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Quantitative assessment of AI-based chest CT lung nodule detection in lung cancer screening: future prospects and main challenges

Marufjon Salokhiddinov[a], Ruth Awotwe[a], Munojat Ismailova[a]
[a]Radiology Department, Republic Zangiota No-2 COVID Specialized Hospital, Uzbekistan

1. Introduction

Lung cancer is the most common cause of cancer-related death. It is known for being particularly aggressive. Early detection of asymptomatic lung cancer is crucial for optimal treatment, which can greatly increase patients' survival rates. Since the beginning of the twentieth century, the incidence in the population has increased several times. Its growth is especially pronounced in industrialized countries, where lung cancer ranks first in the structure of oncological morbidity. Lung cancer also ranks among the top three cancers in terms of incidence rates for both men and women. As the precursor, lung nodules are the main indication of lung cancer. Therefore, lung screening by CT exams has been recommended for identifying and characterizing nodules to detect early lung cancer.

The manifestation of lung nodules in CT images is complicated because of their irregular shapes, broad gray value range, and varied scale [1]. It is a time consuming and challenging task to effectively detect nodules for Radiologists. Additionally, differentiating benign from malignant nodules is another challenging task. Currently, pulmonary nodules incidentally observed on CT exams are handled by following consensus standards [2, 3]. But that has several drawbacks. Because the Radiologist's interpretation of each lesion is a complicated process, the evaluation performance is highly dependent on the experience or skills of the Radiologist, so the diagnosis is not always consistent. Considering the low efficiency of human reading, some patients might miss the ideal opportunity for treatment [4,5,6,7].

The computer-aided automatic solution has been proposed and utilized to address these challenges. It is expected to be able to overcome physical human limitations, such as the limited gray level recognition of the human visual system, fatigue, and distraction [8]. It can also provide diagnostic results in a repeatable and reliable manner. It can therefore be used to reduce Radiologists' workloads, locate nodules that Radiologists might overlook, and improve diagnostic accuracy [4]. Recently-developed artificial intelligence (AI) technology has made the computer-aided automatic solution even more promising. Deep learning, as one subset of AI technology, allows the model to learn high-dimensional abstract features from vast amounts of data and empowers the model to handle complex tasks. AI has demonstrated many compelling advantages and accomplishments [9,10,11,12,13] in imaging diagnosis and/or evaluation.

In this study, we aim to quantitatively assess the performance of AI-assisted reading versus traditional radiology reports in detecting lung nodules and evaluate AI as a method of characterizing and classifying lung nodules in lung cancer screening.

2. Materials and Methods

2.1 Data Preparation and Categorization

The study included 635 patients with a mean age of 52±9 years old. They underwent chest CT exam from May to October 2021 at Republic Zangiota No-2 COVID Specialized Hospital, Uzbekistan. Scans were not included in the study if:

(a) All lung lobes were not fully visible in the field of view
(b) The image contained motion artifacts
(c) The image did not meet Digital Imaging and Communications in Medicine standards
(d) The Radiologists responsible for ground truth labeling were unable to confidently annotate the images [14]

2.2 CT Image Acquisition

For non-contrast-enhanced chest CT scanning, the uCT® 550 scanner (United Imaging Healthcare, Shanghai, China) was used. The collimation of the CT detector was 256 x 0.625 mm, 64 x 0.625 mm, 96 x 0.6 mm, and 320 x 0 x 5 mm, respectively. In the supine position, each subject underwent an inspiratory CT scan during a single breath hold. The tube voltage was set to be either 120 kV or 100 kV depending on the patient size. The dose modulation was on, and the tube current ranged from 50 to 200 mAs. Slice thickness ranged from 0.625 to 1.0 mm.

2.3 Radiologist Interpretation

One Radiologist with over five years of experience reviewed the chest CT images. RadiAnt DICOM Viewer was used to review the studies. The Radiologist was given unlimited reading time and the option to adjust the display based on scan-specific characteristics to ensure optimal reading quality. Nodules in our dataset were divided into five types based on the National Comprehensive Cancer Network (NCCN) recommendations for lung cancer screening (version 2.2019): solid nodules (<5 or >5 mm), subsolid nodules (<5 or >5 mm), and calcified nodules.

