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Creating and Verifying a Deep Learning-Powered Automatic Algorithm for Chest Radiographs to Identify Active Pulmonary Tuberculosis

Bollu Siva Keshava Rao[1], Dr. Priti Maheshwary[2]

[1]Department of Computer Science and Engineering, Rabindranath Tagore University, Bhopal, M.P., India.
bsivakeshav@gmail.com

[2]Department of Computer Science and Engineering, Rabindranath Tagore University, Bhopal, M.P., India.
pritimaheshwary@rediffmail.com

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Abstract:

Chest radiographs (CRs) that demonstrate active pulmonary tuberculosis are required to screen and diagnose conditions related to tuberculosis. An automated system has the potential to improve diagnostic performance while also accelerating the process of TB screening, which is a source of optimism. To build a deep learning-based automatic detection (DLAD) approach, thirteen radiologists who are board-certified went through 54,211 normal CRs and 6,778 CRs with active pulmonary tuberculosis. To ensure that DLAD was effective, six external, multinational datasets were used. To compare the efficacy of DLAD with that of physicians, fifteen doctors including thoracic radiotherapists, board-certified radiotherapists, and non-radiology physicians took part in an observer performance exam. To measure the effectiveness of lesion-wise localization along with image-wise classification, respectively, the area over the ROC (receiver operating characteristic) curves and the area under a separate free-response ROC curve were used. Determined were the DLAD's sensitivity and specificities using two cutoffs: high sensitivity [98%] and high specificity [98%] established by internal validation. It was shown that DLAD achieved a classification performance of 0.977-1.000 and a localisation performance of 0.973-1.000. In contrast to the high-specificity cutoff, which generated sensitivity and specificities ranging from 84.1% to 99.0% and 99.1% to 100%, correspondingly, the high-sensitivity cutoff produced 94.3% to 100% sensitivities and 91.1% to 100% specificities. Both localization (0.993 vs. 0.664-0.925) and classifying (0.993 vs. 0.746-0.971) were areas where DLAD outperformed all physician groups. When it came to reliably identifying active pulmonary TB upon CR, the DLAD fared better than clinicians, particularly thoracic radiologists.

Keywords: Chest Radiographs, Tuberculosis, Deep learning, Active Pulmonary, ROC.

1. Introduction:

About 1.8 million people died from tuberculosis in 2017, making it the most common infectious cause of mortality globally. The World Health Organisation advises screening for active TB in high-risk groups to lessen the burden of illness. With a specificity and sensitivity of 99% as well as 76% for any abnormality, and 88% and 90% for abnormalities linked to TB, chest radiographs (CRs), which are reasonably priced and widely accessible, have been helpful in this respect and have been instrumental in the screening of active tuberculosis. Despite its encouraging results, TB diagnosis on CRs is still a labour & time-intensive procedure that needs an expert's clarification. Expert

radiologists are hard to come by in high-burden nations with inadequate medical resources [1-2]. Under this situation, automated pulmonary TB diagnosis on CRs could prove very beneficial clinically.

There have been many attempts at automatic detection so far. An analysis using a commercially available program revealed a performance area over the curve of the receiver operating characteristics (AUROC) of 0.72 to 0.85, which is regarded as quite high but not ideal for use in a clinical workflow [3]. The deep learning approach, however, showed promising results even in medical picture classifications after its landslide victory in the 2013 Image Net Large-scale Visual Recognition Competition. Regarding pulmonary tuberculosis detection in CRs, just released encouraging findings from a pilot investigation utilising the deep learning approach on 500 TB patients as well as 500 healthy controls across 5 datasets. Since their focus was on image-wise TB classification using a small dataset, they did not address further evaluations such as abnormality localisation, model generalisability, or performance compared to clinicians. With the area developing quickly and the need for easy-to-implement enhancements in TB screening and diagnosis worldwide, these evaluations are crucial in establishing the practical usefulness of new techniques [5-6]. Therefore, the goal of the work was to create an autonomous detection algorithm (DLAD) for active pulmonary TB on CRs based on deep learning and to test its performance using several datasets in contrast to that of medical professionals.

