Quantification of Tomographic Patterns Associated with COVID-19 from Chest CT

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Summary
Automated quantification of abnormalities associated with COVID-19 from chest computed tomography (CT) can help clinicians evaluate the disease and assess its severity and progression. This paper proposes measures of disease severity and a deep learning and deep reinforcement-based method to compute them.
Key Points

- The method computes PO (Percentage of Opacity) and LSS (Lung Severity Score) by segmenting 3D abnormalities associated with COVID-19, namely ground glass opacities (GGO) and consolidations. The PO and LSS quantify the extent of lung involvement and the distribution of involvement across lobes, respectively.
- Given that high opacity abnormalities (i.e., consolidations and sub-solid regions) were shown to correlate with severe symptoms, this paper introduces two new complementary severity measures PHO (Percentage of High Opacity) and LHOS (Lung High Opacity Score). They quantify the extent of high opacity abnormalities and their distribution of involvement across lobes, respectively.
- The combined severity measures (PO, PHO) and (LSS, LHOS) quantify the extent of overall COVID-19 abnormalities and the presence of high opacities, global and lobe-wise, respectively. The performance of the method in estimating PO, LSS, PHO, and LHOS is evaluated on a database of 100 COVID-19 cases and 100 controls from multiple institutions from Canada, Europe, and US. Ground truth is established by computing the same measures from manual annotations of the lesions, lungs, and lobes.

List of Abbreviations

CT Computed Tomography
COVID-19 Coronavirus Disease 2019
PO Percentage of Opacity
LSS Lung Severity Score
PHO Percentage of High Opacity
LHOS Lung High Opacity Score
ABSTRACT

Purpose
To present a method that automatically detects and quantifies abnormal tomographic patterns commonly present in COVID-19, namely ground glass opacities (GGO) and consolidations. Since high opacity abnormalities (i.e., consolidations and sub-solid regions) were shown to correlate with severe disease, the paper introduces two combined severity measures (Percentage of Opacity, Percentage of High Opacity) and (Lung Severity Score, Lung High Opacity Score). They quantify the extent of overall COVID-19 abnormalities and the presence of high opacity abnormalities, global and lobe-wise, respectively, based on 3D segmentations of lesions, lungs, and lobes.

Materials and Methods
The proposed method takes as input a non-contrasted chest CT and segments the lesions, lungs, and lobes in 3D. It outputs two combined measures of the severity of lung/lobe involvement, quantifying both the extent of COVID-19 abnormalities and presence of high opacities, based on deep learning and deep reinforcement learning. The first measure (PO, PHO) is global, while the second (LSS, LHOS) is lobe-wise. Evaluation is reported on CTs of 200 subjects (100 COVID-19 confirmed and 100 controls) from institutions from Canada, Europe and US. Ground truth is established by manual annotations of lesions, lungs, and lobes.

Results
Pearson Correlation Coefficient between method prediction and ground truth is 0.95 (PO), 0.98 (PHO), 0.96 (LSS), 0.96 (LHOS). Automated processing time to compute the severity scores is 10 seconds/case vs 30 mins needed for manual annotations.

Conclusion
A new method identifies regions of abnormalities seen in COVID-19 non-contrasted chest CT and computes (PO, PHO) and (LSS, LHOS) severity scores.
INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease affecting more than 2,400,000 patients worldwide as of April 20, 2020 (1). The disease is caused by the severe-acute respiratory symptom Coronavirus 2 (SARS-Cov2) and has a high case fatality rate of up to 4% (2) with more than 170,000 deaths reported currently. Due to a high reproduction number and infectious nature of the disease, tools for rapid testing and evaluation are vital to track and mitigate the spread. Non-contrast chest Computed Tomography (CT) has been useful to detect, quantify severity, and assess progression of the disease. We propose an automated system that can quantify the abnormalities most often seen in COVID-19, i.e., ground glass opacities and consolidations. The system will output regions of abnormality demarcated in a 3D CT scan and output two combined severity measures of the disease: (Percentage of Opacity, Percentage of High Opacity) and (Lung Severity Score, Lung High Opacity Score). The first measure (PO, PHO) indicates the overall disease spread relative to the volume of the lungs, while the second (LSS, LHOS) is a cumulative measure of the extent of involvement for each lung lobe (Fig. 1). Opacities here include GGO, consolidation and crazy-paving patterns which are all commonly observed in COVID-19. Given that higher opacity abnormalities such as consolidation were shown to correlate with severe symptoms, the measures cover both the extent of disease and the presence of high opacities (3,4). In this paper, we will use the term “high opacity” to mean consolidation of sub-solid regions of high attenuation. We use this term since these regions were determined using an empirical threshold. The ability to determine the extent of disease and quantify the presence of high opacities provides valuable insight for prognosis prediction, risk prioritization, and therapy response (5).
Background: CT imaging for COVID-19