2.4 Artificial Intelligence-assisted Reading

On chest CT images, uAI® Discover Chest[1] (United Imaging Healthcare, Shanghai, China) can automatically identify and measure lung nodules. The CT console automatically sends the CT images to the AI server for lung nodule detection once acquired. It took about 2 to 4 minutes to transfer and process the whole volume images of each patient. In short, this system automatically generates a bounding box that shows the characteristics of the suspected nodule, such as its diameter and volume, as well as its components (solid, part-solid, or nonsolid).

2.5 AI Model Development

Recent research [15,16,17] studies have proposed using deep learning approaches for the detection and classification of lung nodules with CT images, as such approaches have demonstrated significant improvements in both tasks. In this work, the automated processing was performed using United Imaging Intelligence's uAI Discover Chest AI-based approach. For automated nodule detection, the uAI Discover Chest employs cascading feature pyramids and a heterogeneous convolutional neural network in its algorithm. Conventional deep learning approaches can only identify objects at a single scale – they cannot handle items with significant size variations. As shown in Figure 1, the uAI Discover Chest approach uses a 3D feature pyramids network (FPN) with V-Net to specifically solve the large-scale variance problem.

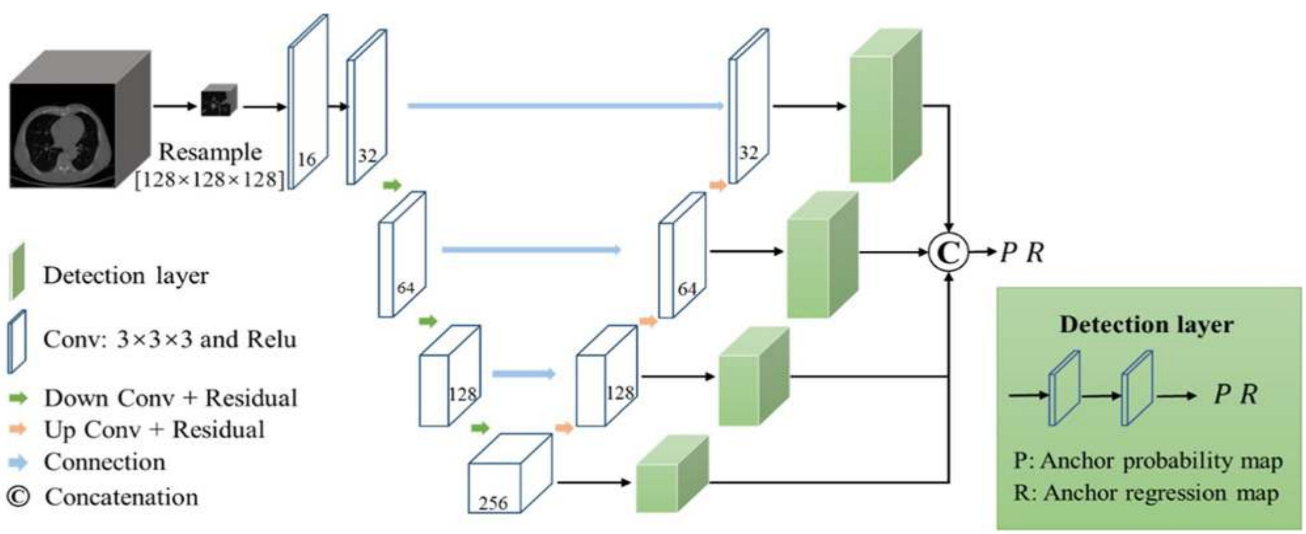

Figure 1. The architecture of the feature pyramid network (FPN).

1 This product is a work in progress; the information in this article represents ongoing research and development. No 510k application has been filed with the FDA. This product is not available for sale in the U.S. for clinical uses and also may not be available for such sales in other countries

2.6 Nodule Categorization

Lung nodules are divided into three main types according to the NCCN guideline [18]: solid, part-solid, and non-solid nodules. Each type has a unique management process. Solid nodules are further divided into strata of <5 and >5 mm, part-solid nodules <5 and >5 mm, and calcified nodules. Typical nodules of different types are shown in Figure 2.