2. Techniques:

This research was approved by the institutional review panels of all collaborating institutions, with the informed consent of the patients waived.

2.1. DLAD Development:

2.1.1. Collection of Data:

Data was retrieved retrospectively from the imaging database of Seoul National University Hospital (SNUH) to investigate the origins of DLAD. As part of this data set, there were 57,482 normal CRs from 48,987 people (male: female = 22c025:26c963; mean standard deviation age 52 ± 17 years) and 8068 CRs with active pulmonary TB (tuberculosis CRs) from 1608 individuals (male: female = 908:698; mean ± standard deviations age 58. 18 years). Normal CRs were found in the search for radiology reports that included CRs acquired between 2011 and 2016. A total of TB culture records (CRs) were collected from individuals with a diagnosis of active pulmonary tuberculosis (TB) and a treatment interval of less than one month from 2014 to 2017.

Individuals were tested for Mycobacterium tuberculosis using a PCR (polymerase chain reaction) or mycobacterial culture. It collected all CRs regardless of whether there were related chest CT images to confirm the amount and variety of data [7-10]. Radiographs were collected from several pieces of equipment and were all taken in a posteroanterior orientation. After the pictures were labelled, 1 298 TB CRs were incorrectly extracted and 3 261 ordinary CRs were taken out of the database. Totalling 54,211 normal CRs and 6768 TB CRs, the DLAD technique was devised. An equal number of normal CRs and TB CRs were randomly distributed across three datasets: one for internal validation, which aimed to check in-house performance; another for tuning, which aimed to optimise

hyperparameters; and finally, for training, there were 53c621 normal CRs and 6458 TB CRs, used to optimise network weights. Patients in one dataset did not always correspond to another. The fact that previous studies have looked at normal CRs in the datasets is worth noting. Nevertheless, this investigation's aims and the algorithms' designs were different from those of the previous research, as was the study's central subject.

2.2 Annotation and Labelling of Images:

Before the implementation of DLAD, all CR pictures were evaluated by board-certified radiotherapists. Standard chest radiographs, previously interpreted as normal in standard practice, were re-evaluated by one of five board-certified radiologists, each with seven years of expertise in interpreting chest radiographs, to exclude the possibility of any aberrant results [11-12]. The tagging and annotation of pictures for TB CRs was carried out by eight radiologists who were board-certified and had 7 to 14 years of experience. Their job was to determine whether the data indicated active pulmonary tuberculosis. Of the total tuberculosis case reports, 1,128 out of 6,768 were annotated for persistent pulmonary TB lesions, accounting for 16.8%. While two radiologists annotated 12.8% of tuberculosis case reports (828/6468) in the training data set, five radiologists marked all TB case reporting in both the tuning and internal verification datasets. For the tuning and internal validation datasets, lesions identified by three or more radiologists were deemed actual lesions. On the other hand, for the training dataset, all marked lesions were considered real [14-15].

2.3 Construction of the Algorithm:

The researcher used a 27-layer deep convolutional neural network with 12 residual connections in this DLAD method. A semi-supervised localisation strategy was used for training as only part of the training information was labelled. The network's final layer was divided into two parts: one for image-wise classification and another for lesion-wise localisation [16]. To exclude non-lung lesions from the network's detection capabilities, the localisation layer has a lung segmentation module.

The researcher randomly resized CRs to cover the different lesion sizes before entering them into the network. The network was designed to be resilient to input from various sources and conditions by utilising image augmentation methods such as geometric procedures (including horizontal flipping, cropping, along rotation) and photometric procedures (including brightness, contrast, gamma jittering, along noise injection). The final estimate was the average of three networks' forecasts, each trained with similar data but using different hyperparameters [17-19]. The classification stage of DLAD takes an input CR and outputs a continuous value ranging from 0 to 1, which is the probability of tuberculosis (TB) at the image level. The localisation layer superimposed a single-channel image over the input CR, with continuous values ranging from 0 to 1, reflecting the per-pixel probability of TB.

