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Case Report

# Asymptomatic coronavirus disease 2019 mimicking metastatic breast cancer on positron emission tomography/computed tomography imaging ☆,☆☆

*Tanmayi S. Pai, MD[a], Carlos Rojas, MD[b], Martha C. Wasserman, MD[b], Ephraim E. Parent, MD, PhD[b], Lauren Cornell, MD[c], Saranya Chumsri, MD[c,*]*

[a] *Department of Internal Medicine, Mayo Clinic, Jacksonville, FL, USA*
[b] *Department of Radiology, Mayo Clinic, Jacksonville, FL, USA*
[c] *Division of Hematology and Medical Oncology, Jacoby Center for Breast Health, Mayo Clinic, Jacksonville, FL, USA*

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ABSTRACT

A 55-year-old asymptomatic woman with newly diagnosed, locally advanced breast cancer undergoing routine staging with 2-deoxy-2[$^{18}$F]fluoro-D-glucose positron emission tomography/computed tomography was found to have multiple hypermetabolic pulmonary nodules on imaging that were concerning for metastatic disease. However, further workup with dedicated chest computed tomography imaging demonstrated multiple bilateral, peripheral nodular lesions with peripheral ground-glass opacity, predominantly in the lower lung zone, that were suspicious for coronavirus disease 2019. The patient ultimately was diagnosed with coronavirus disease 2019 based on detection of viral ribonucleic acid via polymerase chain reaction. Follow-up chest computed tomography scan obtained after 27 days showed complete resolution of the lung lesions. In the setting of a global pandemic, a high index of suspicion for coronavirus disease 2019 in cancer patients is warranted, not only to enable early identification and treatment of a potentially aggressive infection but also to prevent misdiagnosis of metastatic disease.



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* Corresponding author.
E-mail address: chumsri.saranya@mayo.edu (S. Chumsri).

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## Case report

A 55-year-old Arabic woman presented to our breast center in early November 2020 for an evaluation of newly diagnosed breast cancer. The patient presented with abnormalities seen in routine screening mammogram, which subsequently had been confirmed by breast ultrasound at an outside institution in late October 2020. Mammogram and breast ultrasound demonstrated multifocal lesions measuring 1.4 centimeters and 7 millimeters in the upper outer quadrant of her right breast. The patient also was noted to have 3.9-centimeter enlarged right axillary lymphadenopathy. She then had completed a 2-site right breast biopsy and axillary lymph node biopsy. The outside pathology report noted grade 3, hormone receptor-negative, human epidermal growth factor receptor 2 (HER2)-positive invasive ductal carcinoma at both biopsied sites. The right axillary lymph node was also positive for metastatic disease. Due to locally advanced HER2-positive disease, the patient also underwent 2-deoxy-2[$^{18}$F]fluoro-D-glucose positron emission tomography/computed tomography (FDG PET/CT), extending from the skull base to the mid thighs, to evaluate for disease spread. At the time of FDG PET/CT imaging, the patient denied symptoms of coronavirus disease 2019 (COVID-19) including cough, fevers, chills, shortness of breath, gastrointestinal upset, and loss of taste and smell.

The FDG PET/CT images demonstrated multiple hypermetabolic foci in the right breast and multiple hypermetabolic right axillary lymph nodes, consistent with the patient's known breast cancer and nodal metastatic spread of disease. The patient also was noted to have multiple FDG-avid pulmonary nodules with maximum standard uptake value as high as 9.3 in both lungs (Fig. 1). These findings were concerning for pulmonary metastatic disease, and the patient was scheduled to undergo percutaneous biopsy of the pulmonary nodules to confirm metastatic disease. However, given the somewhat atypical appearance of the pulmonary nodules, a dedicated CT of the chest was performed for definitive evaluation prior to biopsy. The diagnostic CT chest without contrast demonstrated multiple rounded pulmonary nodules with ground-glass opacity predominantly in the lower lung zone (Fig. 2). Due to the distribution of these lung lesions with bilateral lower lobe involvement, these findings raised concern for COVID-19 and were less likely to be consistent with metastatic breast cancer. Other infectious causes of pneumonia also were in the differential diagnosis but were considered less likely than COVID-19.