COVID-19 is confirmed via a reverse transcription polymerase chain reaction (RT-PCR) (6). However, the sensitivity of this test may be as low as 60-70% (7) and can cause false negatives in the first few days. Although the role of CT for diagnosis is currently being debated, two preliminary studies (8,9) showed that chest CT imaging of the lung provides improved sensitivity when compared to RT-PCR for patients suspected to have COVID-19. The primary features seen on a lung affected by COVID-19 are peripheral focal or multi-focal ground glass opacities, consolidation and crazy-paving patterns. Another study evaluated CT scans of patients tested positive for COVID-19 across 552 hospitals in China (4). They found that 84.4% of patients exhibiting mild symptoms showed CT changes, whereas 94.6% of patients exhibiting severe symptoms showed CT changes. In a study of 121 patients, Bernheim et al showed that CT changes correlated with disease severity, with increasing lung involvement and abnormalities as the disease progressed (10). A recent radiologist performance study also points to preliminary evidence that radiologists can discriminate COVID-19 from other types of pneumonia (11). The study showed that seven U.S. and Chinese radiologists were able to identify COVID-19 from other types of viral pneumonia with a median sensitivity of 73% and a median specificity of 93%. The studies so far have been performed on patients either suspected or confirmed to be tested positive of COVID-19, therefore it is too early to state that CT can be used as an effective diagnostic or screening tool for evaluation of COVID-19 in general population. However, most patients with COVID-19 exhibit CT abnormalities and the extent of these changes seem to correlate with disease severity. Recently, Fleischner society provided recommendations for use of chest imaging in evaluation of COVID-19 in regions with resource constraints especially with worsening respiratory status, suspected false negative PCR, and more severe. Elsewhere, they indicated that chest imaging can be used to establish a baseline for moderate to severe cases (12). As a result, CT imaging is being adapted as a tool to evaluate COVID-19 in emergency rooms across the world, where other resources for testing are scarce.
MATERIALS AND METHODS

All the authors have either been employed or partially supported by Siemens Healthineers.

Datasets and Annotation.
The datasets were de-identified and retrospectively collected from multiple centers in USA, Canada and Europe, with the respective data source’s ethic clearing processes. Non-contrasted chest CT datasets that completely show lungs in their field of view were used to train two models for lung and lobe segmentation, and abnormality segmentation. Complete details of the datasets are provided in Tables 1 and 2, including age and sex distribution, manufacturer, slice thickness and kernel type.

9749 CT volumes were used in the study, in total. 200 volumes were reserved for testing, and the remaining were used for lung and lesion segmentation training and model selection. 8087 chest CTs for this task are a part of a legacy database that was used in our previous work. 901 volumes were used for training the abnormality segmentation model. Due to limited availability of COVID-19 data, we determined three groups of data that are useful for training the abnormality model: COVID-19 datasets (431), pneumonia datasets (174) and other Interstitial Lung Diseases or ILDs (274). Note that 575 datasets were common to the lung segmentation and lesion segmentation training sets. The distribution of the datasets for each task is visualized in Fig 6. Annotation details for the two tasks are presented in the supplementary section. A separate test set of 100 control volumes and 100 COVID-19 positive volumes was used to evaluate lung and lobe segmentation as well as abnormality segmentation. The control group consist of volumes without pathology that were randomly sampled and visually inspected by a radiologist. 110 COVID-19 positive cases were randomly selected from 2 European and 2 American institutions. Of these, 10 cases were excluded for having very low percentage of abnormalities based on ground truth annotations.
Lung and Lobe Segmentation

