NICE advice

Lung texture analysis for measuring interstitial lung diseases

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is lung texture analysis, which includes the algorithm known as CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Rating) in peer-reviewed publications. It is used for automated measurement of interstitial lung disease, idiopathic pulmonary fibrosis and other fibrotic conditions.
- The **innovative aspect** is that lung texture analysis is a fully automated way of processing images, running analyses and returning the output without clinician involvement.
- The intended **place in therapy** would be in addition to current standard care in people with suspected interstitial lung disease, idiopathic pulmonary fibrosis or other fibrotic conditions.

- The **main points from the evidence** summarised in this briefing are from 3 cohort studies including a total of 300 patients diagnosed with interstitial lung diseases and 1 validation study including 119 patients. They show that lung texture analysis could be an effective addition to standard care in assessing interstitial lung disease.
- **Key uncertainties** around the evidence or technology are that there are no randomised controlled trials in the evidence base; the available studies are mainly retrospective cohort studies. Also, most studies that have been done within a UK context used the same patient dataset.
- The **cost** of Imbio CT lung texture analysis is £40 per analysis (excluding VAT). Unlimited use annual subscriptions are available at a cost of £20,000 per year per site (excluding VAT). This would be in addition to standard care.

The technology

Lung texture analysis (Imbio) is a digital technology that analyses standard chest CT images and maps the presence of abnormal lung textures. Lung texture analysis includes the Computer-Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER) technology. Lung texture analysis can automatically receive standard Digital Imaging and Communications in Medicine (DICOM) high-resolution CT image series from any CT scanner or picture archiving communication systems (PACS) to run lung texture analysis. The results of the analysis are summarised in a 1-page quantitative report that includes a combination of colour-coded images, figures and data to show where abnormal textures are present and how much of the lung is affected. The report can be used by clinicians involved in managing interstitial lung disease to help determine if disease is present and over time to help track stability or progression. It is expected to be used in addition to current practice to increase reader agreement and improve diagnostic accuracy.

Innovations

Lung texture provides a quantitative analysis and 3D visualisation to support personalised diagnosis and care planning. The software can automatically receive standard DICOM high-resolution CT images from any CT scanner or PACS, run lung texture analysis and return the output back to the original patient study in the institution's PACS without physician involvement.

Current care pathway

People with suspected interstitial lung disease or idiopathic pulmonary fibrosis are often referred from their GP to a chest specialist. To confirm the diagnosis and assess the severity of the disease, a CT scan of the lungs is usually needed. High-resolution CT scanning is most used and visually analysed by 1 radiologist. Pulmonary function tests are done to measure total lung capacity including forced vital capacity, an important measurement to assess lung function. A lung biopsy may also be done, where a small sample of lung tissue is taken using a keyhole procedure and examined under a microscope. Lung tissue can also be taken during a bronchoscopy. During a bronchoscopy, a tube with a camera on the end (an endoscope) is passed through the mouth or nose into the airways. Tiny tools on the endoscope are used take a sample of lung tissue.

The following publications have been identified as relevant to this care pathway:

- NICE's COVID-19 rapid guideline on interstitial lung disease
- NICE's guideline on idiopathic pulmonary fibrosis in adults: diagnosis and management
- NICE's quality standard on idiopathic pulmonary fibrosis in adults
- NICE's Pathway on idiopathic pulmonary fibrosis.

Population, setting and intended user

Lung texture analysis is intended to be used in addition to the current methods of assessment for people who have confirmed or suspected idiopathic pulmonary fibrosis, interstitial lung disease or other fibrotic conditions. The technology is designed to help clinicians in diagnosing and managing these conditions by providing a computer-assisted reading of high-resolution CT lung scans, which are done at centres across the UK. Visual assessment of scans can be challenging and time consuming. It is also common to have low levels of agreement between clinicians, even among expert readers.

Costs

Technology costs

The cost of the technology is £40 per analysis (excluding VAT). This can be decreased to

£20 per analysis based on volume. Unlimited use annual subscriptions are £20,000 per year, per site (excluding VAT). Software updates are released 1 to 3 times per year; the cost of updates and customer support are included with no additional charge for current subscriptions.

Costs of standard care

According to NHS National Cost Collection data from 2019/2020, the national average unit cost of a CT scan of 1 area is £91. The new technology will be used in addition to current standard care.