Due to the concern for COVID-19 and other infections, a nasopharyngeal swab for COVID-19, respiratory syncytial virus, and influenza A and B was performed. The patient's polymerase chain reaction (PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with the cobas SARS-CoV-2 assay (Roche Molecular Systems, Inc., Pleasanton, California, United States of America) detected SARS-CoV-2 infection, and she was referred to our institution's COVID-19 clinic for follow up, and treatment. The patient remained mostly asymptomatic, as she only experienced occasional dry cough over the 3-week follow-up period and did not require specific treatment for COVID-19. A follow-up chest CT was performed 27 days after her initial imaging. This chest CT scan showed resolution of the previously seen pulmonary lesions (Fig. 3). The patient was started subsequently on neoadjuvant chemotherapy with docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP), 28 days after she had tested positive for SARS-CoV-2. At the time of this report, the patient has received 2 cycles of TCHP neoadjuvant chemotherapy and tolerated the treatment very well without significant toxicities. She remains asymptomatic from COVID-19.

Of note, at the time of this patient's imaging studies, all patients entering our hospital were screened at the entrances for COVID-19 symptoms. All patients, whether symptomatic or not, were required to wear a cloth or surgical mask in the hospital. All radiologists and nuclear medicine technicians were provided with standard 3-layer surgical masks for daily continuous use. All employees, regardless of COVID-19 exposure status, were required to return to work if they were asymptomatic and provide daily attestations to their health and lack of COVID-19-related symptoms. PCR tests were performed only for symptomatic employees. As COVID-19 was confirmed in our patient after her visits and imaging, staff members were informed of their possible exposure as soon as the result was available and were advised to continue with daily self-screening.

## Discussion

Since its discovery in late December 2019, the novel coronavirus known as SARS-CoV-2 has spread internationally, infecting patients across the globe with the disease described as COVID-19 [1]. COVID-19 typically presents with flu-like symptoms such as fever, cough, and fatigue, although in some patients, severe acute respiratory failure due to severe lung injury and multiorgan failure have been documented. At the time of this writing, over 29 million people in the United States have been infected with SARS-CoV-2, and over 541 thousand deaths from COVID-19-related causes have been documented since the first reported infection in the United States on January 20, 2020 [2,3]. While the majority of patients infected with SARS-CoV-2 will be symptomatic, it has been reported that approximately 45%-75% of SARS-CoV-2 infections may be asymptomatic at the time of testing [4,5]. However, asymptomatic patients may still have subclinical lung abnormalities demonstrable on chest CT scan. In the study from patients on the Princess Cruise ship returning to Yokohama, Japan, 331 (46.5%) out of 712 passengers who tested positive for SARS-CoV-2 were asymptomatic. A chest CT scan was obtained for 70 of these asymptomatic patients, and 54% of these patients had abnormal lung opacities or consolidations [6].

It has been postulated that cancer patients face significant challenges related to the COVID-19 pandemic [7]. Patients fearful of COVID-19 are less likely to enroll in cancer clinical trials [8], and providers facilitating these trials may struggle to provide adequate continuity of care or intravenous therapies [9]. More than 200 trials have been suspended as a result of the COVID-19 pandemic. Data regarding COVID-19-specific mortality in cancer patients are variable. A matched case control analysis from 2 New York-Presbyterian hospi-

