules.

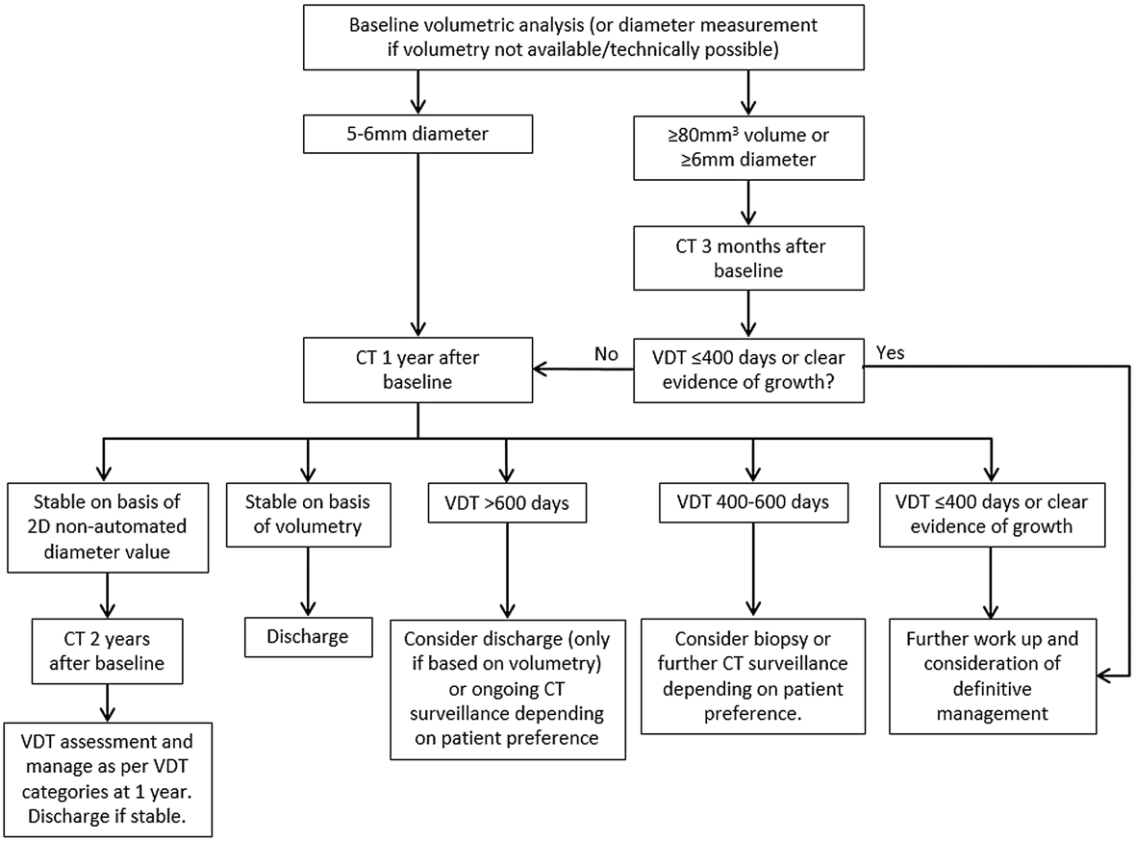
**Figure 1 Initial assessment of solid lung nodules**




* Some nodules seen may be attached to or very near the lining of the lungs (perifissural nodules), these are often pulmonary lymph nodes

Figure 2 shows the recommended pathway for CT surveillance of solid lung nodules. The overall aim of this approach is to use the presence and speed of the nodule growth to discriminate between benign and malignant nodules. The nodule growth should be assessed by estimating its volume-doubling time (VDT). The surveillance period for sub-solid nodules is longer (4 years) than for solid nodules (1 year with volume and 2 years with diameter measurements).

**Figure 2 CT surveillance of solid lung nodules**




The BTS guidelines are currently being updated.

### *3.2.4 Current methods of detecting nodules and measuring nodule volume and growth on CT scans*

Currently, in routine clinical practice, radiologists or other healthcare professionals such as radiographers detect lung nodules on chest CT scan images without assistance from any software. The healthcare professional reviewing the scan may or may not be specialised in reviewing chest CT images (for example a thoracic radiologist).

In the TLHC programme, the healthcare professionals reviewing the scans are radiologists specialised in reviewing chest CT images. They are either radiologists who regularly lead at their local lung cancer multidisciplinary team or radiologists who yearly, as part of their normal clinical practice, report more than 500 thoracic CT scans of which a significant proportion are lung cancer CT scans (Targeted screening for lung cancer with low radiation dose CT: standard protocol prepared for the Targeted Lung Health Checks Programme). Also software for automated detection of lung nodules has been

used in the TLHC programme. The British Society of Thoracic Imaging and the Royal College of Radiologists' radiology-related considerations for the TLHC include advice on software.