2.4 Evaluation of DLAD Capabilities:

External validation was carried out using six datasets to confirm DLAD's generalisation performance, after an internal performance assessment with an internal verification dataset. For external dataset validation, two open-source datasets and data collected in the past from four different institutions were used. There were both typical and tuberculosis-related CRs in the four

hospitals' datasets [20-22]. To ensure an accurate evaluation of DLAD's performance, CRs with corresponding CT images were included, in contrast to the data set's growth, to set a definitive standard for classification (i.e., normal CR compared to tuberculosis CR) and localisation (i.e., the location of the tuberculosis lesion in a tuberculosis CR).

The following items were considered for inclusion in the TB CRs: C-reactive protein samples were collected from patients with active pulmonary TB during 2016 and 2017, with a minimum of one month between the beginning of therapy and the collection of C-reactive protein samples. With CT-related CRs spaced no more than one month apart. The TB lesions were annotated separately using CT images by the board-certified radiologists at every facility. For conventional CRs, the following were the inclusion criteria [23-24]: CRs were acquired between May and June of 2018, with similar normal CT scans performed at intervals of one month or less. The CT scans were confirmed to be normal by radiologists from each of the participating institutions. Instances of overlapping with a developing dataset were not found in the validated external data set from SNUH. Two datasets attained from the US National Library of Medication are accessible to the public. The TB testing initiatives in Shenzhen, China, & Montgomery County, Maryland, both provided normal and TB CR datasets, respectively. All CRs were reviewed for tuberculosis lesions and nonparenchymal TB by two experienced thoracic radiologists who scrutinized through the two public databases. The two radiologists examined the CRs independently before reevaluating them together whenever they disagreed. The DLAD was designed to target pulmonary tuberculosis, thus removing 16 TB CRs from the Shenzhen dataset and 4 from the Montgomery dataset since pleural effusion was not always associated with tuberculosis.

2.5 Test of Observer Performance:

An observer performance test was carried out to compare the DLAD and physician performances and to determine whether DLAD may improve doctors' performances. Five thoracic radiologists with thirteen to twenty-six years of experience, five board-certified radiologists with seven to five years of experience, and five non-radiology doctors made up the three groups of readers with different levels of expertise. There were two sessions for the exam. Without DLAD's help, each reader evaluated each CR in session 1 on their own, in a random sequence. The localisation of TB lesions on each case report (CR) and the classification of CRs as moreover consuming lively pulmonic TB findings or not were requested of the physicians. To facilitate localisation, doctors were requested to mark every lung abnormality associated with active TB (ignoring abnormalities that were unlikely to be connected to the disease) and to indicate on a 5-point scale how confident they were about each annotated lesion [25].

Readers assessed each CR once again in session 2, this time with DLAD's help. Each reader was invited to affirm or modify their choice as necessary after examining their own original choices from session 1 and the DLAD data session 1 readers did not use DLAD and instead evaluated each CR in a random sequence. The purpose of this study was to have physicians identify the TB lesions on each case report and to categorise the cases as having active pulmonary tuberculosis or not. To pinpoint the exact location of TB, doctors had to use a 5-point confidence scale to mark any lung anomalies associated with the disease, disregarding any that were not likely to represent the disease, about

every lesion that has been marked (Regarding the observer's performance test interface, see Supplementary Figures 1 and 2.).

2.6 Analyses Statistical:

The entire statistical analysis was carried out using R, specifically the RJafroc package, which was developed by the R Project for Statistical Computing in Vienna, Austria. To assess the accuracy of the classification process for each picture, use the receiver-operating characteristic (ROC) analyses; to assess the accuracy of the localisation process for each lesion, the researchers used jackknife alternative free-response ROC (JAFROC) studies. As levels of trust for ROC with JAFROC analyses, accordingly, for DLAD assessment, we used the maximum pixel-wise possibility in a real lesion along with the image-wise probabilities worth of each CR. In image-wise classification, the doctors' degree of confidence was determined by using the most confidently classified lesions in each picture. The results assessed of the ROC and JAFROC studies by calculating the area under the ROC curves (AUROCs) and the various free-response curves of ROC (AUAFROCs), respectively. A suggested procedure was used to check the statistical significance.