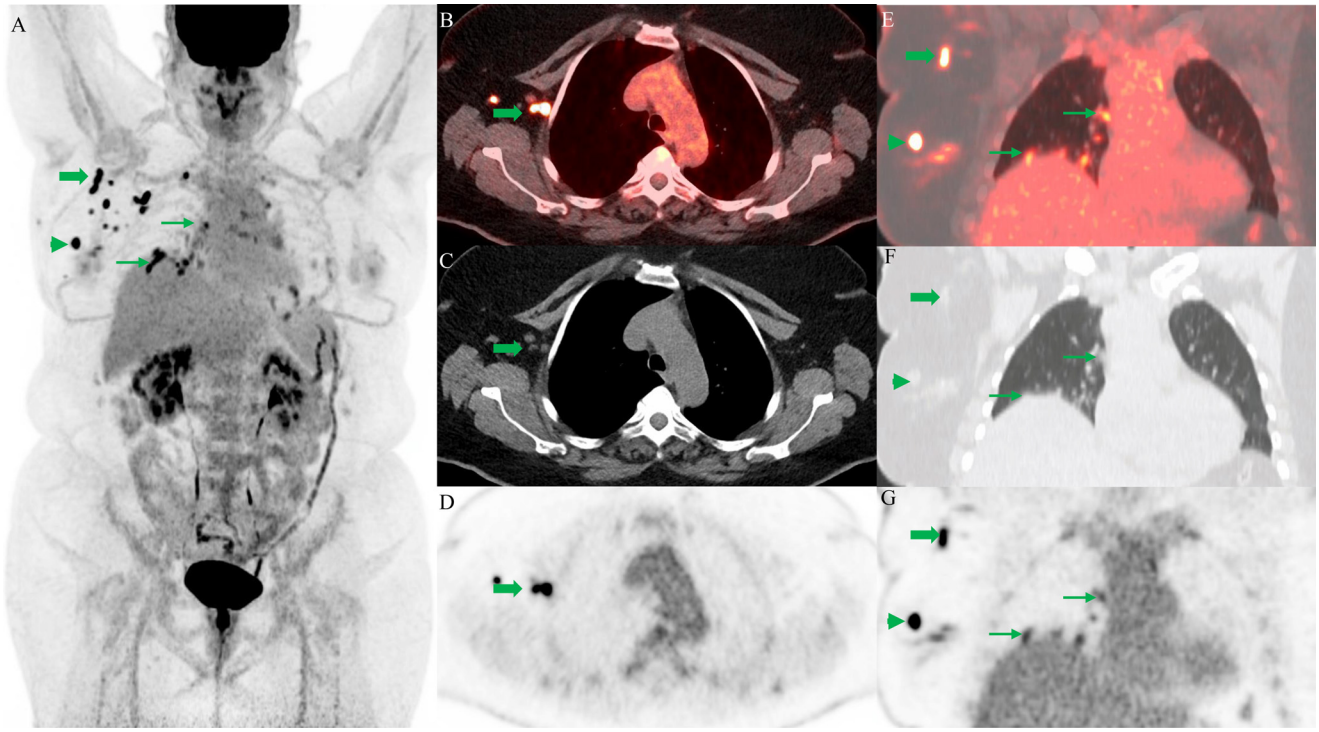


**Fig. 1 – Selected images from the FDG PET/CT in this patient with recently diagnosed right breast cancer. Coronal FDG PET maximum intensity projection (MIP; A) demonstrates multifocal hypermetabolic right breast lesions (arrowhead) with several additional hypermetabolic right axillary lymph node deposits (thick arrow) and pulmonary nodules in both lungs (thin arrows). Transaxial fused FDG PET/CT (B) CT (C) and PET (D) show several hypermetabolic right axillary lymph nodes (thick arrows) with proven metastatic involvement. Coronal fused FDG PET/CT (E) CT (F) and PET (G) show the primary hypermetabolic breast carcinoma (arrowheads), right axillary nodal disease (thick arrows) and ground glass and partially solid pulmonary nodules in the right lung (thin arrows).**