The BTS guidelines for the investigation and management of pulmonary nodules recommend that the size of an identified nodule is quantified as the volume of the nodule. To do this a volumetry software needs to be used. In current practice, this is often a software that is part of the PACS system or it may be a module on a software that comes with the CT scanner. In measuring the size of the part-solid nodules, the diameter of the solid part of the nodule is considered. In ground-glass nodules, the diameter of the entire nodule is measured.

This software may not have the capability of comparing subsequent scans to automatically measure the volume-doubling time. When this feature is not available or not used, the volume-doubling time is usually calculated by inputting the nodule measurements using the BTS Pulmonary Nodule Risk Calculator (also available as a Cancer Research UK and BTS produced smartphone and tablet application). In addition to growth, for ground-glass nodules any later appearance of a solid part is assessed.

It is also possible that a volumetry software is not available or measuring the nodule volume by the software is not possible because of the quality of the image or the location of the nodule within the lung. In these instances, the largest diameter of the nodule is measured and the volume-doubling time is estimated based on the diameter measurements. Clinical experts explained that diameter measurements are still widely used in the NHS.

### *3.2.5 Diagnosis and staging of lung cancer*

To guide the treatment of lung cancer, information about type and spread of the lung cancer (stage) are needed. The NICE guideline on diagnosis and management of lung cancer recommend choosing investigations that give the most information about diagnosis and staging with the least risk to the person. The type and sequence of investigations may vary but the investigations typically include a positron emission tomography-CT (PET-CT) scan and an image-guided biopsy. Other methods that may be used include MRI, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA).

### *3.2.6 Treatment for lung cancer*

After diagnosis, treatment for lung cancer is based on several factors, such as overall health, the type, size, position, and stage of cancer. The treatment

may include surgery, chemotherapy, radiotherapy, immunotherapy or other targeted therapy drugs or a combination of these (NICE guideline on diagnosis and management of lung cancer).

NICE pathway for treating lung cancer provides further details on treatment of both non-small-cell lung cancer and small-cell lung cancer.

### 3.3 Patient issues and preferences

Finding a lung nodule may cause anxiety and worry, particularly if the CT scan was done without expectation of finding lung nodules and especially if it is not clear whether the nodule is malignant or not. If this leads to a person having CT surveillance, the time of not knowing whether the nodule is malignant would be even longer. Some people may be worried about repeated radiation exposure if surveillance is needed. Earlier diagnosis would be beneficial because this would allow for earlier treatment and the potential for improved patient outcomes but overdiagnosis could lead to harms from unnecessary biopsies and treatment. Where treatment is not possible such as for people with limited life-expectancy or with multiple co-morbidities, the finding of nodules and the diagnosis of lung cancer could cause unnecessary anxiety. People may wish to discuss in advance of the CT scan what might happen if a lung nodule is found. Consistency in how assessment and care is provided across the NHS is important to people.

## *4 Comparator*

Chest CT scan review by a radiologist or another healthcare professional (such as a radiographer) without software for automated detection and analysis of lung nodules. The reviewer of the scan may use software to help measure the volume an identified lung nodule (see section 3.2.2), but this software does not automatically detect or measure lung nodules. When volumetric software is not used, nodule diameter is used to define the nodule size and nodule growth. The healthcare professional reviewing the scan may or may not be specialised in reviewing chest CT images.

Clinical experts highlighted that the experience of radiologists in reviewing CT scans for lung nodules will vary, for example from general trauma radiologists to thoracic radiologists. They further commented the level of expertise of the healthcare professional reviewing the scan may change the impact of the software. For example, less experienced reviewers may be more likely to act on nodules detected by the software, even if they disagree. As highlighted in section 3.2.4, the standard protocol for the Targeted Lung Health Checks programme (TLHC) includes specific requirements for radiologists reviewing the CT scans in the programme.