The students & the cases were both preserved as random effects in investigations of the reader collection, but in analyses of individual viewers, only the instances were analysed as random effects. In addition, for lesion-based localisation, evaluate the specificities and sensitivity of image-based classification and the actual detection rate, which is defined as the ratio of correctly located lesions to the overall quantity of lesions. A high-sensitivity threshold of 98% for image-wise identification & a high-specificity cut of 99% was obtained from in-house validation findings, which were used to classify tests as positive or negative. These cutoff values were then used to generate the DLAD's output probability. Medical professionals considered every detected lesion to be positive. McNemar was used to test and compare the degrees of sensitivity, and reliability of detection rates. A difference of statistical significance was shown by results with a value of P less than 05. To fix the problem of numerous comparisons, several methods were used.

3. Result:

3.1 Evaluation and Verification of DLAD Function:

For DLAD, the AUROC was 0.989 (95% CI, 0.977-0.998) and the AUAFROC was 0.978 (96% CI, 0.967-0.989) in the validation dataset internal review. With a sensitivity level of 0.0267 and a specificity level of 0.5362, the classification limits were determined by DLAD's output probability. The results of DLAD's testing on external validation datasets are shown in Figure 1(a,b). While AUAFROCs were in the range of 0.974 to 1.001, AUROCs were in the range of 0.978 to 1.001.

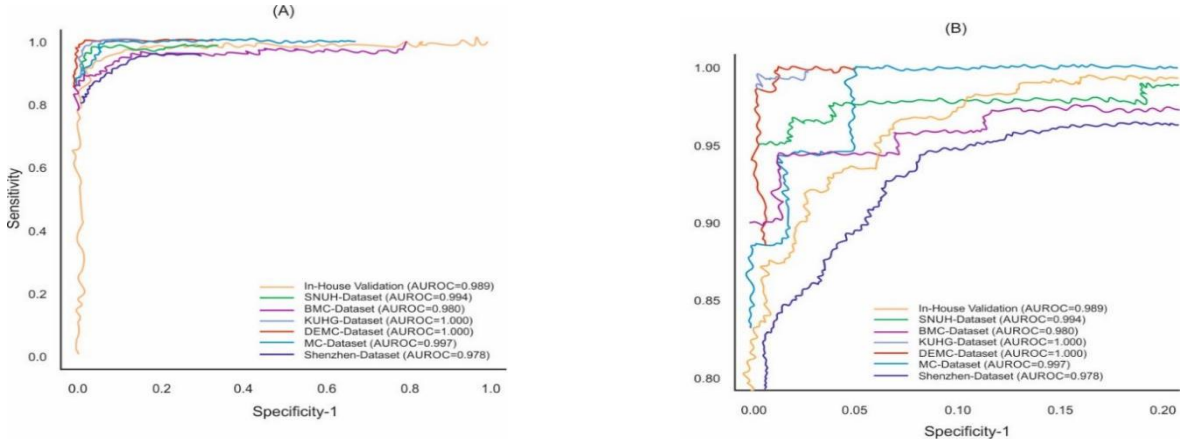

Figure 1. Internal and external validation of the deep learning-based automated detection algorithm (DLAD).

3.2 Test of Observer Performance:

For the first session, the AUROCs for pooled non-radiology doctors were 0.747, 0.947, and 0.972, respectively; for the same group, the AUAFROCs were 0.664, 0.900, & 0.925. The second session's AUROCs were 0.850 aimed at one reading group, 0.961 for another, and 0.971 for the third, while the corresponding AUAFROCs were 0.781, 0.924, and 0.942. Among the four reader groups compared to DLAD and doctors, DLAD performed better on the AUROC and AUAFROC tests (Figure 2 a,b).