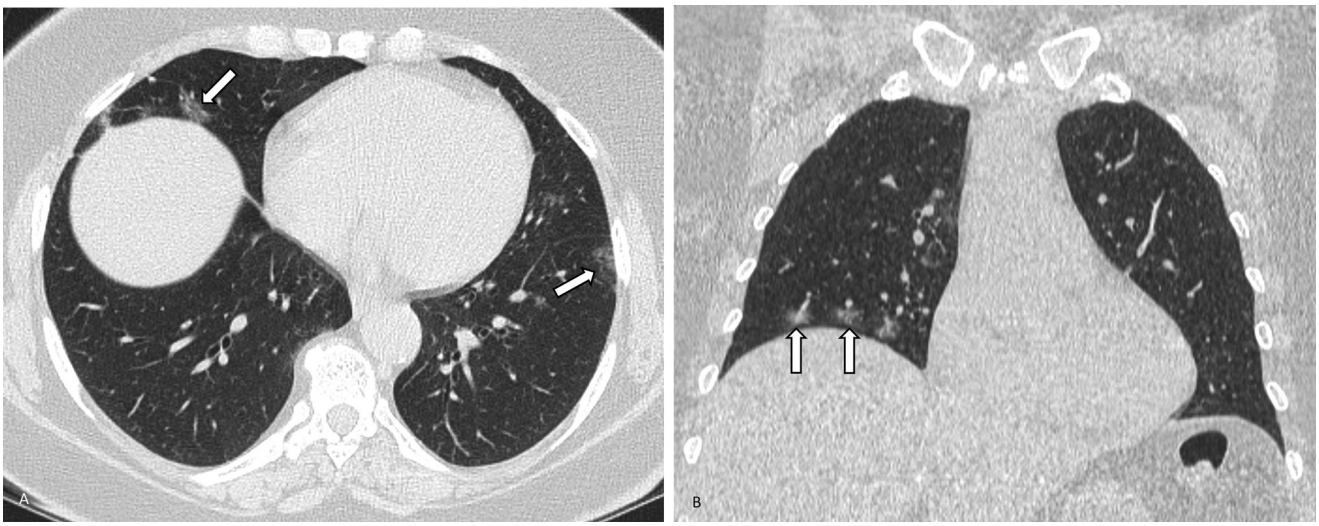


**Fig. 2 – (A) Axial CT image of the chest without contrast performed 1 day after FDG PET/CT demonstrating multiple, peripheral, bilateral ground-glass opacities with rounded morphology (white arrows). (B) Coronal CT image of the chest without contrast showing ground-glass opacities with rounded morphology (white arrows) with a lower lung zone predilection.**