# 5 Scope of the assessment

**Table 2 Scope of the assessment**

| | |
|---|---|
| **Decision question** | Does the use of software for automated detection and analysis of lung nodules from CT scan images represent a clinically and cost-effective use of NHS resources? |
| **Populations** | 1. People who have no confirmed lung nodules, lung cancer and who are not having staging investigations or follow-up imaging for primary cancer elsewhere in the body, who have a CT scan that includes the chest:<br>• because of signs or symptoms suggestive of lung cancer (symptomatic population)<br>• for reasons unrelated to suspicion of lung cancer (incidental population)<br>• who attend lung cancer screening (inclusion of the screening population will be confirmed following the upcoming lung cancer screening recommendations of the National Screening Committee)<br><br>2. People having CT surveillance for a previously identified lung nodule.<br><br>Where data permits, the following subgroups may be considered:<br>• Ethnicity<br>• People who have a CT scan with or without contrast<br>• For the incidental population, by reason for CT scan. |
| **Interventions** | CT scan review by a radiologist or another healthcare professional using any of the following software for automated detection and analysis of lung nodules:<br>• AI-Rad Companion Chest CT (Siemens Healthineers)<br>• AVIEW LCS+ (Coreline Soft)<br>• ClearRead CT (Riverain Technologies) *<br>• contextflow SEARCH Lung CT (contextflow) **<br>• InferRead CT Lung (Infervision) *<br>• JLD-01K (JLK Inc.)<br>• Lung AI (Arterys)<br>• Lung Nodule AI (Fujifilm)<br>• qCT-Lung (Qure.ai)<br>• SenseCare-Lung Pro (SenseTime) |

| | |
|---|---|
| | • Veolity (MeVis) *<br>• Veye Lung Nodules (Aidence)<br>• VUNO Med-LungCT AI (VUNO)<br>* indication for use specifies use in asymptomatic population, therefore the software cannot be assessed in symptomatic population<br>** indication for use specifies use in symptomatic population, therefore the software cannot be assessed in incidental or screening populations<br>Please note: specific indications for use for some of the technologies are unclear because only information in the public domain was available |
| **Comparators** | CT scan review by a radiologist or another healthcare professional without software for automated detection and analysis of lung nodules from CT scan images (using diameter or volume to measure nodule size) |
| **Healthcare setting** | Secondary care or settings used for CT scans done as part of lung cancer screening |
| **Outcomes** | Intermediate measures for consideration may include:<br>• Accuracy to detect nodules<br>• Accuracy to assess volume of nodule or change in volume (when interventions are used as part of CT surveillance)<br>• Concordance between interventions to detect nodules<br>• Characteristics of detected nodules<br>• Proportion of detected nodules that are malignant<br>• Radiologist reading time<br>• Radiology report turnaround time<br>• Technical failure rate<br>• Impact of test result on clinical decision-making<br>• Number of people having CT surveillance<br>• Number of CT scans in taken as part of CT surveillance<br>• Number of people having a biopsy or excision<br>• Number of cancers detected<br>• Stage of cancer at detection<br>• Time to diagnosis<br>• Acceptability and experience of using the software |
| | Clinical outcomes for consideration may include: |

| | |
|---|---|
| | • Morbidity (including any adverse events caused by assessment or treatment)<br>• Mortality |
| | Patient-reported outcomes for consideration may include:<br>• Health-related quality of life<br>• Acceptability of use of the software |
| | Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:<br>• Cost of software (including integration to PACS)<br>• Cost of staff training<br>• Cost of data storage<br>• Cost of further diagnostic tests<br>• Cost of treatment (including costs of any adverse events) |
| | The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year. |
| **Time horizon** | The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. |

# *6 Other issues for consideration*

## 6.1 Evidence from use of the technologies in screening

The available evidence on the software may predominantly come from the screening context. There may be uncertainty about whether the findings from this setting are generalisable to the use case in this scope.

## 6.2 Software updates

The lung nodule software may have periodic updates and upgraded versions with new functionality may become available. These updates may have an impact on the accuracy to detect and measure the nodules. This means that evidence based on earlier versions of the software may not accurately reflect the effectiveness of the current versions.

## 6.3 Factors that may affect the performance of the technologies

Several factors such as the use of contrast in the CT scan, thickness of the CT sections, the lung volume, the nodule size and its location within the lung and whether the scan covers the entire lung may affect the performance of the software (Devaraj et al. 2017).

### 6.4 Use as part of CT surveillance of a detected lung nodule

If a healthcare setting has and uses the assessed software to initially detect lung nodules from CT scans, any subsequent CT surveillance may also use the software for monitoring the detected lung nodule.

There may be uncertainty about the extent to which the technologies, when used for CT surveillance of an identified lung nodule, lead to either greater or earlier (in terms of stage of cancer) detection of lung cancer. Surveillance involves multiple CT scans, so any malignancy detected by the intervention and not by the comparator (or vice versa) may be detected by a subsequent scan at a later time. The clinical significance of any such earlier detection may be unclear. The NICE diagnostics advisory committee recently noted, in an ongoing assessment of a further technology related to lung nodules (EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules), that there is currently no evidence that stage progression of malignant nodules happens in the timeframe of CT surveillance (section 3.10 of the EarlyCDT Lung diagnostics consultation document).