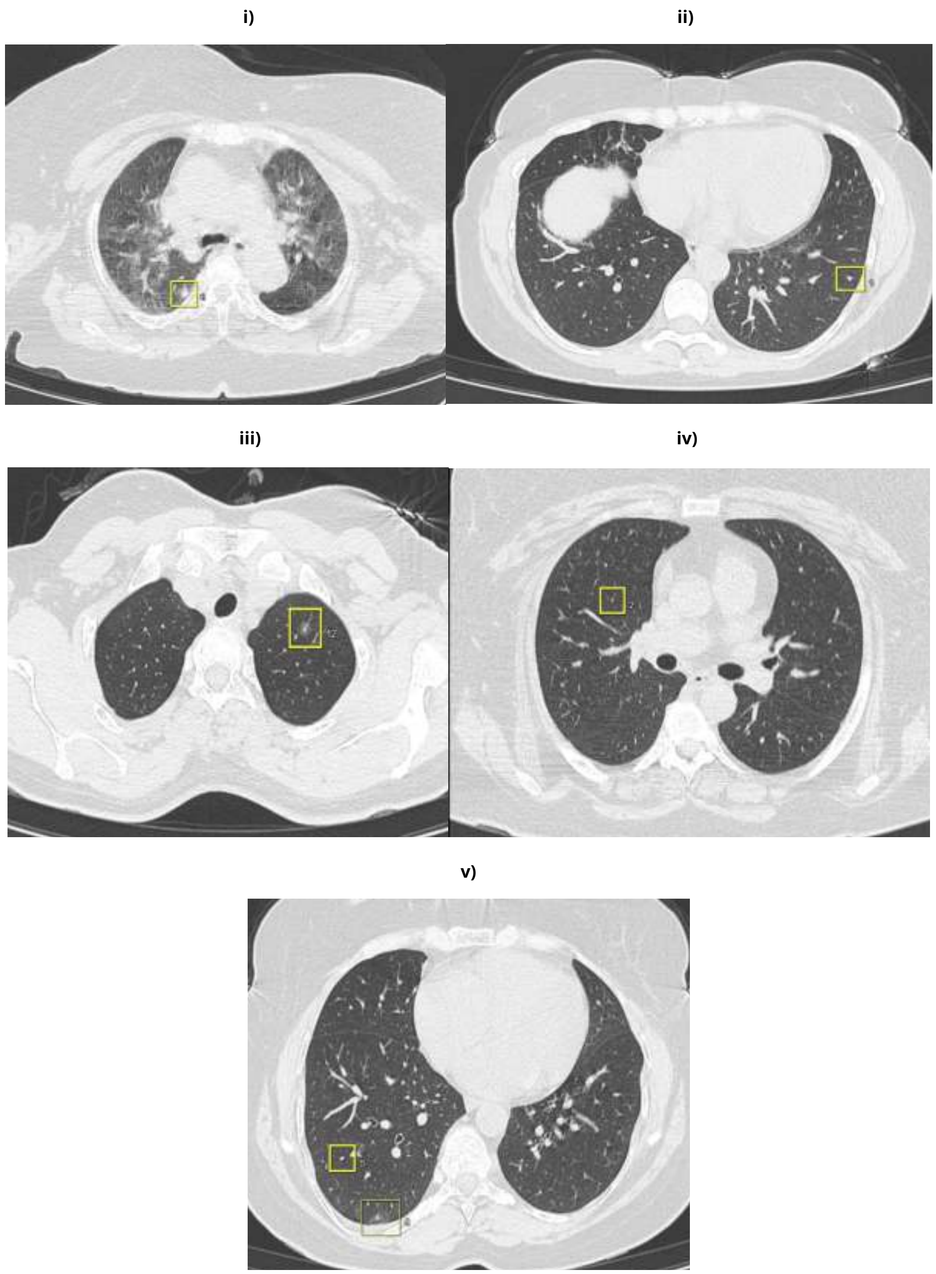

Figure 2. Nodule Categorization according to NCCN. i) Solid >5 mm, ii) Solid <5 mm, iii) Subsolid >5 mm, iv) Subsolid <5 mm, v) Calcified.

2.7 Panel Review

Two Radiologists with 15 and 20 years of experience in chest radiology were included in the review panel to evaluate the results reported by the Radiologist and AI system. The review panel was to establish a reference standard for the presence of nodules. Based on the standard, the figure of merit (FOM) could be calculated by including the number of false negatives, true negatives, false positives, and true positives. For instance, a lung nodule was regarded as a false-positive nodule if it was discovered by a Radiologist or detected by AI-assisted reading but was not confirmed by the review panel. The system interface of the uAI Discover Chest assisted lung nodule evaluation is shown in Figure 3.