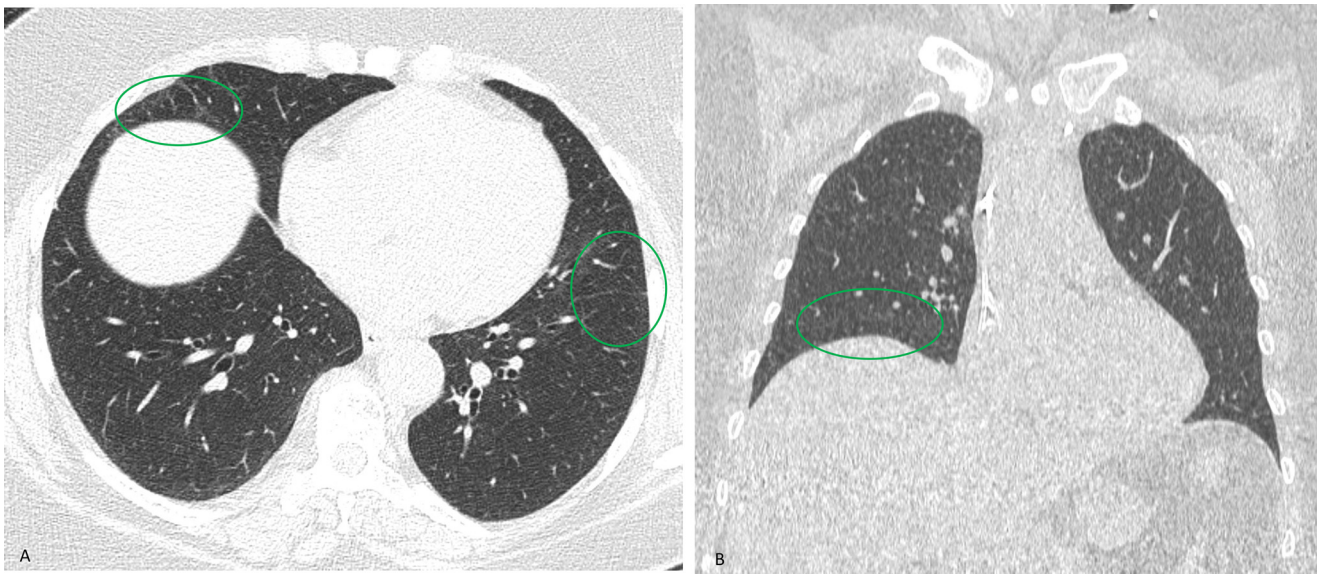


**Fig. 3 – (A) Axial and (B) coronal CT images of the chest without contrast performed 27 days later demonstrated interval resolution of ground glass opacities (circled areas).**

tals showed that cancer patients developed similar severity and outcomes to patients without cancer [10]. However, other studies demonstrated high mortality rates in cancer patients compared to patients without malignancy [11,12]. Reported mortality rates varied from 3.7% to over 60%, and hematological malignancies appear to be associated with higher mortality compared to solid organ malignancies [12]. In a retrospective study performed at Memorial Sloan Kettering Cancer Center, while cytotoxic chemotherapy administration was not significantly associated with severe COVID-19 outcomes, cancer patients experiencing neutropenia from chemotherapy prior to SARS-CoV-2 infection had worse outcomes, with a 4.2-fold increase in severe COVID-19 events. Severe events were defined as one or more of the following criteria: documented hypoxemia, respiratory failure, ICU admission or intubation, or death [13]. This study's results posited a major concern for administering chemotherapy regimens that confer significant risk of neutropenia in asymptomatic cancer patients with SARS-CoV-2 infection. This patient's TCHP regimen, a commonly used neoadjuvant chemotherapy regimen for patients with locally advanced HER2-positive breast cancer, is associated with a 46.1% risk of neutropenia [14].

Perhaps another critical effect on cancer patients' care lies in delays in cancer treatment in patients who test positive for COVID-19. A systematic review and meta-analysis of 34 studies found that a 4-week delay in surgery, chemotherapy, and/or radiation therapy is associated with an increased risk of mortality in 7 cancers, including breast cancer, although estimates varied [15]. Amid an ongoing pandemic, the potential for large numbers of preventable cancer deaths due to delays in both cancer- and COVID-19-related diagnoses and care cannot be overstated. In this patient's case, initiation of this patient's chemotherapy was postponed for a minimum of 21 days in accordance with Centers for Disease Control guidelines.

Radiological signs of COVID-19 vary and can be nonspecific, particularly on chest radiographs [16]. Evidence regarding diagnosis of COVID-19 based on FDG PET/CT imaging is limited to case reports, which highlight how the acute inflammatory state of COVID-19 pneumonia manifests as PET avidity [17,18]. Unfortunately, the hypermetabolic activity seen on FDG PET/CT can be indicative of other infectious or inflammatory processes such as metastatic cancer, as was thought to be the case in this patient. Thus, dedicated chest CT imaging may be needed to elucidate findings from other imaging modalities that are suggestive of COVID-19. As illustrated in this patient's case, this additional chest CT, which showed multiple, peripheral, bilateral ground-glass opacities in a lower lobe-predominant distribution, raised concern for COVID-19 [19]. Additionally, influenza pneumonia and organizing pneumonia from other etiologies, such as connective tissue disease and drug toxicity, can have a similar imaging appearance. Our case highlights the importance of being vigilant for unusual patterns of FDG uptake, caused by infectious and inflammatory etiologies, in PET/CT scans in order to avoid misdiagnosis of metastatic disease in cancer patients. Furthermore, due to the potentially high risk of serious complications from COVID-19, it is critical to be cognizant of potential asymptomatic COVID-19 in cancer patients starting cytotoxic chemotherapy, particularly regimens associated with a high rate of neutropenia.

## Patient consent

The patient described in this case report provided informed consent for use of her case details and imaging.

## REFERENCES


[1] Pascarella G, Strumia A, Piliego C, Bruno F, Buono RD, Costa F, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med 2020;288:192–206. doi:10.1111/joim.13091.

