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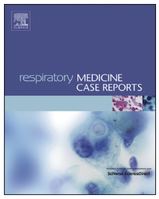

Case Report

Reevaluation of missed lung cancer with artificial intelligence

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ABSTRACT

Lung cancer is often missed on chest radiographs, despite chest radiography typically being the first imaging modality in the diagnosis pathway. We present a 46 year-old male with chest pain referred for chest X-ray, and initial interpretation reported no abnormality within the patient's lungs. The patient was discharged but returned 4 months later with persistent and worsening symptoms. At this time, chest X-ray was again performed and revealed an enlarging left perihilar mass with post-obstructive atelectasis in the left lower lobe. Follow-up chest computerized tomography scan confirmed lung cancer with post-obstructive atelectasis, and subsequent bronchoscopy-assisted biopsy confirmed squamous cell carcinoma. Retrospective analysis of the initial chest radiograph, which had reported normal findings, was performed with Chest-CAD, a Food and Drug Administration (FDA) cleared computer-assisted detection (CAD) software device that analyzes chest radiograph studies using artificial intelligence. The device highlighted the perihilar region of the left lung as suspicious. Additional information provided by artificial intelligence software holds promise to prevent missed detection of lung cancer on chest radiographs.

1. Introduction

Lung cancer is the second most common type of cancer in both men and women, and the leading cause of cancer death, making up almost 25% of all cancer deaths [1]. Chest radiography is typically the first imaging modality in the diagnosis pathway [2,3] and is the most common diagnostic imaging examination performed in emergency departments [4–6]. Despite this, lung cancer is often missed on chest radiographs [7–10]. Specifically, misdiagnosis on chest radiographs leads to approximately 90% of missed lung cancer cases [9,11]. Overall, missed lung cancer is a significant source of concern among physicians and an important medicolegal challenge [9,11].

The breadth of pathologies that can appear on chest radiographs is vast, and physicians play a crucial role in the visual detection of these pathologies in order to effectively manage and treat patients. In particular, lung cancer is often missed on chest radiographs, leading to delayed diagnosis and treatment. Lung cancer may not always appear on chest radiographs. When it is visible, lung cancer can have a variable appearance on radiography. At earlier stages it often appears non-calcified and nodular in shape. Identification of any new opacity with these characteristics should prompt a physician to recommend a computerized tomography (CT) scan for further characterization. Early detection of malignant pulmonary nodules in patients has been shown to reduce lung cancer related mortality by up to 20% [12]. In patients diagnosed with lung cancer, it is not unusual to discover chest abnormalities during retrospective

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observation of previous radiologic exams [9]. Factors that contribute to missed lung cancer on a chest X-ray include observer error, tumor characteristics, and technical considerations [9].

Augmenting physicians with artificial intelligence tools has been shown to improve accuracy [12–15]. These tools improve detection accuracy by highlighting suspicious regions of interest (hereafter ROIs) in radiographs and other medical imaging modalities and learn to do so by analyzing large volumes of data. As of August 2021, there were 126 artificial intelligence tools cleared by the Food and Drug Administration (FDA) for radiology, 31 of which were related to chest imaging and only 7 of which were for chest radiography [16]. Imagen Technologies' Chest-CAD is one such FDA-cleared tool - it identifies suspicious ROIs in chest radiographs and can be used by physicians.

We present a case of missed lung cancer on chest radiograph and discuss potential opportunities for artificial intelligence to reduce the likelihood of such a miss in the future.

2. Case presentation

A 46 year-old male presented to the emergency department at 2 a.m. with chest pain. The patient had no prior medical or surgical history; 0.75 pack-year smoking history; and no history of alcohol abuse. There was no prior imaging for comparison. Physical exam was non-contributory and within normal limits. As part of the patient's evaluation the patient received labs, which were within normal limits, as well as a 2-view chest X-ray (Fig. 1) obtained at 3 a.m. The radiology report (Fig. 2) did not identify an abnormality within the patient's lungs.

The patient was discharged and returned 4 months later with persistent and worsening symptoms that included cough, chest pain, and shortness of breath. A subsequent 2-view chest X-ray (Fig. 3) revealed an enlarging left perihilar mass with post-obstructive atelectasis in the left lower lobe.