2.8 Statistical analysis

In this study, 1082 nodules were included from the data of 635 patients, further classified as 778 (<5mm = 513 and >5 mm = 265) solid nodules, 283 (<5mm = 186 and >5 mm = 97) subsolid nodules and 21 calcified nodules. Statistical analysis was performed using MedCalc®, version 19.3 (MedCalc Software Ltd). Sensitivity and accuracy were measured to evaluate the performance of lung nodule detection, using the following equations, respectively:

$$Sensitivity = \frac{TP}{(TP+FN)} \quad (1)$$

$$Accuracy = \frac{TP+TN}{TP+FP+TN+FN} \quad (2)$$

where TP is the true positive, TN is the true negative, FP is the false positive, and FN is the false negative. FP is an outcome where the model incorrectly predicts a nodule in the lung CT without its existence.

3. Results

In the detection of solid nodules, the sensitivity and accuracy were 96.80% and 94.08% for AI-reading and 89.50% and 85.34% for radiological observation, respectively. The sensitivity and accuracy for <5 mm solid nodules were 96.80% and 94.34% with AI-reading and 91.70% and 88.65% with radiological observation, and for >5 mm solid nodules were 96.90% and 93.58% with AI-reading and 85.10% and 79.02% with radiological observation, respectively.

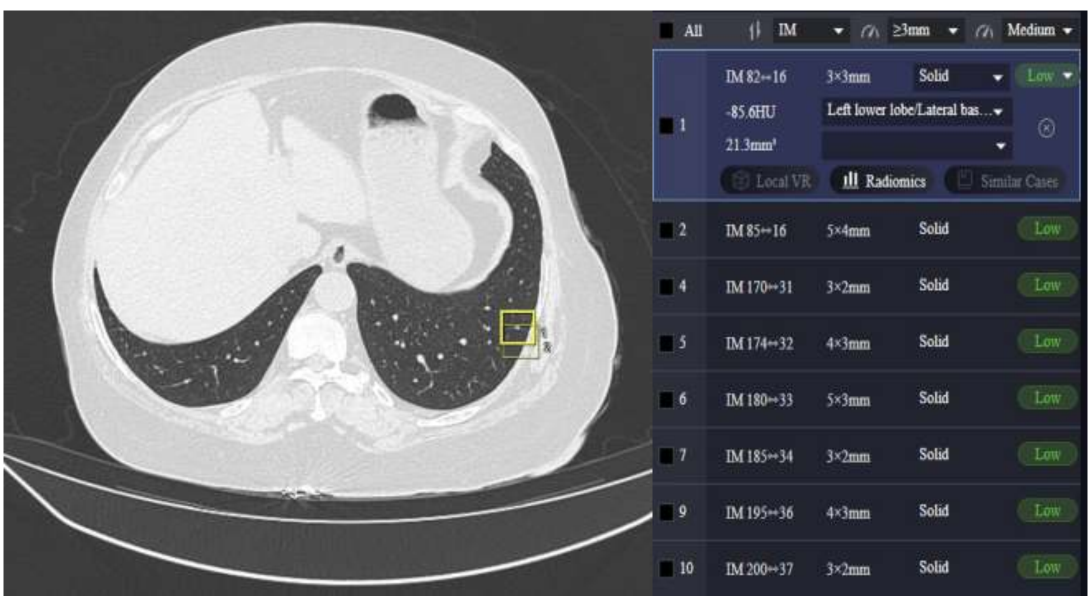

Figure 3. uAI® Discovery Chest-assisted lung nodule evaluation system interface

A similar analysis was performed for sub-solid and calcified nodules. The sensitivity and accuracy were 93.34% and 89.04% for AI-reading and 80.00% and 75.26% for radiological observation, respectively, in the sub-solid nodule detection. The sensitivity and accuracy for <5 mm sub-solid nodules were 93.80% and 90.21% with AI-reading and 87.10% and 82.32% with radiological observation, and for >5 mm sub-solid nodules were 92.50% and 86.86% with AI-reading and 67.40% and 63.36% with radiological observation, respectively.

The sensitivity and accuracy of the AI-reading-based calcified nodule detection were 95.34% and 95.34%, and 88.90% and 76.19% for Radiologist observation, respectively. The comparison of the detection performance between AI reading and Radiologist observation for all solid, subsolid, and calcified nodules is shown in Figure 4. Figure 5 displays the bar graph of the sensitivity and accuracy of AI reading and Radiologist observation for <5 mm and >5 mm solid and subsolid nodules detection.