Resource consequences

Lung texture analysis is currently being integrated into clinical care at Royal United Hospitals Bath. The technology is also offered as part of thoracic radiology reading services by Heart and Lung Health, a UK-based thoracic radiology reading service comprised of NHS consultants providing services to NHS and private hospitals.

Lung texture analysis is compatible with existing CT scanners and PACS systems. There are minimal to no changes needed in facilities or infrastructure, although CT protocols may need updating to automatically forward scans to the Imbio software. The technology can be provided as either an on-site software-only service, or a cloud-based service depending on NHS site preference.

Regulatory information

Lung texture analysis is a CE-marked class IIa medical device under the Medical Devices Directive (MDD).

Equality considerations

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

No equality issues were identified in the development of this briefing.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Four studies are summarised in this briefing. There are several abstracts and other studies with mainly smaller patient populations that have not been summarised in this briefing.

Three retrospective cohort studies with 135 (Jacob et al. 2017), 110 (Ungprasert et al. 2017) and 55 people (Maldonado et al. 2014) have been included. One validation study (Bartholmai et al. 2013) was also included.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

There have been a significant number of studies done to analyse using lung texture analyses in assessing interstitial lung diseases. One of the strengths of the evidence base on the NHS context is that many of the studies have outcomes that are commonly used in NHS practice. Most studies are retrospective cohort studies using scan data from databases, rather than results from randomised controlled trials or long-term observational studies. A literature review by Jankharia and Angirish (2021) outlines the investigatory and validation studies that have been done in relation to Computer-Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER) technology. The review includes images from the Imbio lung texture analysis software to show how the results are presented and analysed by radiologists. There are also several abstracts which have not yet been published as full articles that could potentially be useful in assessing the benefit of implementing lung texture analysis within the NHS.

Lung texture analysis is intended to be used in clinical practice as a supplement to visual analysis of CT scan results, to help increase radiologist agreement and identify features

that may have been missed by readers. The evidence base consists of studies that compare quantitative CT analysis to visual CT analysis, pulmonary function tests and other imaging techniques. Also, many diagnoses are incorporated under interstitial lung diseases and the evidence base encompasses a significant number of these conditions.

Jacob et al. (2017)

Study size, design and location

A retrospective study of 135 people who were diagnosed with hypersensitivity pneumonitis and underwent CT imaging at the Royal Brompton Hospital, London between 2007 and 2011. The study was done at 1 site in the UK.

Intervention and comparators

Computer-based CT analysis (CALIPER), compared with visual CT scoring and pulmonary function tests.

Key outcomes

The following CT features were scored visually: ground glass opacity, reticulation, honeycombing, consolidation, gas trapping and traction bronchiectasis. For CALIPER CT analysis, pulmonary vessel volume was also estimated. Pulmonary function measures examined included: forced expiratory volume in 1 second, forced vital capacity, diffusing capacity for carbon monoxide, carbon monoxide transfer coefficient, residual volume, total lung capacity and composite physiologic index.

Linkages between visual and CALIPER scores for shared interstitial CT patterns were strongest for honeycombing (r=0.77) and fibrosis extent (r=0.62), while they were weakest for ground glass opacities (r=0.21). On CALIPER CT analysis, total interstitial lung disease extent showed stronger linkages with forced vital capacity, diffusing capacity for carbon monoxide and composite physiologic index than corresponding visual CT scores. Of all the CT variables scored visually or by CALIPER, pulmonary vessel volume showed the strongest links with pulmonary function tests.

Strengths and limitations

The current accepted gold standard for identifying clinical deterioration in people with

interstitial lung disease is the measurement of forced vital capacity. Therefore, CT analysis through visual and computer-based methods were specifically compared with this outcome measure. Every person included in the study was subject to all 3 interventions: CALIPER CT analysis, visual CT analysis and pulmonary function tests. Two radiologists independently evaluated each CT scan; they had 5 and 7 years thoracic imaging experience. A significant limitation of the study was that not all people had histopathological proof of diagnosis. Although it can be highlighted that this is reflective of the population usually seen in clinical practice.

Ungprasert et al. (2017)

Study size, design and location

A retrospective cohort study of 110 patients who were diagnosed with idiopathic inflammatory myopathies-associated interstitial lung disease (IIM-ILD) undergoing CT imaging and pulmonary function tests at baseline and 1 year at the Mayo Clinic, Rochester, Minnesota between 2003 and 2011. The study was done at 1 site in the US.