The algorithm generates lung and lobe segmentation mask on a given CT data set. First, multi-scale deep reinforcement learning (13) is used to robustly detect anatomical landmarks in a CT volume. The carina bifurcation is used to identify the lung region of interest (ROI). When this is not detected by the system, the sternum tip is used as a landmark. The size and the relative location of the lung ROI to the landmark are specified according to annotated lung datasets. Next, the lung ROI image is resampled to a 2mm isotropic volume and fed into a Deep Image-to-Image Network (DI2IN) (14) to generate the lung segmentation. Finally, the ROI segmentation mask is remapped to have the same dimension and the resolution as the input data. The DI2IN has been first trained on a large cohort of patients with various diseases (miscellaneous in Table 1), then fine-tuned with a cohort with abnormal patterns including (ILDs, Pneumonia and COVID in Table1), to improve the robustness of the lung segmentation over the infected areas.

COVID-19 Related Abnormality Segmentation

We formulate the segmentation of the COVID-19 related abnormality patterns as a semantic segmentation problem involving binary classes. A DenseUNet (15) with anisotropic kernels is trained to transfer a 3D chest CT volume to a semantic segmentation mask of the same size. We use a single label to define all voxels within the lungs that fully or partially contain ground glass opacity or consolidations as the positive voxels (see Annotation Details in supplementary section). The rest of the image areas within the lungs and the entire area outside the lungs are defined as negative. The network is trained as an end-to-end segmentation system. The 3D output segmentation is filtered by the lung segmentation as described above. The technical details of the network architecture and the training strategy are summarized in the supplementary material.
COVID-19 Severity Measures

The severity of COVID-19 in each subject is measured by the combined metrics (PO, PHO) and (LSS, LHOS) as defined below.

1) **Percentage of Opacity (PO)**: The Percentage of Opacity is calculated as the total percent volume of the lung parenchyma that is affected by disease:

\[ PO = 100 \times \frac{\text{volume of predicted abnormalities}}{\text{volume of lung mask}} \]

2) **Percentage of High Opacity (PHO)**: The Percentage of High Opacity is calculated as the total percent volume of the lung parenchyma that is affected by severe disease i.e., high opacity regions including consolidation. The high-opacity regions were identified using a threshold on -200 HU from the abnormality segmentation:

\[ PHO = 100 \times \frac{\text{volume of high opacity region}}{\text{volume of lung mask}} \]

3) **Lung Severity Score (LSS)**: The Lung Severity Score is computed to measure the extent of lung involvement across each lobe as described by Bernheim et al (10). For each lobe, the percentage of affected lobe is calculated and scored between 0-4.

- 0: lobe is not affected.
- 1: 1-25% of the lobe is affected.
- 2: 25-50% of the lobe is affected.
- 3: 50-75% of the lobe is affected.
- 4: 75-100% of the lobe is affected.
The scores for each of the 5 lobes are summed up to get the total LSS, resulting in a total score range from 0-20. 0 indicates that none of the lobes are involved and 20 indicates that all 5 lobes are severely affected.

4) Lung High Opacity Score (LHOS): The Lung High Opacity Score is computed to measure the extent of abnormalities with severe disease. For each lobe, the percentage of high opacity is calculated and scored between 0-4.

- 0: lobe is not affected, or abnormalities do not have any consolidation.
- 1: 1-25% of the lobe has high opacity abnormalities.
- 2: 25-50% of the lobe has high opacity abnormalities.
- 3: 50-75% of the lobe has high opacity abnormalities.
- 4: 75-100% of the lobe has high opacity abnormalities.

The scores for each of the 5 lobes are summed up to get the total LHOS, resulting in a total score range from 0-20. 0 indicates that none of the lobes have a high opacity abnormality and 20 indicates that all 5 lobes are severely affected by high opacity consolidations.

