The role of chest computed tomography in the management of COVID-19: A review of results and recommendations

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Impact statement

The impact of the COVID-19 pandemic has been worldwide, and clinicians and researchers around the world have been working to develop effective and efficient methods for early detection as well as monitoring of the disease progression. This minireview compiles the various agency and expert recommendations, along with results from studies published in numerous countries, in an effort to facilitate the research in imaging technology development to benefit the detection and monitoring of COVID-19. To the best of our knowledge, this is the first review paper on the topic, and it provides a brief, yet comprehensive analysis.

Abstract

The rapid and dramatic increase in confirmed cases of COVID-19 has led to a global pandemic. Early detection and containment are currently the most effective methods for controlling the outbreak. A positive diagnosis is determined by laboratory real-time reverse transcriptase polymerase chain reaction (rRT-PCR) testing, but the use of chest computed tomography (CT) has also been indicated as an important tool for detection and management of the disease. Numerous studies reviewed in this paper largely concur in their findings that the early hallmarks of COVID-19 infection are ground-glass opacities (GGOs), often with a bilateral and peripheral lung distribution. In addition, most studies demonstrated similar CT findings related to the progression of the disease, starting with GGOs in early disease, followed by the development of crazy paving in middle stages and finally increasing consolidation in the later stages of the disease. Studies have reported a low rate of misdiagnosis by chest CT, as well as a high rate of misdiagnosis by the rRT-PCR tests. Specifically, chest CT provides more accurate results in the early stages of COVID-19, when it is critical to begin treatment as well as isolate the patient to avoid the spread of the virus. While rRT-PCR will probably remain the definitive final test for COVID-19, until it is more readily available and can consistently provide higher sensitivity, the use of chest CT for early stage detection has proven valuable in avoiding misdiagnosis as well as monitoring the progression of the disease. With the understanding of the role of chest CT, researchers are beginning to apply deep learning and other algorithms to differentiate between COVID-19 and non-COVID-19 CT scans, determine the severity of the disease to guide the course of treatment, and investigate numerous additional COVID-19 applications.

Keywords: COVID-19, chest computed tomography, COVID-19 severity, COVID-19 progression

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Introduction

In December of 2019, a global outbreak of a novel coronavirus infection now known as COVID-19 began in Wuhan, Hubei Province, China.[1,2] Coronavirus infections in humans are within the range of viruses that cause the common cold as well as more severe respiratory diseases, the most notable in recent years being severe acute respiratory syndrome (SARS)[3–5] and Middle East respiratory syndrome (MERS).[6–8] Widespread human-to-human transmission has resulted in a global pandemic. The rapid and dramatic increase in confirmed cases of COVID-19 has been a cause for alarm, although the mortality rate for COVID-19 is lower than either SARS or MERS, which were approximately 10 and 37%, respectively.[9] The World Health Organization (WHO) declared a global health emergency on 30 January 2020. As of 2 June 2020, the virus has spread to 216 countries, infected 6,194,533 people, and caused more than 376,320 deaths.[10] Thus, the WHO reported mortality rate is approximately 6%. However, the WHO has estimated that 80% of cases are mild or asymptomatic, and in the literature, asymptomatic carriers

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of COVID-19 have been estimated to comprise 17.9–33.3% of all infected cases,[11,12] thus many more have probably been infected than have tested positive for the disease, which indicates a lower mortality rate.

Background

With the rapid global spread of the virus, it is essential to provide effective and efficient diagnosis as well as the ability to monitor the progression of disease. Early detection and containment remain the most effective methods for controlling the outbreak.[13] A positive diagnosis is determined by laboratory testing with real-time reverse transcriptase polymerase chain reaction (rRT-PCR) of respiratory secretions. The Center for Disease Control has indicated viral testing as the only specific method of diagnosis. However, with the number of people affected on the rise in every region of the world, performing laboratory testing as the first line of detection is difficult, not only due to the limited number of kits, but also the possibility of false negative results. The total true positive rate for rRT-PCR for throat swab samples was reported to be approximately 30% for mild cases and 50% for severe cases.[14] The sensitivity and availability of the tests is increasing in response to the pandemic. In the meantime, the use of chest CT has been recommended as an effective form of initial screening and monitoring of the disease progression, due to the primary involvement of the respiratory system.[15] Chest CT is a routine imaging tool for the diagnosis of pneumonia and is a simple test that is widely available and provides a fast diagnosis. The use of chest CT for early detection and monitoring of COVID-19 would therefore be highly beneficial. The goal of this study is therefore to evaluate this potential by reviewing the role of chest CT thus far in the detection and management of COVID-19. These findings will be helpful to multidisciplinary researchers as well as clinicians in investigating and addressing the management of COVID-19 in the coming months.

