Deep Learning Localization of Pneumonia
2019 Coronavirus (COVID-19) Outbreak
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METHODS
A total of 10 frontal chest radiographs from 5 patients treated in China and the United States were sourced from 5 recent COVID-19 epidemiologic and case-study publications.1,4-7 Publication figures with frontal chest radiographs were downloaded as JPEG files and manually cropped to only include the frontal radiograph. These images were used as inputs for our DL algorithm, implemented as a U-Net trained with 22K radiologist-annotated radiographs, which produces pneumonia probability maps overlaid onto an input radiograph.

RESULTS
Radiographs and the corresponding pneumonia probability maps are shown for each x-ray in Figure 1. Figure 1A shows serial chest radiographs of a COVID-19+ patient from the United States consistent with the evolving atypical pneumonia and progression over several days.4 Our algorithm predicted and consistently localized areas of pneumonia with increasing likelihood, as the subtle airspace opacities increased over time. It is worth noting that each radiograph was analyzed by the algorithm independently without awareness of the time course or relationship of previous films.

Figure 1B shows 6 additional radiographs for 4 COVID-19+ patients acquired in Chinese hospitals spanning 4 other publications. The group of 5 radiographs on the left side of the panel is from 1 patient over a 7-day span showing progression of a mostly right basilar and perihilar airspace opacities. The 3 radiographs on the right are from different patients. Two illustrate cases showing diffuse bilateral airspace opacities consistent with pneumonia1,5 and another case showing a right infrahiatal consolidation subsequently confirmed by computed tomography.7 In each case, the predicted probability map correctly localizes the findings and assigns likelihoods that mirror the severity of the imaging findings.

COMMENT
These results illustrate a surprising degree of generalizability and robustness of the DL approach that we recently proposed, suggesting that it may have utility in early diagnosis and longitudinal follow-up of suspected pneumonia, including patients with COVID-19 pneumonia. Although our results are not an exhaustive proof of cross-hospital performance, these results imply that cross-institutional generalizability is feasible, standing in contrast to what is generally perceived in the field.8 This is despite considerable variation in the respiratory effort, image contrast, technique, and resolution between each of these published images. It is possible that the decrease in pneumonia likelihood on day 3 in panel A is related to the

BRIEF INTRO
The ongoing coronavirus (COVID-19) outbreak beginning in December 2019 in Wuhan, China, has spread rapidly, with confirmed cases in multiple countries. This virus causes a severe lower respiratory tract infection, with ∼75% of COVID-19+ hospitalized patients developing a viral pneumonia. Seventeen percent of hospitalized patients go on to develop acute respiratory distress syndrome, and often fatal lung injury representing diffuse alveolar damage on pathologic examination.1 The 2% mortality rate associated with COVID-19+ in China is less than that seen with previous zoonotic coronavirus outbreaks such as SARS (10% mortality) and MERS (30% mortality); it is 20-fold higher than that associated with seasonal influenza according to CDC estimates for 2019-2020.2 Chest radiographs are often obtained as part of the diagnostic workup to triage and daily follow-up of patients with suspected pneumonia, including COVID-19 infection. The rapid recognition of pneumonia in these patients may allow for early isolation precautions and administration of supportive therapies.

Deep learning (DL), a form of artificial intelligence, is beginning to show promise for supporting the diagnostic interpretation of chest x-rays. We recently described a DL approach to augment radiographs with a color probability map,1,5 overlay to improve the diagnosis of pneumonia.3 In contrast, this paper describes an approach to augment radiographs with a color probability map of pneumonia, including COVID-19 pneumonia. The rapid recognition and daily follow-up of patients with suspected pneumonia, including COVID-19 pneumonia, is less than that seen with seasonal influenza according to CDC estimates for 2019-2020.2 Chest radiographs are often obtained as part of the diagnostic workup to triage and daily follow-up of patients with suspected pneumonia, including COVID-19 infection. The rapid recognition of pneumonia in these patients may allow for early isolation precautions and administration of supportive therapies.

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change inspiratory effort or in the x-ray technique between the outpatient and inpatient settings. A larger study will be necessary to assess the generalizability of this algorithm across institutions. Nevertheless, these results support the idea that DL algorithms will become increasingly valuable as they become further integrated into the clinical diagnostic workflow.

Our application to the current COVID-19 outbreak provides a tangible example of how physicians and radiologists can work with artificial intelligence. This has the potential to augment the diagnostic abilities of physicians at the point of care, highlighting subtle abnormalities that may be missed by less experienced physicians, and triage patients for computed tomography. It may also help physicians track the daily evolution of the pulmonary manifestations over a patient’s hospitalization before development of diffuse alveolar damage or acute respiratory distress syndrome. As virual epidemics such as COVID-19 place a greater strain on the health care system, it may also provide a mechanism of workload relief and earlier advanced interpretation. Although further study is required to evaluate the effectiveness of this algorithm across multiple institutions, these results provide further evidence that this approach could be a powerful tool for physicians and other health care providers to provide more reliable early diagnosis of infection.

REFERENCES

1. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet (London, England). 2020; 6736:1–7.
2. CDC. Disease burden of influenza. 2019. Available at: www.cdc.gov/flu/about/burden/index.html. Accessed February 18, 2020.
3. Hurt B, Kligerman S, Yen A, et al. Augmenting interpretation of chest radiographs with deep learning probability maps. *J Thorac Imaging*. 2020. Doi: 10.1002/pds.1109.

4. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382:929–936.

5. Song F, Shi N, Shan F, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology*. 2020:200274.

6. Ng M-Y, Lee EY, Yang J, et al. Imaging profile of the COVID-19 infection: radiologic findings and literature review. *Radiol Cardiothorac Imaging*. 2020;2:e200034.

7. Kong W, Agarwal PP. Chest imaging appearance of COVID-19 infection. *Radiol Cardiothorac Imaging*. 2020;2:e200028.

8. Zech JR, Badgeley MA, Liu M, et al. Variable generalization performance of a deep learning model to detect pneumonia in chest radiographs: a cross-sectional study. *PLoS Med*. 2018;15:1–17.