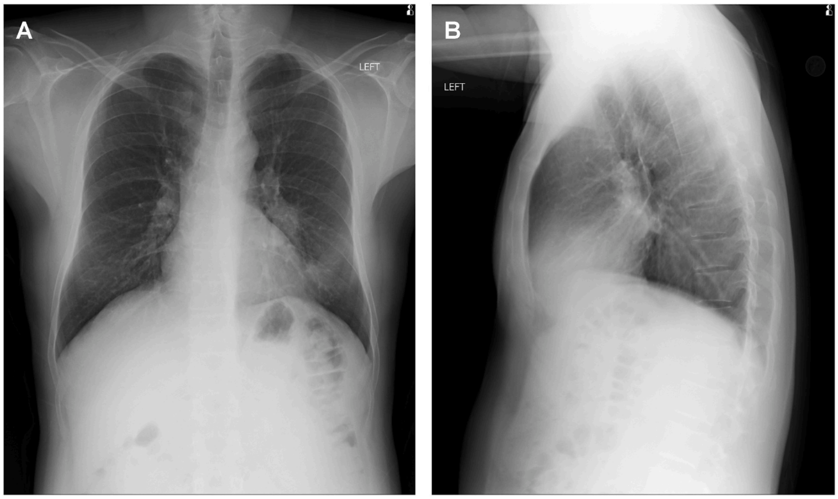
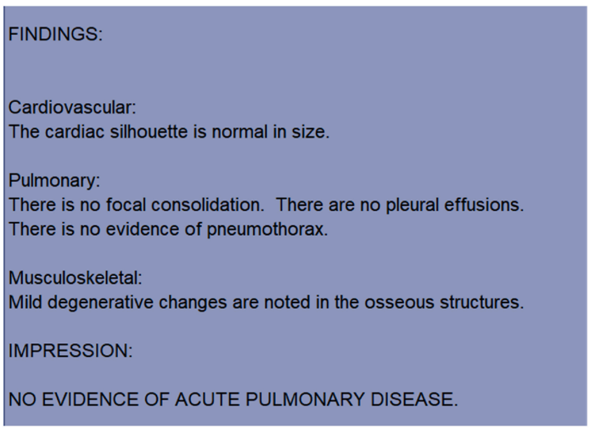


Fig. 1. Posterior-anterior (A) and lateral chest X-ray (B) demonstrating a subtle left infrahilar nodular opacity with a region of atelectasis in the left lower lung, best seen on the frontal view.


FINDINGS:

Cardiovascular:
The cardiac silhouette is normal in size.

Pulmonary:
There is no focal consolidation. There are no pleural effusions.
There is no evidence of pneumothorax.

Musculoskeletal:
Mild degenerative changes are noted in the osseous structures.

IMPRESSION:

NO EVIDENCE OF ACUTE PULMONARY DISEASE.

Fig. 2. The radiology report for the initial chest X-ray, where the findings demonstrated in Fig. 1 are not described.

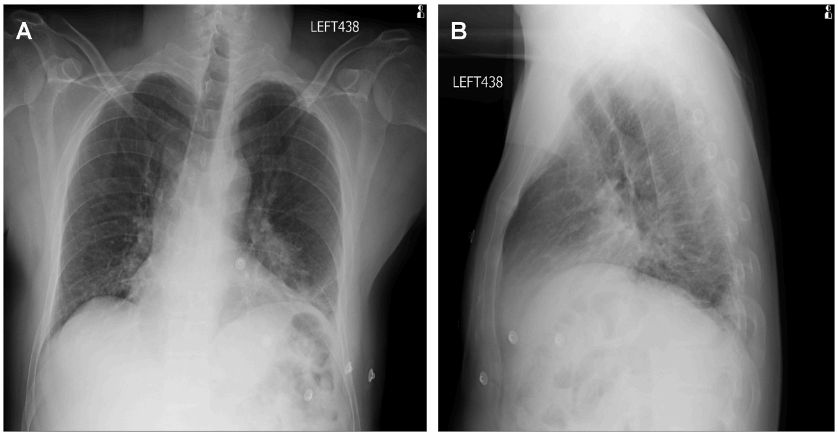


Fig. 3. Posterior-anterior (A) and lateral chest X-ray (B) demonstrating an enlarging left perihilar mass with post-obstructive atelectasis in the left lower lobe when compared to earlier chest X-ray taken 4 months prior.