Overview of chest CT findings in early COVID-19 studies

Numerous studies of COVID-19 cases have reported the appearance of typical imaging features on chest CT of confirmed cases that may be helpful in future screening. In addition, these features can be monitored through subsequent scans for determination of the effectiveness of the treatment. An initial study of 41 patients in Wuhan indicated that all patients demonstrated abnormalities in chest CT images, with 98% of the patients having bilateral involvement. Patients that had been admitted to the ICU exhibited bilateral multiple lobular and subsegmental areas of consolidation, while non-ICU patients showed bilateral ground-glass opacities (GGOs) and subsegmental areas of consolidation. Subsequent CT images showed bilateral GGOs but resolved consolidation.[1] Another initial study of 81 patients admitted to one of two hospitals in Wuhan reported abnormal chest CT findings even in asymptomatic cases, with rapid evolution from focal unilateral to diffuse bilateral GGOs that progressed or coexisted with consolidations within 1–3 weeks.[16] A study of 101 cases of COVID-19 from four institutions in Hunan, China also determined that most patients had GGOs or mixed GGOs and consolidation, vascular enlargement in the lesion(s), and traction bronchiectasis. In addition, lesions present were more likely to have a peripheral distribution and bilateral involvement, as well as exhibit lower lung predominance and a multifocal tendency.[17] A study of an early casualty of a staff member of the Wuhan seafood market suspected of being the origin of the disease indicated patchy bilateral GGOs with peribronchial and peripheral/subpleural distribution.[18] Another early study indicated multifocal nodular opacities in multiple lobes, and confirmed decreased density of the opacities and development of GGOs and reversed halo signs following six days of treatment. This study also reported that the initial laboratory testing was negative but a subsequent test was positive, which suggests that the CT may be more indicative in the early stages of the infection.[19] A study of the passengers onboard the Diamond Princess cruise ship, on which the disease spread rapidly in early February of 2020, even found GGOs with partial consolidation on numerous asymptomatic patients that tested positive for COVID-19.[20]

Of 21 patients in another study, 71% had involvement of more than two lobes in the chest CT, 57% had GGOs, 33% had opacities with a rounded morphology, 33% had a peripheral distribution of disease, 29% had consolidation with GGOs, and 19% had crazy-paving patterns. Fourteen percent of patients had normal CT scans, which likely supports the WHO statement that many cases are mild and asymptomatic. Another important note to make is the complete absence of lung cavitation, discrete pulmonary nodules, pleural effusions, and lymphadenopathy on all of the CT scans.[21] Building upon that study, 121 patients were evaluated in a subsequent study and the results indicated that 56% of patients had a normal CT scan within the first two days of symptom onset. However, after a longer time, the CT findings were more frequent and consistent, including consolidation, bilateral and peripheral disease, greater total lung involvement, linear opacities, crazy-paving pattern, and the reverse halo sign. Bilateral lung involvement was observed in 28% of early patients (0–2 days after symptom onset), 76% of intermediate patients (3–5 days), and 88% of late patients (6–12 days).[22] One study found that chest CT demonstrated a low rate of 3.9% of missed diagnosis of COVID-19. The results also confirmed the above findings in reporting that 90% of scans in positive COVID-19 cases showed GGOs, with or without consolidation, as well as vascular enlargement in 82% of cases, interlobular septal thickening in a crazy-paving pattern in 70.6% of cases, and air bronchogram signs in 69% of cases.[23] A summary study of 919 patients with COVID-19 indicated GGOs in 88% of the cases, bilateral involvement in 87.5%, posterior involvement in 80.4%, multilobar involvement in 78.8%, peripheral distribution in 76%, and consolidation in 31.8%.[24] A study of 108 patients indicated GGOs in 60%, GGOs with consolidation in 41%, vascular thickening in 80%, crazy-paving pattern in 40%, air bronchogram in 48%, and halo sign in 64%. The distribution of the lung legions in 90% of cases was peripheral and the shape was patchy in 86% of the cases.[25] One study evaluated the difference in CT scans based on patient age groups. The study confirmed that the most common features were patchy lesions and GGOs with or without consolidation in the 98 patients in their study. Patients older than 45 years of age had more bilateral lung, lung lobe, and lung field involvement as well as greater lesion numbers than patients less than 18. In addition, GGOs accompanied by interlobular septa thickening or a crazy-paving pattern, consolidation, and air bronchogram were more common in patients above 45 years than those less than 45.[26] These results may explain some of the small inconsistencies in the above studies, as the results are not differentiated by patient age. A recent study that compiled 147 publications from the China outbreak reported that of 8711 patients with COVID-19, over 95% of the patients had abnormal presentations on chest CT, with approximately 74% having bilateral infiltration, 73% peripheral distribution, 70% GGOs, and 30% consolidation. In addition, the reported mortality rate among all the patients in the studies was only 3%.[27]