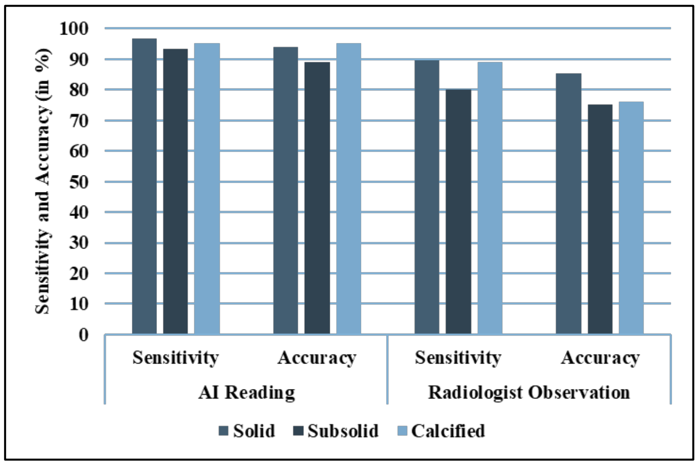

Figure 4. Bar graph of the sensitivity and accuracy of AI reading and Radiologist observation for solid, subsolid and calcified nodules detection.

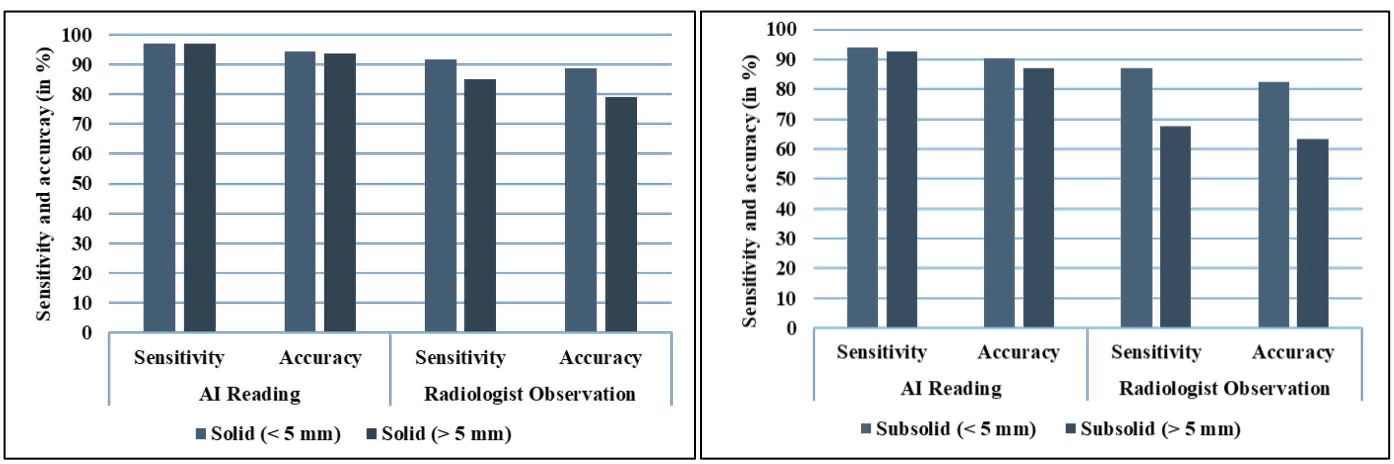

Figure 5. Bar graph of the sensitivity and accuracy of AI reading and Radiologist observation for a) <5 mm and >5 mm solid nodules and b) <5 mm and >5 mm subsolid nodule detection.

4. Discussion

The performance of AI reading and Radiologist observations were quantitively assessed in detecting multiple type nodules including solid, subsolid, and calcified ones. The assessment showed that the performance of AI was better than Radiologist performance in all nodule categories. This study suggests that AI was more sensitive and accurate in detecting the nodules. It is consistent with most other studies that AI is a reliable and sensitive method to use in lung nodule detection.

Compared to earlier studies [19,20,21], uAI Discover Chest introduced several key advanced techniques. First, it used a classification network to further reduce false positives and to analyze large-scale data. The model demonstrated a significantly higher identification rate in sensitivity and accuracy than Radiologists achieved. By utilizing the threshold ReLU, this heterogeneous network not only reduced the overfitting problem but also improved detection performance. The detection of solid nodules had the highest sensitivity as compared to sub-solids and calcified lesions. The results obtained in this work showed that the overall performance of uAI Discover Chest algorithm in detecting lung nodules of different sizes and different types depicted better outcomes as compared to the Radiologist's assessment, especially in detecting nodules that the Radiologist missed.