Intervention and comparator

Computer-based CT analysis (CALIPER) supported by 1 radiologist's visual analysis, compared with pulmonary function tests.

Key outcomes

Correlation between baseline CALIPER measurements (low attenuation areas, ground glass opacity, reticular density, honeycombing and total interstitial abnormalities) and pulmonary function test measurements (total lung capacity, diffusing capacity for carbon monoxide, forced expiratory volume in 1 second, forced vital capacity and oxygen saturation) as well as correlation between changes in measurements at 1 year were tested using Spearman correlation coefficients.

At baseline, total interstitial abnormalities as measured by CALIPER had a significant negative correlation with total lung capacity, diffusing capacity for carbon monoxide and oxygen saturation. Analysis by sub-type of interstitial abnormality revealed significant negative correlations between ground glass opacity and reticular density with total lung capacity and diffusing capacity for carbon monoxide. A significant negative correlation between ground glass opacity and oxygen saturation was also observed. At 1-year follow

up, the only significant negative correlation was change of total interstitial abnormalities compared with changes in total lung capacity and oxygen saturation.

Strengths and limitations

One radiologist reviewed the high-resolution CT scans at baseline and subsequent timepoints in a blinded fashion to correct any errors that happened in the CALIPER software. The study was also the first to show evidence of CALIPER utility beyond idiopathic pulmonary fibrosis and hypersensitivity pneumonitis. The follow up at 1 year allows the evaluation of CALIPER use at different timepoints. A major limitation of the study was that there was no standardised protocol for doing high-resolution CTs and pulmonary function tests; these were done at the discretion of the clinicians which could introduce selection bias. Also, less than 50% of people had these assessments at 1 year, resulting in a small number of eligible people for the follow-up analysis.

Maldonado et al. (2014)

Study size, design and location

A retrospective cohort study of 55 idiopathic pulmonary fibrosis patients evaluated at the Mayo Clinic, Rochester, Minnesota between 2000 and 2010. All patients had 2 high-resolution CTs within a 3-month to 15-month interval, and pulmonary function tests within 30 days of the selected scans. The study was done at 1 site in the US.

Intervention and comparators

Computer-based CT analysis (CALIPER), compared with visual analysis of CT scan by 2 thoracic radiologists and pulmonary function tests.

Key outcomes

The correlation between total lung volume measured by CALIPER and total lung capacity measured by pulmonary function tests was very good for both timepoints 1 (r=0.77) and 2 (r=0.87). Correlation between radiologist 1 and CALIPER for interstitial lung disease scoring was mild to moderate for timepoint 1 (range 0.29 to 0.63) and timepoint 2 (0.24 to 0.64). Correlation between radiologist 2 and CALIPER for interstitial lung disease scoring was mild to moderate for timepoint 1 (range 0.29 to 0.48) and timepoint 2 (0.28 to 0.64).

Strengths and limitations

The study directly investigated the agreement between CALIPER CT analysis and radiologists' visual analysis separately. There was a mild to moderate correlation between observations for both clinicians. This suggests that CALIPER may be a useful tool to help readers agree about CT scan results. An additional strength of the study is that the pulmonary function tests were done within 30 days of the respective CT scans. A limitation of this study is that it needed people to have had 2 high-resolution CTs. In clinical practice this is usually not possible because most people will only have the images from 1 high-resolution CT available. Although the study aimed to quantify correlation between CALIPER and visual CT analysis, this does not consider errors that could have been made using either of the 2 methods.

Bartholmai et al. (2013)

Study size, design and location

A validation study which used statistical analysis and graphical representation of the CALIPER software results, to assess correlation with other measurements in 119 patients with proven diagnosis of interstitial lung disease from the Lung Tissue Research Consortium (LTRC) database. The study was conducted at 1 site in the US.

Intervention and comparators

Computer-based CT analysis (CALIPER), compared with visual analysis of CT scan and pulmonary function tests.

Key outcomes

To verify that the automated classification of lung abnormalities by CALIPER matched those of expert radiologist description of disease, regional matching to severity and character of disease determined by the interpreting radiologist was done using Spearman's correlation coefficients. Significant correlations were found for ground glass opacity ($r=0.19$ to 0.42, $p<0.039$), honeycombing ($r=0.27$ to 0.56, $p<0.003$) and reticular infiltrate ($r=0.18$ to 0.47, $p<0.05$) quantitative scores and corresponding visual scores.