RESULTS

Training of Lung and Lobe Segmentation

We used 8792 chest CT volumes for training the 3D segmentation of lung and lobes. The DI2IN has been first trained on a data set from 8087 patients (8006 for training, 81 for validation) without the prevalence of viral pneumonia, then it has been fine-tuned on another data set from 1136 patients (1076 for training, 60 for validation) with abnormality patterns including ground glass opacities, consolidation, effusions, masses, etc., to improve the robustness of the lung/lobe segmentation over the infected areas. It was finally tested on a data set from 200 patients, consisting of 100 COVID-19 and 100
controls (16). The sample size and the data partition of the COVID19 positive patients are determined by balancing the patients from the US and Europe.

**Training of Abnormality Segmentation**

For the training of abnormality segmentation, we used a combination of COVID19, viral pneumonia, and other Interstitial Lung Diseases (ILDs) datasets, totaling 901 CT scans (431 COVID-19, 174 viral pneumonia, and 296 ILD). Atypical pneumonia datasets including SARS, MERS, and other viral pneumonia have similar abnormalities as COVID-19 (17) and are used as reasonable proxies to complement the COVID-19 training dataset together with CT datasets that include other ILDs that present with GGO and consolidation. These datasets are used in the training dataset to learn the patterns relevant in COVID-19. For the testing set, both the initial annotation and final review was done by a board-certified radiologist. For testing, we used the same 200 datasets as for the lung and lobe segmentation, which includes 100 COVID-19 and 100 controls (16).

**Computation of Combined Measures of Disease Severity**

From the predicted abnormality segmentation, we compute the two proposed combined measures of disease severity: (PO, PHO) and (LSS, LHOS) for the 200-test data set that consists of 100 COVID-19 and 100 controls.

We compute a Pearson correlation coefficient between each metric calculated on the predicted masks (abnormality, lung, and lobes) and ground truth masks (abnormality, lung, and lobes). We compute this statistic for both positives and negatives together, and for COVID-19 positive cases only. The latter computation is performed to show the linear correlation between the predicted and ground truth scores for patients with lung abnormalities only. We also compute the Kendall’s rank correlation test for COVID-19 positive cases, which considers the distribution of scores across the range of the score. Fig 3 shows the scatter plot between ground truth and predicted metrics. The Pearson coefficients for both
positive and negative cases together are 0.95, \( p=5.57\times10^{-6} \) (PO); 0.98, \( p=1.73\times10^{-139} \) (PHO); 0.96, \( p=1.98\times10^{-63111} \) (LSS); and 0.96, \( p=2.74\times10^{-111} \) (LHOS). The detailed results of all statistics can be seen in Table 3. All correlations are statistically significant, demonstrating the system’s ability to predict lung severity measures in COVID-19 datasets. The \( R^2 \) and standard error of each linear correlation was also computed, to show the linear fit between ground truth and predicted data (Table 4). The combined disease severity measure (PO, PHO) indicates the percentage of the lung affected, as well as the percentage of the lung that has high opacities, indicating consolidation. Likewise, the severity measure (LSS, LHOS) indicates the cumulative scores of the extent and severity of the lobes affected, indicating the distribution of the abnormalities.

Fig 4. shows the combined measures (PO, PHO) and (LSS, LHOS) in 2-dimensional plots. The diagonal in the left plot indicates that PO is equal to PHO. A subject’s marker falling on the diagonal would indicate that 100% of the abnormalities present on their lung CT are high opacity or consolidation. Note that all the markers for abnormalities greater than 0 fall below the line, indicating various levels of consolidation present. The closer a subject’s marker is to the diagonal, the more consolidation there is in their lungs. In the right plot of Fig 4, the diagonal indicates that LSS is equal to LHOS. A marker on the diagonal here indicates that all the lobes that are involved have high opacity. When a subject’s marker falls below the diagonal, it means that either some lobes do not have high opacities or that they have less extent of high opacities. Fig 5 shows the qualitative results for COVID-19 positive cases along with their scores. Fig 5(a) shows six cases where our algorithm identifies the abnormality regions accurately. For example, the upper left corner case results in \((PO, PHO) = (55.9\%, 7.6\%)\). That means that 55.9% of the lung volume is affected by disease and 7.6% of the lung volume has high consolidation abnormalities. Fig 5(b) shows one example of abnormality segmentation (left) along with high opacity regions identified through thresholding (left). Fig 5(c) shows two cases which were identified as outliers due to their PO score.
differing by more than 20% from the ground truth. The algorithm misses fainter areas of opacity (left) and tends to over segment into normal areas between the abnormal opacities (right).