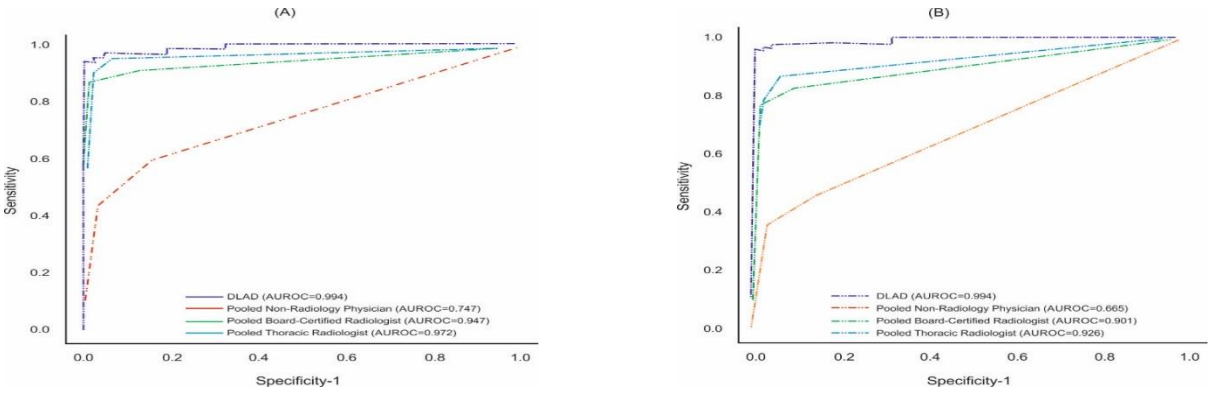

Figure 2. Diagnostic performance comparison between physician groups and deep learning-based automated detection system (DLAD)

When tested in AUROC, DLAD outperformed 13 out of 15 doctors; when tested in AUAFROC, it outperformed every reader. No significant gains in AUROC were detected across any of the reading groups when comparing sessions 1 and 2. Notably, substantial enhancements were seen across all three reader groups for AUAFROC (refer to Supplementary Figure 3).

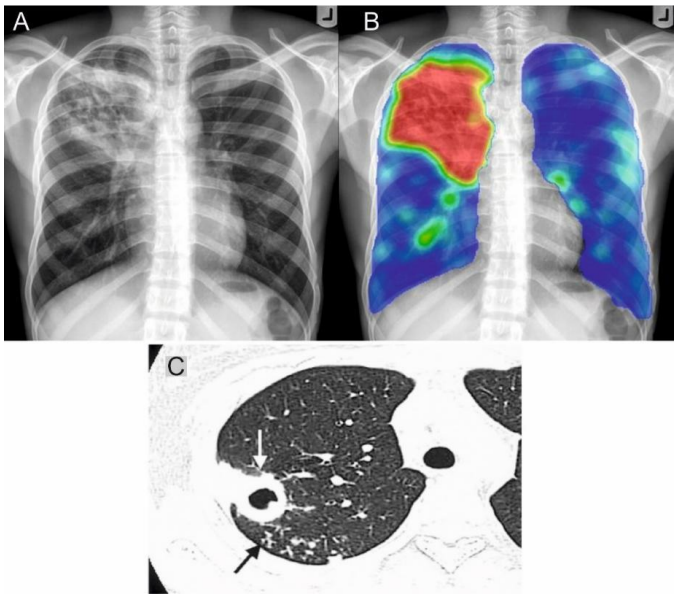

Figure 3. An Example from the performance test for observers

The chest radiogram of a 25-year-old female persistent with several satellite nodules and a cavitary mass is shown in Figure 3 (a). The mass and the computed tomography scans showed good correspondence. The likelihood ratio of 0.9663 for active pulmonary TB was obtained in this instance by the deep learning–based automated detection method, and the lesion was accurately localised in the right upper lung area (Figure 3. b) by the classification activation map. When pulmonary TB is active, radiologic abnormalities such as these are common (Figure 3. c).