Monitoring the severity and progression of COVID-19 with chest CT

Studies investigating the CT imaging features based on the severity of the disease found that the severity is evident on the CT images based on the proliferation of the features. For example, bilateral involvement was seen in 50% of mild cases, 65% of common cases, and 100% of severe and critical cases. Also, GGOs, consolidation, and other typical COVID-19 markers ranged from not being seen in the mild cases to appearing in 100% of the critical cases.[28] Studies specifically evaluating the use of CT in monitoring the progression of the disease over time emphasized the importance of follow-up CT scans, by demonstrating that the CT scans could be used to predict the prognosis of patients, as well as evaluate the treatment response of patients over the course of the disease. CT images from the studies indicated the typical features of COVID-19 in early scans and the alleviation of those features confirming the recovery of the patients. For example, Figure 6 in one study[16] evaluating the CT findings for 81 early patients in Wuhan details the progression of the disease for a 42-year-old woman from presentation at day 3 through the last image before discharge on day 18. The first image demonstrates multifocal consolidations affecting the bilateral, subpleural lung parenchyma. By day 7, the extent of the lesions had increased, and they had become heterogeneous, with internal bronchovascular bundle thickening. Day 11 demonstrates previous opacifications dissipating into GGOs and irregular linear opacities. Finally, day 18 indicates further resolution of the lesions, and the patient was discharged two days later.[16] Another study monitoring the progression of the disease in 21 rRT-PCR confirmed COVID-19 cases reported GGOs, crazy-paving patterns, and consolidation in the majority of patients, with a peak of disease around 10 days from the onset of initial symptoms. After the peak, they reported gradual resolution of consolidation and crazy-paving patterns.[29] Another disease progression study also agreed with the studies above in finding GGOs in 85.6% of cases, mixed GGOs with consolidation in 62.7%, vascular enlargement in 78%, and bilateral lung involvement in 79.7% of the cases.[30] One study presented a 36-week pregnant woman in Wuhan, China, in which comparison of the CT scan acquired two days after admission with the initial CT scan showed the progression of the disease. The decision was made from the scans to perform a Caesarean section, a decision which would have been much more difficult to make in the absence of CT.[31]

Correlation of testing with rRT-PCR and chest CT

Specifically evaluating the effectiveness of rRT-PCR and chest CT, one study reported positive rates of 59 and 88%, respectively. Positive chest CT was identified through the existence of the typical features detailed in the previous sections. Using rRT-PCR as a reference, the sensitivity of chest CT was 97%. Analyzing both tests, 60–93% of patients had initial positive chest CT consistent with COVID-19 before the initial positive rRT-PCR test results. Forty-two percent of patients showed improvement on follow-up chest CT scans before the rRT-PCR results turned negative.[32] Another study presented findings of five patients who initially tested negative by rRT-PCR but eventually tested positive through repeated tests. All patients exhibited chest CTs with GGOs and/or mixed GGOs and consolidation.[33] A third study reported similar findings, with 97% sensitivity by the initial CT scan, as compared to the initial rRT-PCR sensitivity of 83.3%. Among the patients for which the rRT-PCR test was initially negative, half tested positive in the second round of testing after a few days, while the other half finally tested positive in the third round of testing after several days.[34] A recent study compiled results from over 4000 patients and reported that the sensitivity of CT was 86%, while rRT-PCR needed to be repeated up to three times before giving an accuracy of 99%.[35] These studies indicate the potential of chest CT to provide more accurate results than rRT-PCR in the early stages of the COVID-19 disease, which is critical in terms of ensuring treatment and isolation begin immediately. Therefore, the use of both chest CT and rRT-PCR has proven important in ensuring that cases are not missed and are identified as early as possible. Patients with CT findings typical of COVID-19 but negative rRT-PCR results should be isolated, and rRT-PCR testing should be repeated to avoid misdiagnosis.