A CT scan (Fig. 4) was performed that evening, within hours of the second chest X-ray, which confirmed lung cancer with post-obstructive atelectasis.

Subsequent bronchoscopy-assisted biopsy confirmed squamous cell carcinoma. The patient was later treated with pneumonectomy, chemotherapy, and radiation, but passed away within one year following this initial CT scan due to complications from this lung cancer.

This case was retrospectively reviewed with Imagen's FDA-cleared software, Chest-CAD, based on an artificial intelligence algorithm indicated for use in adult patients with chest radiographs. Chest-CAD uses deep learning, a branch of artificial intelligence that learns from patterns in data, to analyze chest radiographs and identify suspicious ROIs in chest radiographs. The artificial intelligence algorithms were trained with hundreds of thousands of studies annotated by multiple experts. Chest-CAD analysis identified suspicious ROIs in the lungs (Fig. 5), with one ROI encompassing early lung cancer in the left lung. A heatmap (Fig. 6), which is an intermediate processing output of Chest-CAD and not shown to the end user, clearly focused on the known left infrahilar malignancy and post-obstructive left lower lung atelectasis. A heatmap is not part of the output of the FDA cleared device and provided here for illustrative purposes.

3. Discussion

In this case report we demonstrate the promising results of applying Imagen Technologies' Chest-CAD artificial intelligence tool to the chest X-ray of a patient whose lung cancer was not initially detected by the radiologist.

Prior work has recognized the burden of missed lung cancer on chest radiography [7,9,17]. Indeed, early studies of the factors leading to overlooked lung lesions date back to the middle of last century [18,19]. Despite extensive technological advancement, the issue of missed lung lesions persists [7,9,17], and multiple factors including observer error can contribute to missed lung cancer on chest X-rays [9–11]. A 19% miss rate was measured on identifying non-small cell lung cancer on chest radiographs [20], and radiological examinations overall have a retrospective error rate of 30% [21].

Studies have shown that tumor detectability rate is strongly influenced by its location [9]. In particular, this case demonstrates the challenge of identifying lung cancer in the hilar regions, which are known to be prone to missed lesions [9]. There is natural variabil-

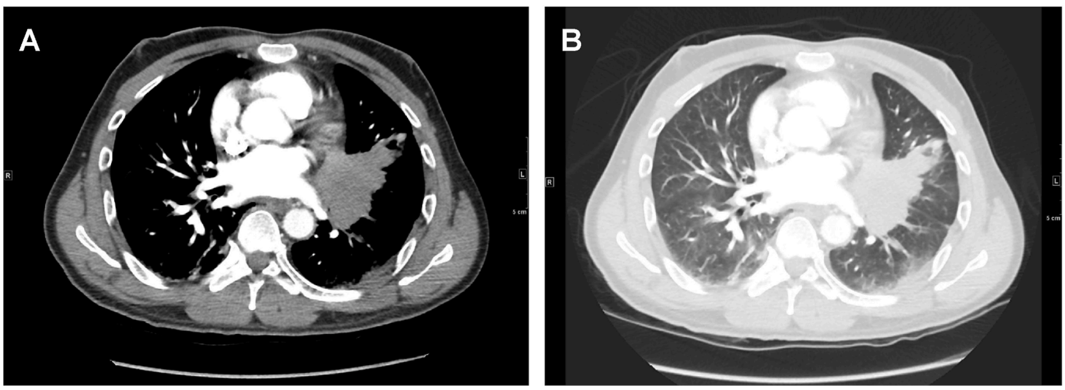


Fig. 4. Two examples of the axial CT scan of the chest with differing window level and width to highlight soft tissue (A) and lungs (B) that reveal a left lower lobe mass with post-obstructive atelectasis.