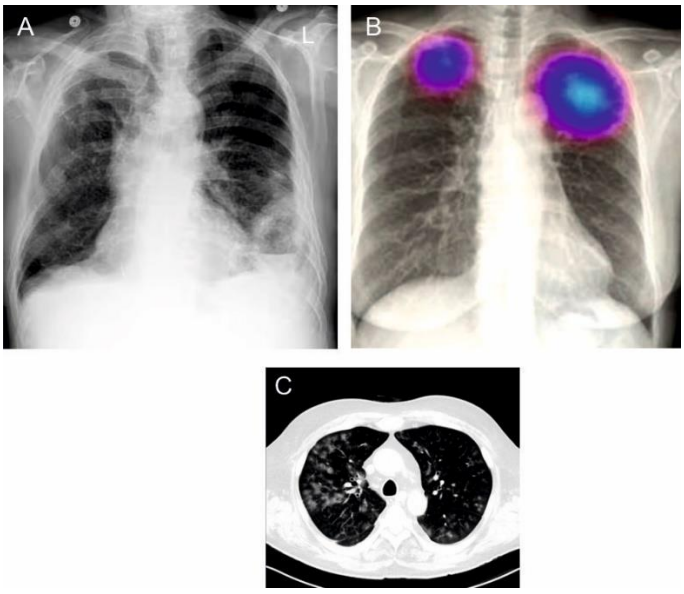

Figure 4. Observer Performance Test Example

Figure 4. (a) shows the results of a chest radiograph taken of a female patient 59 years old; the DLAD, an automated detection technique based on deep learning, yielded a probability value of 0.9526, along with a matching classifying activation map (Figure 4. b), which were first overlooked by two readers (non-radiology doctors) on the associated computed tomography picture (Figure 4. c).

After reviewing the DLAD data, readers who had previously incorrectly classified a chest radiograph changed their classification.

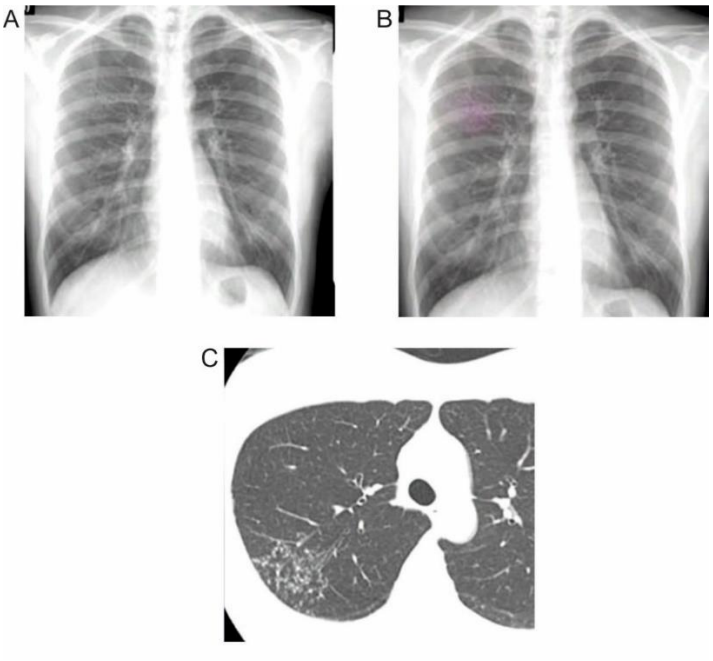

Figure 5. An Example from the performance test for observers.

A 35-year-old female patient's chest radiograph (Figure 5. a) and after looking over the DLAD data, two of the fifteen readers seven of whom had originally missed the lesion corrected their reading (Figure 5. b). The accompanying computed tomography picture (Figure 5. c) showed a little nodular infiltrate in the right upper lung region. The lesion was successfully localised using the deep learning-based automated detection method (DLAD), which also produced a likelihood value of 0.1625.