The ability to differentiate between COVID-19 pneumonia and other pneumonias

One study compared the chest CT scans of 11 patients with COVID-19 pneumonia with scans of 22 patients having non-COVID-19 pneumonia. The study found no statistical difference in imaging features between the two sets of scans. The typical COVID-19 imaging features were found in both groups in similar percentages: GGOs in 100% of COVID-19 and 90% of non-COVID-19, mixed GGOs in 63.6% versus 72.7%, and consolidation in 54.5%

versus 77.3%. However, the chest CT scans for patients testing positive for COVID-19 demonstrated GGOs predominantly located in the peripheral zone in 100% of patients, as compared to 31.8% of the negative patients. Therefore, the study concluded that findings highly suspicious of COVID-19 were imaging patterns of multifocal, peripheral, pure GGOs, mixed GGOs, or consolidation with slight predominance in the lower lung and findings of more extensive GGOs than consolidation during the first week of illness.[36] In a recent study investigating the ability of both Chinese and American radiologists to differentiate between more than 200 COVID-19 cases and 200 non-COVID-19 pneumonia cases, six of the seven radiologists demonstrated a specificity greater than 93%. In addition, a peripheral distribution was found to distinguish COVID-19 from other viral pneumonia in 63–80% of the cases.[37]

Discussion

The studies largely concur in their findings that the early hallmarks of COVID-19 infection are GGOs, often with a bilateral and peripheral lung distribution. In addition, most studies demonstrated similar CT findings related to the progression of the disease, starting with GGOs in early disease, followed by the development of crazy paving in middle stages and finally increasing consolidation in the later stages of the disease. Finally, studies agree in the absence of ancillary chest CT findings such as lymphadenopathy, pleural effusions, pulmonary nodules, and lung cavitation. These findings are supported by CT images we have acquired from patients diagnosed with COVID-19 at the University of Oklahoma Health Sciences Center, which are provided in Figure 1(a) to (f), which demonstrate the hallmarks progressing from GGOs in (a) to consolidation in (f). Additional images may be found in the open data repository maintained by the Radiological Society of North America (RSNA).[38]

Studies have reported a low rate of misdiagnosis by chest CT, as well as a high rate of misdiagnosis by the rRT-PCR tests. Specifically, chest CT provides more accurate results in the early stages of COVID-19, as well as abnormal findings in some asymptomatic cases. The American College of Radiology (ACR) initially recommended that CT not be used for diagnosis but has updated that recommendation due to the lack of widespread availability of COVID-19 laboratory testing as well as sensitivity issues. They now indicate that while caution should be taken in the approach, CT can be a useful method for making informed decisions on performing laboratory COVID-19 testing on a patient and immediately proceeding with isolation measures and treatment accordingly.[39] A recent publication presented an expert consensus statement endorsed by the RSNA, Society of Thoracic Radiology, and the ACR, which stated that although the use of CT for the detection of COVID-19 is not recommended by most radiological societies, the number of CT scans performed for persons suspected of having COVID-19 has increased, and they anticipate that the use of CT in clinical management as well as incidental findings potentially attributable to COVID-19 will continue to evolve.[40]