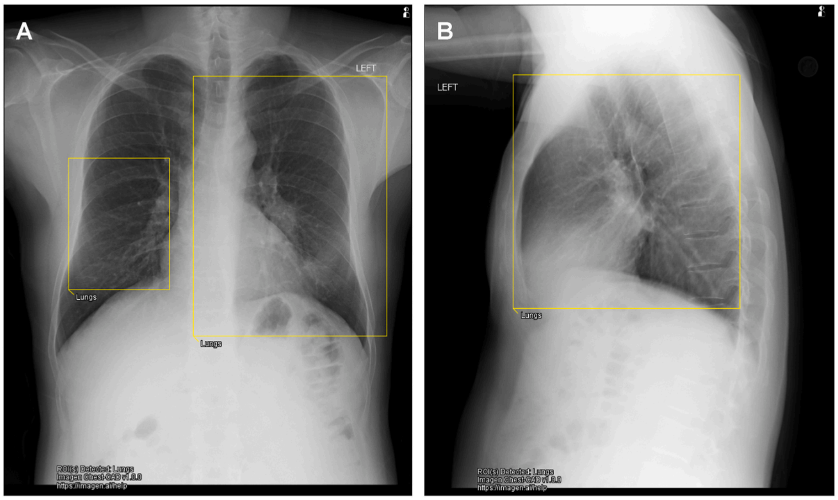


Fig. 5. Posterior-Anterior (A) and lateral chest X-ray (B) demonstrating Chest-CAD output that identified suspicious ROIs in the lungs.

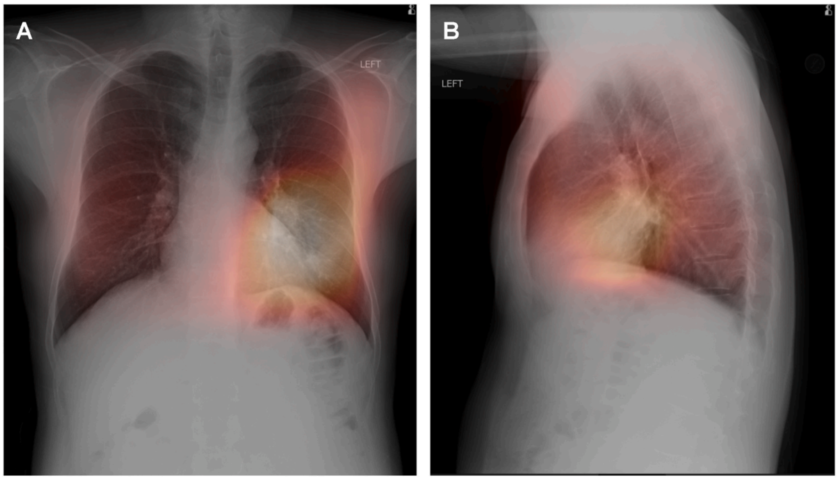


Fig. 6. Posterior-Anterior (A) and lateral chest X-ray (B) demonstrating why Chest-CAD identified the lungs as having suspicious ROIs. The heatmaps are focused on the known left infrahilar malignancy and post-obstructive left lower lung atelectasis.

ity in the appearance of the normal hila, which leads to difficulty in discerning whether opacity in this region represents a true underlying pathology rather than variant anatomy. For example, Muhm et al. showed that 65% of the pulmonary lesions originating in the hila or paratracheal regions were overlooked in a screening program [22].

There are other reasons that likely led to this misdiagnosis. The study was performed at 2am, and clinically important interpretation errors have been previously demonstrated to occur more frequently overnight compared with the day [23]. Imaging modality context switching is also a concern. As opposed to an outpatient worklist focused on chest imaging, an emergency department worklist typically involves switching frequently between modalities, patient ages, and anatomy regions. For example, an emergency department worklist may switch between a brain CT on an elderly patient with a fall, followed by a pediatric renal ultrasound, followed by a chest radiograph on an adult patient with chest pain. Additionally, this patient lacked prior imaging for comparison. Finally, physicians' decision-making may also be affected by low probability bias. A 46 year-old with a nonspecific history of chest pain and less than 1 pack-year of smoking history is unlikely to have lung cancer on their first available chest radiograph, and this low probability can bias a physician toward complacence.

We retrospectively analyzed this case with Chest-CAD, with the goal of assessing whether this device could have prevented the missed lung cancer and whether it could aid physicians in the future on similar cases. Chest-CAD accurately detected and localized the ROI that contained lung cancer on the initial chest radiographs, where the cancer was missed. Chest-CAD's findings demonstrated that artificial intelligence tools have the potential to significantly improve diagnostic accuracy on chest radiographs; though broader studies are necessary to show that artificial intelligence tools can systematically improve radiologists' accuracy.