While twelve readers showed significant gains in AUAFROC during session two, five readers showed remarkable improvements in AUROC. The findings demonstrated that the non-radiology doctors in the pool performed significantly better in session 2 in terms of compassion, specificity, and accurate recognition rates, while the board-certified radiotherapist in the pool performed significantly better in terms of sensitivity and true uncovering rates. Only in session 2 did the combined thoracic radiologists show a statistically significant improvement in the error-free detection rate. Representative photos from an observer's performance test are shown in Figures 3–5.

4. Conclusion:

The researcher achieved amazing results in both the in-house dataset and six separate datasets after developing and validating DLAD algorithms for active pulmonic TB on CRs. Image-wise categorisation and lesion-wise localisation were two areas where DLAD surpassed most physicians, even thoracic radiologists. Researchers demonstrated that DLAD improved the localisation of lesions by physicians.

The DLAD algorithm has the following strengths: First, tested DLAD with 6 independent datasets of CRs from various nations and quality levels. DLAD performed better than a commercial software

package in all permutations, demonstrating good generalisability. Second, DLAD to a variety of doctors, including thoracic radiologists. Despite earlier research comparing commercial software to skilled nonexpert readers, its performance was shown to be inferior to radiologists. The work is the first to reveal an automated system that can diagnose active pulmonary TB better than doctors and thoracic radiologists.

Finally, the third and most prevalent application of automated detection methods in clinical settings was to evaluate the DLAD in a second reader. DLAD improved the sensitivity and specificity of non-radiology physicians. DLAD increased sensitivity in radiologists who have earned their board certification. At last, our DLAD made it possible to localise lesions and classify images individually. It is debatable if image-wise classification is more therapeutically relevant than localising each tuberculosis lesion on CR. Doctors' confidence in the DLAD model can increase if localisation helps them comprehend the model's output. Understanding how a deep learning model explains its output is crucial for determining its reliability. Doctors may be hesitant to adopt black box algorithms due to the lack of transparency around its inputs and outputs, which might lead to catastrophic mistakes in medical applications. By surpassing thoracic radiologists' (DLAD) localisation performance in lesion-wise and by enhancing doctors' localisation performance after DLAD data analysis, our DLAD seems to be capable of depicting the decision reasoning.

The DLAD has two potential uses in the medical field. To begin with, the DLAD has the potential to serve as an additional pair of eyes in clinical practice, enhancing the efficiency and effectiveness of doctors treating active TB, particularly in primary care and community-based settings where general practitioners, not radiologists, should be interpreting clinical reports. Second, when it comes to TB CR classification, our DLAD beats thoracic radiologists, which might mean it can screen patients or triage CRs who need professional advice. Many restrictions on our research are in place. A retrospective normal and TB CR dataset was used to validate DLAD first. The real reality would be quite different from our current environment. There could be other anomalies, and the prevalence of active tuberculosis in the lungs might be much lower than what we saw in our study. Prospective studies to validate existing DLAD in clinical settings may be able to build on our results. Secondly, instead of CT, radiologists decide on the reference standards for the development dataset. That reference standard may be reflective of reality as, in actual practice, doctors visually examine CRs to detect and track active pulmonary tuberculosis.

Due to the importance of evaluating diagnostic performance, CT-based methods used external validation datasets with standards of reference for TB and actual normal CRs. When tested on datasets used for third-party verification, DLAD performed satisfactorily.

Third, active tuberculosis in the lungs is the focus of our DLAD algorithm. The result was a failure to handle TB pleurisy and other important thoracic diseases, such as lung cancer. It is also not known whether DLAD can differentiate active pulmonary tuberculosis from different pulmonary abnormalities or detect radiologic abnormalities outside of the lung. These challenges should be addressed in future studies. To sum up, the DLAD outperformed most physicians, including thoracic radiotherapists, in the detection active pulmonic TB on CR.

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