To further the role of chest CT through computer-assisted detection processes, researchers are beginning to apply deep learning and other algorithms to differentiate between COVID-19 and non-COVID-19 CT scans and monitor the progression and severity of the disease, which will lead to an even greater benefit in detection and monitoring of COVID-19. One study presented a deep learning model developed to extract visual features from volumetric chest CT scans for COVID-19 detection and differentiation from non-COVID-19 scans. They reported a 90% sensitivity and 96% specificity for detecting COVID-19, and an 87% sensitivity and 92% specificity for detecting non-COVID-19 pneumonia.[41] Another study compared multiple convolutional neural network models to classify CT samples with COVID-19, influenza viral pneumonia, or no infection, and reported a sensitivity of 98.2% and a specificity of 92.2% in differentiating between the three outcomes.[42] Another study assigned risk scores when applying a multi-view deep learning fusion model, with a score of 1 indicating 100% certainty of a COVID-19 diagnosis. Figure 5 of the study[43] demonstrates images of four patients, two of which were confirmed COVID-19 cases and two with bacterial pneumonia. The scores of the COVID-19 cases were 0.801 and 0.946, while the bacterial pneumonia scores were 0.461 and 0.315. In addition, the GGOs were clearly indicated in the COVID-19 patient images, but not present in those of the patients with bacterial pneumonia.[43] These and additional studies[44–47] have demonstrated that computer-assisted screening models provide specific and reliable COVID-19 detection by digitizing and standardizing the image information containing the typical features of the disease. This will be very important in the future detection and diagnosis of COVID-19. Computer-assisted algorithms have also been used in numerous additional areas of COVID-19 research, including the taxonomic classification of COVID-19 genomes,[48] survival prediction of severe patients,[49] identification and prioritization of potential drug candidates,[50] automated detection and monitoring of the disease progression over time,[51] development of neural network classifiers for a large-scale screening of COVID-19 patients based on their respiratory patterns,[52] generation of novel drug-like compounds for COVID-19 treatment,[53] and identification of potential candidates for vaccine components.[54,55]

The potential risks of chest CT include the radiation dose, which is typically 7 mSv as compared to 0.1 mSv for chest X-ray.[56] However, that amount is typical in the background radiation one would experience in a period of two years and has been determined an acceptable risk for disease detection and diagnosis purposes. While chest X-ray has a much lower dose, it is insensitive in the early stages and for mild cases of COVID-19,[57] and chest CT has demonstrated improved detection of COVID-19 over chest X-ray.[58] In addition, chest CT is more sensitive for early parenchymal lung disease, disease progression, and alternative diagnoses, including acute heart failure from COVID-19 myocardial injury.[59] Therefore, the use of chest CT over X-ray would be necessary in an environment where infected individuals need to be tested and isolated as early as possible, but if individuals are asked to stay at