The use of the software for CT surveillance may have benefits for radiologists if the automated nodule detection and growth assessment saves time taken to review scans.

### 6.5 Expertise of healthcare professional reviewing CT scan

As noted in section 4, the experience of the healthcare professional reviewing a CT scan, with or without the assessed software, is likely to affect the impact of introducing the software into NHS practice. If data allows, clinical and cost effectiveness analysis considering the expertise of the reviewer should be provided.

## *7 Potential equality issues*

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

People with lung cancer may be classified as having a disability and therefore protected under the Equality Act 2010 from the point of diagnosis. Incidence rates for lung cancer in the UK are highest in people aged 85 to 89 (Cancer Research UK 2016-2018). Lung cancer is more common in men than in women. But over time, whereas lung cancer rate in men has become lower, the rate in women has increased. There are differences in the rates of lung cancer between ethnic groups. In men, lung cancer is most common in white

men and men of Bangladeshi family background. In women, lung cancer is most common in white women. The incidence and mortality of lung cancer are higher in deprived communities.

Some people may find it challenging to lie still and to hold their breath or both during a chest CT scan. Some people may find it difficult to understand the instructions for what to do during the scan.

If the software has been developed and validated in populations in which particular groups (such as people from different ethnic groups or people with lung conditions other than cancer) have been underrepresented, it may perform differently in these groups than data suggests.

# *8 Potential implementation issues*

According to the clinicians and companies, adopting the software does not require extensive training.

## 8.1 Integration into radiologists' workflow

The Royal College of Radiologists' guidance on integrating artificial intelligence with the radiology reporting workflows (RIS and PACS) notes that artificial intelligence software must be integrated in reporting workflows seamlessly and in a way that does not add extra burden to radiologists. If the software does not fully integrate into the radiologists' workflow within the Picture Archiving and Communication System (PACS) where CT scan images are reviewed and reported, using the software may increase review time. Loading new software, opening further screen windows, or having additional steps to retrieve, analyse or report the images adds to the radiologists review and reporting tasks and time. Some software may not include the rules for reporting recommended by the BTS pulmonary nodule guidelines. Clinical experts raised concerns about how the software integration might affect the stability of the PACS system.

## 8.2 IT capacity and compatibility

There are some concerns about the level of IT support and capacity needed to install and use the software. There are also concerns about the software's ability to analyse images created using different CT scanners and its compatibility with other computer packages or systems. A report generated by an external software may not be compatible with the Radiology Information System (RIS). It is also possible that the CT scan where the nodule is first identified is done at a different centre than the follow up CT scan. If different lung nodule software are used to assist to review the scans, it may be difficult

for the reporting radiologist to compare the scans and assess the nodule growth.

### 8.3 Governance issues

When the software use cloud-based servers for the image analysis, there may be issues about adequate protection of patient data. There may also be questions about software updates (potentially automatic) and what these updates mean for the clinical performance of the software.

## *9 Authors*

**Suvi Härmälä**
Topic Lead

**Thomas Walker**
Technical Adviser

December 2021

# Appendix A Glossary of terms

**Brock model**
A prediction model used to estimate the risk that lung nodule is malignant following the initial chest CT scan in the care pathway for lung nodules. The risk is calculated based on multiple factors including age, sex, nodule size, number of nodules and nodule location.

**Herder model**
A prediction model used to estimate the probability that a lung nodule is malignant following the PET-CT scan in the care pathway for lung nodules. The risk calculation is based on multiple factors similar to those used in the Brock model but it also includes PET-CT findings of metabolic activity.

**Volume-doubling time (VDT)**
Volume-doubling time is the time in days it takes for a growing lung nodule to double its volume. It is calculated after follow up CT scans in surveillance of lung nodules to assess whether the nodule is likely to be malignant and further assessment or treatment is needed.

## Appendix B Abbreviations

| | |
|---|---|
| BTS | British Thoracic Society |
| PACS | Picture Archiving and Communication System |
| PET-CT | Positron-emission tomography CT |
| TLHC | Targeted Lung Health Checks programme |
| VDT | Volume-doubling time |

## Appendix C References

Devaraj A, Van Ginneken B, Nair A et al. (2017) Use of Volumetry for Lung Nodule Management: Theory and Practice. Radiology 284(3): 630–644.