DISCUSSION

In this work we proposed a method to automatically quantify regions with ground glass opacity and consolidation in chest CT scans using state-of-the-art deep learning algorithms. The abnormalities detected by our system are the most common chest CT findings in COVID-19. The system outputs the 3D contours of the CT abnormalities and computes two combined severity measures (Percentage of Opacity, Percentage of High Opacity) and (Lung Severity Score, Lung High Opacity Score).

Clinical value of our system

Automated characterization of disease can be extremely useful to facilitate rapid response in assessing the extent of lung infection and progression of the disease in patients exhibiting symptoms of COVID-19. Evaluation of a chest CT can be used to answer several questions in a clinical setting such as triage of a patient, diagnosis, assessment of severity and progression, and response to therapy. Recently, lung severity measures have been proposed for COVID-19 that demonstrate correlation to disease severity and progression (10,18–21). Manual calculation of these scores produces a two-fold problem: either the affected regions are annotated precisely, which is a time-consuming process, or the affected regions are assessed subjectively, which translates into low reproducibility of the assessment. A precise automated measurement of lung severity scores will address both the speed and reproducibility problems. In addition to quantitative outputs, the abnormality segmentation produced by the system can also be used for visual interpretation and inspection.

The automatic computation of (PO, PHO) and (LSS, LHOS) as provided by our system is useful in several clinical scenarios:
• **Severity assessment**: An objective quantitative measure of severity is provided by (PO, PHO) and (LSS, LHOS). This measure can be used in triage, to prioritize patients requiring hospital or ICU admittance, and to assess the prognosis of a patient.

• **Progression assessment**: In several instances, the patient might be imaged multiple times to assess disease progression or to assess response to drugs. In order to make these decisions, an objective metric or a score that can assess the extent of disease is vital. The (PO, PHO) and (LSS, LHOS) scores can be useful when evaluating a patient’s lung status over time. Such a tool could also be used in scientific research studies that are documenting the temporal radiological change of COVID-19 pneumonia and clinical trials studying drug responses.

• **Early detection**: Although the evidence is preliminary, the system could be used as an effective tool in conjunction with RT-PCR tests to increase overall sensitivity of COVID-19 detection, especially in scenarios where there are limited resources and a crunch for time.

An automated system that can perform this disease severity assessment can be of great use to hospitals that have a shortage of manpower combined with a high-volume of patients during the outbreak (5).

**Technical Contributions**

To our knowledge this is one of the first systems to provide an automatic, efficient, and detailed evaluation of tomographic CT patterns associated with COVID-19. We also believe that this is the first system to propose and show how to automatically compute severity measures such as (PO, PHO) and (LSS, LHOS) that characterize not only the extent of disease in the lungs, but also the extent of high opacity abnormalities, both globally and lobe-wise. This performance is facilitated by the experience of a multidisciplinary team of clinicians, machine learning experts, and engineers, whose combined clinical and technical knowledge helped to solve robust landmark detection in chest CT, 3D lung and lobe segmentation, and 3D segmentation of abnormalities associated with COVID-19.
Limitations and Future Work

The system was trained with specific abnormalities that were relevant to COVID-19 such as ground glass capacities and consolidations. Presence of other abnormalities in or around the lung such as pleural effusion could produce challenges to the algorithm. In the future, the system will be trained comprehensively to account for abnormalities other than GGO and consolidation. Moreover, the algorithm will be improved using more training data in boundary conditions, which cause under segmentation with faint regions and over segmentation with highly abnormal regions as seen in Fig 5 (c).

The system produces a quantification of abnormalities in a lung CT scan only. It is hard to ascertain the diagnosis based on this information alone. In the future, we will evaluate the feasibility of distinguishing COVID-19 from other types of pneumonias and ILDs. We will conduct studies to correlate the imaging findings computed in this work to clinical factors and outcomes. A similar study can be performed with X-ray chest images as well, which will be a part of our future investigations.