Access to artificial intelligence tools like Chest-CAD could have alerted the radiologist that there was a region within the patient's lungs requiring more focused analysis. Radiologists have three tasks with every study: (1) identifying the salient findings when present; (2) interpreting the findings for clinical importance and recommending next steps; and (3) communicating those findings to the clinical team. Artificial intelligence can be particularly helpful with the first task. A large component of the extensive medical training a radiologist undergoes is related to learning as much as possible about pathologies, including their presentation on imaging and their management; however, that knowledge cannot be used if those findings are missed. Radiologists and other physicians that regularly interpret X-ray images need assistance in reducing perceptual error, but even with the use of artificial intelligence they still have a vital role to play in interpreting the value of the artificial intelligence findings for clinical importance and helping to determine next steps for the patient.

4. Conclusion

Lung cancer is a challenging diagnosis on chest radiography. Chest radiographs are typically the first images obtained in a clinical setting. Even though there are more advanced imaging modalities available for chest imaging (e.g., CT), patients generally will not have an opportunity to undergo them if their initial chest radiograph is misdiagnosed. Therefore, correct identification of lung cancer in chest X-rays assisted with artificial intelligence tools such as Chest-CAD can prevent delayed diagnosis and treatment. Furthermore, although CT is the ideal imaging modality for detecting lung cancer, the US Preventative Task Force recommends annual screening for lung cancer with LDCT in adults aged 50–80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Since this patient was 46 years-old and had a 0.75 pack-years smoking history, he would not have qualified for routine low dose CT screening. An artificial intelligence tool such as Chest-CAD can be a vital assistant to chest radiograph interpretation by increasing detection accuracy of disease, like the lung cancer presented here. Despite this promising example, further studies are needed to determine if artificial intelligence tools can help reduce diagnostic errors and improve patient care.

Consent for publication

No consent was obtained nor required for the writing of this manuscript, as it is waived by Mount Sinai Health Systems' IRB policy.

Author contributions

Concept and design: SS, FAO, RMJ, and RVL. Acquisition of data: SS and SV. Interpretation and analysis of data: SS. Drafting of the manuscript: SS, MA, and FAO. Critical revision of the manuscript: SS, MA, FAO, NK, SV, RMJ, and RVL. Literature review: SS, MA, FAO, and NK.

Declaration of interest

Financial support for the research was provided by Imagen Technologies. Authors SS, MA, FAO, NK, SV, RMJ, and RVL are employees and equity holders at Imagen Technologies.

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References

[1] Lung Cancer Statistics | How Common is Lung Cancer? n.d. https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html (accessed August 25, 2021).

[2] How to Detect Lung Cancer | Lung Cancer Tests n.d. https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/how-diagnosed.html (accessed August 25, 2021).

[3] S.H. Bradley, S. Abraham, M.E. Callister, A. Grice, W.T. Hamilton, R.R. Lopez, et al., Sensitivity of chest X-ray for detecting lung cancer in people presenting with symptoms: a systematic review, Br J Gen Pract J R Coll Gen Pract 69 (2019) e827–e835, https://doi.org/10.3399/bjgp19X706853.

[4] E.J. Hwang, J.G. Nam, W.H. Lim, S.J. Park, Y.S. Jeong, J.H. Kang, et al., Deep learning for chest radiograph diagnosis in the emergency department, Radiology 293 (2019) 573–580, https://doi.org/10.1148/radiol.2019191225.

[5] C. Galvez, J. Arenas-Jimenez, J.D. Campo, S. Maroto, M. Sirera, F. Lirio, Diagnostic imaging pathways in the setting of acute chest wall trauma, J Vis Surg 6 (2020), https://doi.org/10.21037/jovs.2019.11.08.

[6] Radiology (ACR) RS of NA (RSNA) and AC of. chestrad. RadiologyinfoOrg n.d. https://www.radiologyinfo.org/en/info/chestrad (accessed August 25, 2021).

[7] D. Tack, N. Howarth, Missed lung lesions: side-by-side comparison of chest radiography with MDCT, in: J. Hodler, R.A. Kubik-Huch, G.K. von Schulthess (Eds.), Dis. Chest Breast Heart Vessels 2019-2022 Diagn. Interv. Imaging, Springer International Publishing, Cham, 2019, pp. 17–26, https://doi.org/10.1007/978-3-030-11149-6_2.