Significant correlations were noted between CALIPER measurements and physiologic parameters that are accepted as biomarkers for disease severity in interstitial lung

disease. Percentage of reticular infiltrates correlated significantly ($p<0.001$) with changes in 6-minute walk total distance ($r=-0.32$), forced vital capacity ($r=-0.63$), diffusing capacity for carbon monoxide ($r=-0.65$) and total lung capacity ($r=-0.44$). Similarly, significant inverse correlation ($p<0.001$) existed between lung classified as normal by CALIPER and physiologic tests: 6-minute walk total distance ($r=0.32$), forced vital capacity ($r=0.66$), diffusing capacity for carbon monoxide ($r=0.59$) and total lung capacity ($r=0.56$).

Strengths and limitations

The study was the first to describe the use of CALIPER in interstitial lung diseases and validate it using correlation with visual analysis and pulmonary function measurements. The most significant limitation of the study was that it was done at the same institute where the technology was developed.

Sustainability

There is no evidence on the sustainability of this technology.

Recent and ongoing studies

No ongoing or in-development trials were identified.

Expert comments

Comments on this technology were invited from clinical experts working in the field. The comments received are individual opinions and do not represent NICE's view.

All of the experts were familiar with this technology, but only 1 had used it before.

Level of innovation

All the experts agreed that lung texture analysis is a novel technology for the assessment of interstitial lung diseases and it would be used as well as current radiologist assessment of CT imaging, which is subject to errors of interpretation. There is a lack of appropriately trained thoracic radiologists within the NHS, while a general radiologist can often misread CT images and incorrectly label lung features which leads to misdiagnosis. Therefore, the

technology would add value for general radiologists in non-specialist centres. Another expert commented that the technology is most likely to provide utility in specialist centres for people with interstitial lung disease and that it is unlikely for general respiratory clinicians to be employing this type of technology.

Potential patient impact

Three of the 4 clinical experts commented that the technology may help to standardise the level of reporting through objective quantification of CT scans in people with interstitial lung disease. This will allow better identification of people who are showing disease progression and track changes over time in a more reproducible manner than current standard practice. The improved accuracy of diagnosis and reduction in individual variation between CT reporting could provide huge benefits for people. One of the experts explained how improved diagnostic accuracy would allow earlier treatment, potentially improving quality of life and survival in people with interstitial lung disease.

Potential system impact

Three experts commented on the improved accuracy of diagnosis, making sure people have the right treatments at the right time, which would speed up treatment pathways and reduce wastage of inappropriate treatments. The benefit to individual people of a more efficient treatment pathway would reduce both the cost and burden of treatment across the healthcare system. Two of the experts suggested that the technology would be useful in clinical trials where accurate quantification of interstitial lung disease is needed to identify novel treatments for diseases such as idiopathic pulmonary fibrosis. The technology can provide a biomarker of disease phenotype that can be used in the context of a clinical trial.

General comments

All of the experts anticipated that the technology will cost more than current standard care, though 2 experts explained that routine use of the technology might lead to productivity benefits by reducing radiologists' reporting time. All of the experts highlighted that potential users of the technology will need training to interpret the quantified data. None of the experts listed any adverse events or potential risks associated with the technology if the automated CT analysis is reviewed by a radiologist. Two of the experts suggested that real-world NHS experience of the technology is lacking and that it has not

really been validated as a tool to be used in clinical practice. This could be overcome by a larger pilot study in a specialist interstitial lung disease centre to show value.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Nazia Chaudhuri, consultant respiratory physician and lead of interstitial lung disease unit, Manchester University NHS Foundation Trust. Did not declare any interests.
- Dr Jonathan Rodrigues, consultant radiologist, Royal United Hospitals Bath NHS Foundation Trust. Royal United Hospitals Bath is a research centre for Imbio which receives non-financial support and free use of Imbio's portfolio of products for clinical research. Partner at Heart and Lung Health Imaging which offers Imbio lung density and lung texture analysis.
- Professor Sujal Desai, consultant radiologist, Royal Brompton and Harefield Hospitals and National Heart and Lung Institute. Did not declare any interests.
- Dr Ian Forrest, consultant respiratory physician, Newcastle upon Tyne Hospitals NHS Foundation Trust. Did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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