[2] CDC COVID Data Tracker. Centers for Disease Control Web site. Available at: https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days. [accessed 24.03.21].

[3] Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med 2020;382:929–36. doi:10.1056/NEJMoa2001191.

[4] Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. Ann Intern Med 2020;173:362–7. doi:10.7326/M20-3012.

[5] Yanes-Lane M, Winters N, Fregonese F, Bastos M, Perlman-Arrow S, Campbell JR, et al. Proportion of asymptomatic infection among COVID-19 positive persons and their transmission potential: a systematic review and meta-analysis. PLoS One 2020;15:e0241536. doi:10.1371/journal.pone.0241536.

[6] Tabata S, Imai K, Kawano S, Ikeda M, Kodama T, Miyoshi K, et al. Clinical characteristics of COVID-19 in 104 people with SARS-CoV-2 infection on the Diamond Princess cruise ship: a retrospective analysis. Lancet Infect Dis 2020;20:1043–50. doi:10.1016/S1473-3099(20)30482-5.

[7] Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol 2020;21:1023–34. doi:10.1016/S1470-2045(20)30388-0.

[8] Fleury ME, Farner AM, Unger JM. Association of the COVID-19 outbreak with patient willingness to enroll in cancer clinical trials. JAMA Oncol 2021;7(1):131–2. doi:10.1001/jamaoncol.2020.5748.

[9] Upadhaya S, Yu JX, Oliva C, Hooton M, Hodge J, Hubbard-Lucey VM. Impact of COVID-19 on oncology clinical trials. Nat Rev Drug Discov 2020;19:376–7. doi:10.1038/d41573-020-00093-1.

[10] Brar G, Pinheiro LC, Shusterman M, Swed B, Reshetnyak E, Soroka O, et al. COVID-19 severity and outcomes in patients with cancer: a matched cohort study. J Clin Oncol 2020;38(33):3914–24.

[11] Lee L, Cazier JB, Starkey T, Briggs S, Arnold R, Bisht V, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. Lancet Oncol 2020;21:1309–16. doi:10.1016/S1470-2045(20)30442-3.

[12] Saini KS, Tagliamento M, Lambertini M, McNally R, Romano M, Leone M, et al. Mortality in patients with cancer and coronavirus disease 2019: a systematic review and pooled analysis of 52 studies. Eur J Cancer 2020;139:43–50. doi:10.1016/j.ejca.2020.08.011.

[13] Jee J, Foote MB, Lumish M, Stonestrom AJ, Wills B, Narendra V, et al. Chemotherapy and COVID-19 outcomes in patients with cancer. J Clin Oncol 2020;38(30):3538–46.

[14] Schneeweiss A, Chia S, Hickish T, Harvey V, Eniu A, Hegg R, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). Ann Oncol 2013;24:2278–84. doi:10.1093/annonc/mdt182.

[15] Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ 2020;371:m4087. doi:10.1136/bmj.m4087.

[16] Kanne JP, Little BP, Chung JH, Elicker BM, Ketai LH. Essentials for radiologists on COVID-19: an update—Radiology Scientific Expert Panel. Radiology 2020;296:E113–14. doi:10.1148/radiol.2020200527.

[17] Albano D, Bertagna F, Bertoli M, Bosio G, Lucchini S, Motta F, et al. Incidental findings suggestive of COVID-19 in asymptomatic patients undergoing nuclear medicine procedures in a high-prevalence region. J Nucl Med 2020;61:632–6. doi:10.2967/jnumed.120.246256.

[18] Qin C, Liu F, Yen TC, Lan X. (18)F-FDG PET/CT findings of COVID-19: a series of four highly suspected cases. Eur J Nucl Med Mol Imaging 2020;47:1281–6. doi:10.1007/s00259-020-04734-w.

[19] Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, et al. Radiological Society of North America Expert Consensus Document on reporting chest CT findings related to COVID-19: endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. Radiol: Cardiothorac Imaging 2020;2:e200152. doi:10.1148/ryct.2020200152.