[8] S. Stapley, D. Sharp, W. Hamilton, Negative chest X-rays in primary care patients with lung cancer, Br J Gen Pract 56 (2006) 570–573.

[9] A. del Ciello, P. Franchi, A. Contegiacomo, G. Cicchetti, L. Bonomo, A.R. Larici, Missed lung cancer: when, where, and why? Diagn Interv Radiol 23 (2017) 118–126, https://doi.org/10.5152/dir.2016.16187.

[10] P.M. Turkington, N. Kennan, M.A. Greenstone, Misinterpretation of the chest x ray as a factor in the delayed diagnosis of lung cancer, Postgrad Med J 78 (2002) 158–160, https://doi.org/10.1136/pmj.78.917.158.

[11] C.S. White, A.I. Salis, C.A. Meyer, Missed lung cancer on chest radiography and computed tomography: imaging and medicolegal issues, J Thorac Imaging 14 (1999) 63–68.

[12] M. Van De Luecht, W.M. Reed, The cognitive and perceptual processes that affect observer performance in lung cancer detection: a scoping review, J Med Radiat Sci 68 (2021) 175–185, https://doi.org/10.1002/jmrs.456.

[13] J.G. Nam, E.J. Hwang, D.S. Kim, S.-J. Yoo, H. Choi, J.M. Goo, et al., Undetected lung cancer at posteroanterior chest radiography: potential role of a deep learning–based detection algorithm, Radiol Cardiothorac Imaging 2 (2020) e190222, https://doi.org/10.1148/ryct.2020190222.

[14] J.T. Wu, K.C.L. Wong, Y. Gur, N. Ansari, A. Karargyris, A. Sharma, et al., Comparison of chest radiograph interpretations by artificial intelligence algorithm vs radiology residents, JAMA Netw Open 3 (2020) https://doi.org/10.1001/jamanetworkopen.2020.22779, e2022779–e2022779.

[15] R. Lindsey, A. Daluiski, S. Chopra, A. Lachapelle, M. Mozer, S. Sicular, et al., Deep neural network improves fracture detection by clinicians, Proc Natl Acad Sci 115 (2018) 11591–11596, https://doi.org/10.1073/pnas.1806905115.

[16] FDA Cleared AI Algorithms n.d. https://models.acrdsi.org/(accessed August 25, 2021).
[17] P.K. Shah, J.H.M. Austin, C.S. White, P. Patel, L.B. Haramati, G.D.N. Pearson, et al., Missed non–small cell lung cancer: radiographic findings of potentially resectable lesions evident only in retrospect, Radiology 226 (2003) 235–241, https://doi.org/10.1148/radiol.2261011924.
[18] G.Z. Brett, The presymptomatic diagnosis of lung cancer, Proc R Soc Med 59 (1966) 1208–1214.
[19] R.N. Cooley, Radiographic detection of preclinical and asymptomatic cancer of the lung, Am J Roentgenol 107 (1969) 440–442, https://doi.org/10.2214/ajr.107.2.440.
[20] L.G.B.A. Quekel, A.G.H. Kessels, R. Goei, J.M.A. van Engelshoven, Miss rate of lung cancer on the chest radiograph in clinical practice, Chest 115 (1999) 720–724, https://doi.org/10.1378/chest.115.3.720.
[21] C.S. Lee, P.G. Nagy, S.J. Weaver, D.E. Newman-Toker, Cognitive and system factors contributing to diagnostic errors in radiology, Am J Roentgenol (2013), https://doi.org/10.2214/AJR.12.10375.
[22] J.R. Muhm, W.E. Miller, R.S. Fontana, D.R. Sanderson, M.A. Uhlenhopp, Lung cancer detected during a screening program using four-month chest radiographs, Radiology 148 (1983) 609–615, https://doi.org/10.1148/radiology.148.3.6308709.
[23] A.G. Patel, V.J. Pizzitola, C.D. Johnson, N. Zhang, M.D. Patel, Radiologists make more errors interpreting off-hours body CT studies during overnight assignments as compared with daytime assignments, Radiology 297 (2020) 374–379, https://doi.org/10.1148/radiol.2020201558.