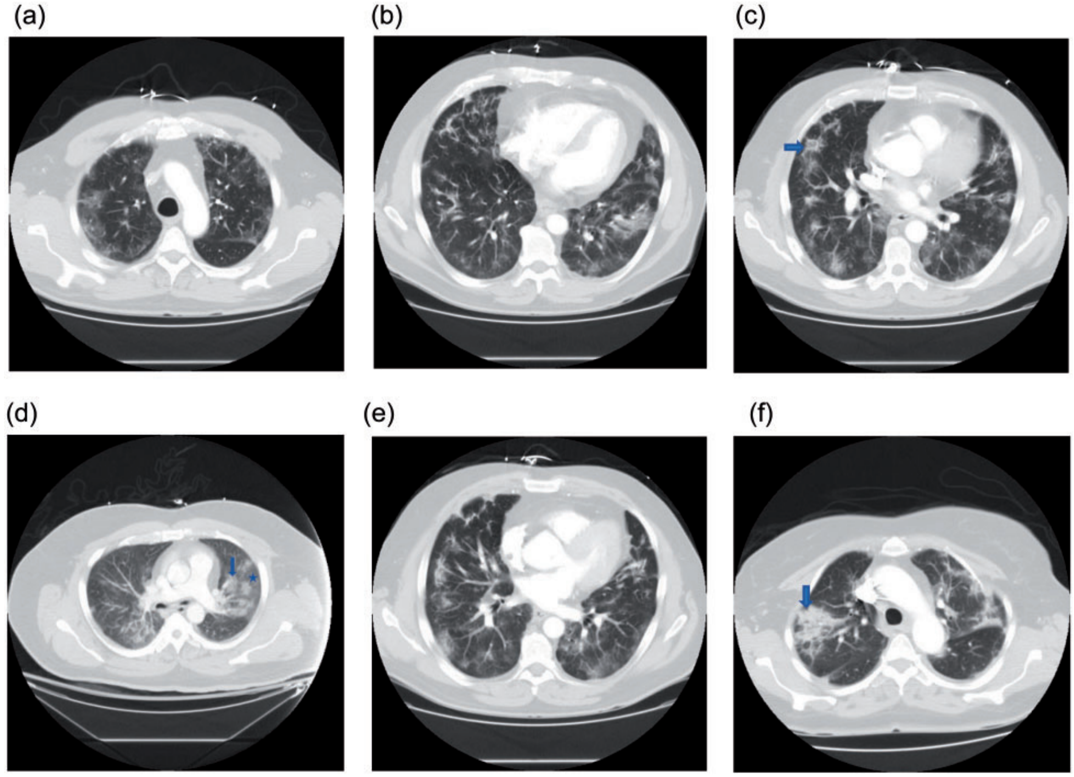

Figure 1. Chest CT images from COVID-19 patients at the University of Oklahoma Health Sciences Center, demonstrating the progression of the disease: (a) GGOs, (b) linear opacities, (c) reverse halo sign (blue arrow), (d) consolidation (blue arrow) in setting of GGOs (blue star), (e) crazy-paving pattern (GGOs with interstitial changes), and (f) consolidation (blue arrow).

home such as in New York City until the symptoms are advanced, chest X-ray is often abnormal by the time the patient is imaged. Thus, the selection of chest CT versus chest X-ray could be made based on the situation. For hospital scenarios, chest X-ray may also be useful due to the portability, which allows imaging within an infected patient's isolation room and eliminates the risk of transmission along the route or within the room with the CT scanner, as well as avoids the time and effort to disinfect the machine after each patient. Chest X-ray may also be useful in limiting the radiation dose to which the patient is exposed during prolonged or consistent monitoring of the disease progression. The two modalities could be used in conjunction with one another to ensure the highest detectability while also reducing the dose.

A recent study in Washington, where the first United States cases were reported, has detailed the policies and procedures with which the hospital has handled the COVID-19 outbreak, in an effort to control the virus by early detection and treatment, as well as prevention of disease dissemination. They do not routinely use chest CT to screen patients unless access to the rRT-PCR test or results is limited. However, they have created their own rRT-PCR tests onsite and indicate a much higher sensitivity than that previously reported with commercially available tests.[60] Also recently, a multidisciplinary panel comprised principally of radiologists and pulmonologists from 10 countries with experience managing COVID-19 patients evaluated the utility of imaging within scenarios representing risk factors, community conditions, and resource constraints. They recommended not using imaging as a screening test for asymptomatic or mild features of COVID-19 unless they are at risk for disease progression. They do recommend imaging for patients with moderate to severe features of COVID-19 regardless of the rRT-PCR results, as well as patients with COVID-19 and evidence of worsening respiratory status.[61] These recommendations are consistent with the findings in the literature, as the COVID-19 features were not always seen on mild and asymptomatic cases, but they were consistently seen on severe cases.

Conclusion

Numerous studies largely concur in their findings that the early hallmarks of COVID-19 infection are GGOs, often with a bilateral and peripheral lung distribution. In addition, most studies demonstrated similar CT findings related to the progression of the disease, starting with GGOs in early disease, followed by the development of crazy paving in middle stages and finally increasing consolidation in the later stages of the disease. Finally, studies agree in the absence of ancillary chest CT findings such as lymphadenopathy, pleural effusions, pulmonary nodules, and lung cavitation. Studies have reported a low rate of misdiagnosis by chest CT, as well as a high rate of misdiagnosis by the rRT-PCR tests. Specifically, chest CT provides more accurate results in the early stages of COVID-19, when it is critical to begin treatment as well as isolate the patient to avoid the spread of the virus. While rRT-PCR will probably remain the definitive final test for COVID-19, until it is more readily available and can consistently provide higher sensitivity, the use of chest CT for early stage diagnosis and isolation has proven valuable in avoiding misdiagnosis and controlling the spread as well as monitoring the progression of the disease. To further the role of chest CT and the computer-assisted detection process, researchers are beginning to apply deep learning and other algorithms to differentiate between COVID-19 and non-COVID-19 CT scans, determine the severity of the disease to guide the course of treatment, and investigate numerous additional COVID-19 applications. The goal of this review-in-brief is to facilitate the research in imaging technology development to benefit the detection and monitoring of COVID-19.

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