Nevertheless, this study had a limitation that need to be addressed in the future. There was no true gold standard available for the comparison of outcomes. For the evaluation in this study, a reference standard was carried out by the two Radiologists having an experience of 8 years and 7 years respectively. In such cases, there is a possibility of missing out fewer lung nodules which may lead to an inconsistency of obtained results. According to recent research, the performance of a cutting-edge artificial intelligence system for lung nodule detection and characterization is comparable to that of skilled Radiologists. Numerous AI studies discuss cutting-edge architectures for finding lung nodules, with the Radiologists' consensus as the reference standard [22,23,24].

Finding all lung cancers, not all nodules, is the ultimate goal. Therefore, future research should concentrate on a reference standard that measures cancer detection and is based on histopathological evidence or follow-up imaging for at least 2 years (depending on morphology to judge the stability of lesions). Unfortunately, there are no publicly available datasets with a sizable number of CT-detected malignant nodules [25]. The NLST database is the largest database that is open to the public, but the metadata does not specify which nodules were biopsied. Therefore, even with all the available screening scans and knowledge of the pathological evidence, it is not always clear which CT lesions were cancerous.

However, the issue of lack of data is currently being addressed by a variety of approaches, one of which is the creation and dissemination of databases that are open to the public. For instance, in 2017, the National Institutes of Health disseminated one hundred thousand labeled chest radiographs [26,27] in their collection. The labels of the data were obtained by applying the technology of natural language processing into reading the radiology reports. It makes it possible to implement bigger databases and skip the human labeling step. It will also resolve the imperfection in statistical significance and make it conducive to further study.

The methods employed in lung nodule image classification have shown massive progress from user-defined to technological feature-based methods. Though the accuracy achieved with the user-defined features is over 90%, as seen in the work of Liu and Hou [28], and Wei and Cao [29], it is solely based on the professional understanding and analysis of nodules which is very subjective and lacks uniformity and standardization. Performance can be improved by combining it with other methods like generic features. Most research studies have resorted to using AI tools in developing algorithms, which are most efficient in identifying features of imaging and making precise differentiation, improving lung cancer detection [30]. AI can be employed to improve the efficiency of Radiologists in nodule detection. It must meet several requirements, such as processing speed, cost of training, maintenance, and implementation to detect various shapes, and low numbers of false positives, for Radiologists to use it routinely [31,32].

The use of a convolutional neural network (CNN) like the generative adversarial network (GAN) is another method that can be utilized to circumvent the lack of large datasets [33]. This method involves the generation of data sets that are fabricated to contain characteristics that are analogous to those of a specific training dataset. These GANs could be taught to learn representative features in a totally unsupervised fashion through the process of training [31]. The labeling step can be skipped entirely because the features are generated rather than chosen from images that already exist in the database. GANs can either be integrated into supervised strategies or used on their own without supervision.

5. Conclusion

In conclusion, the experiment's results demonstrated that the uAI Discover Chest outperformed the Radiologists' assessment on average in terms of lesion identification sensitivity. Furthermore, the performance of the uAI

Discover Chest algorithm to identify lung nodules is consistent and less subjective compared to assessments made by skilled Radiologists regardless of lung nodule size. Results obtained in this study also suggest that the use of uAI Discover Chest for clinical screening can greatly benefit Radiologists in making a substantial diagnosis. The uAI Discover Chest can be considered an effective tool due to its advantages such as consistent performance, faster processing, and high clinical efficiency.

6. Image/Figure Courtesy

All images are the courtesy of Republic Zangiota No-2 COVID Specialized Hospital, Taskent, Uzbekistan.

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Author Biography

Dr. Marufjon Salokhiddinov

Head of Department
Radiology Department,
Republic Zangiota №2 COVID
Specialized Hospital
Uzbekistan

Dr. Marufjon Salokhiddinov completed his BSc in Medicine from Tashkent Medical Academy and a one-year internship in Neurology, followed by MSc in Medical Imaging, at the University of Aberdeen, UK. After the completion of his MSc, he was employed at the Department of Radiology, Tashkent Medical Academy. Since 2020, Dr. Marufjon has been working as an M.D. Radiologist at Republic Zangiota No-2 Clinical Hospital, Tashkent, Uzbekistan. Dr. Marufjon has been awarded with several prizes including "El-yurt Umidi" funded MSc by the Government of Uzbekistan, Young Investigator Award by WFN, and Best Poster Awards from WCN, ESR, WFITN, and AAN. He has published several research articles at national and international conferences/congresses.

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