Disclaimer: The concepts and information presented in this paper are based on research results that are not commercially available.
Annotation Details

ITK-Snap was used for ground truth annotation of lung, lobe, and abnormality segmentation task. The window level and width are adjusted to 425 and 1500. The annotation task was performed by a team of 25 expert annotators under the supervision of 3 board-certified radiologists. Every dataset was reviewed and corrected by a radiologist for any areas missed or to be removed from the final mask.

The lung lobe masks were initialized by a pre-trained segmentation model. The mask follows the lung boundary against the mediastinum and soft tissue chest wall. The lung lobe segmentation mask covers the lung parenchyma from the division of the primary to secondary bronchus onwards. The mask adjusted to lung parenchymal window for best visualization of opacities includes any areas of consolidation, collapse and other abnormalities. The lung lobe annotation was performed by separating the whole lung into three right lobes and two left lobes at the fissure boundaries with different mask labels. A subset of the training dataset of 8087 chest CT was annotated previously.

For the ground truth of the abnormality a single label mask included all areas of ground glass opacity and consolidation within both lung fields however pleural effusion was excluded in the mask. For crazy paving pattern the mask excluded normal areas of the lung with precision contouring of the mask.

The average time for annotation and review of the lung and lobe masks is 2 hours.

Abnormality Segmentation Network Architecture

The training images are firstly resampled to the resolution $1 \times 1 \times 3\text{mm}$. The image intensity is clipped using the standard lung window with the width 1500 HU and level $-600$ HU before being normalized to
We use the predicted lung masks described in Sec. II-B to compute the geometric center of the lungs and then crop the image with a fixed bounding box of size $384 \times 384 \times 384$. For data augmentation, we perturb the image intensity within a random interval $[-20,20]$ and then flip the image in one of the three dimensions by 50% chance. The tensor 3D dimensions are kept in z-y-x order throughout training and inference.

We use a UNet (15) resembling architecture with convolutional blocks containing either $1 \times 3 \times 3$ or $3 \times 3 \times 3$ CNN kernels to deal with the anisotropic image resolutions. The network architecture is illustrated in Fig. 5. The 3D input tensor is first fed into a 3D $1 \times 3 \times 3$ convolutional layer followed by batch normalization and LeakyReLU. The features are then propagated to 5 DenseNet blocks (22). For the first two DenseNet blocks, the features are downsampled by a $1 \times 2 \times 2$ convolution with a stride of $1 \times 2 \times 2$. These anisotropic downsampling kernels are designed to preserve the inter-slice resolution of the input tensors. The last 3 DenseNet blocks have isotropic downsampling kernels with the stride of $2 \times 2 \times 2$. The input to each decoder block is obtained by concatenating the encoder output features with the same resolution and the features upsampled from the previous decoder. The upsampling kernels are built with transpose convolutional kernels with the sizes and strides same to the corresponding DenseNet blocks. The final network output is derived by projecting the feature maps to 2 feature channels and being activated by the softmax activation. The network parameters are randomly initialized.

We use the Jaccard index as the training loss function. The loss function $L(p, y)$ between the probability prediction tensor $p$ and the ground truth tensor $y$ is only computed within the precomputed lung segmentation as

$$L(p, y) = 1 - \frac{p \cdot y + \epsilon}{p \cdot p + t \cdot t - p \cdot t + \epsilon}$$
where $\varepsilon = 1$ is the smoothing factor and $\cdot$ represents the tensor inner product operator. The loss function is optimized using Adabound (23) with an initial learning rate 0.001. The final model used for testing is selected using a validation set with 10% of the training set patients that is randomly sampled.

The training and testing pipeline were implemented using Pytorch.

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# Tables

Table 1: Properties of training and testing data used for lung and lobe segmentation. IQR: Interquartile range.

|                      | Training                                                                 | Testing                                                                 |
|----------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|
| # Data Sets          | Total: 9223, COVID-19: 148, Viral Pneumonia: 161, ILD: 827, Miscellaneous: 8087 | Total: 200, COVID-19: 100, Normal: 100                                  |
| Data Origin          | Multiple clinical sites in Europe, Canada, USA                            | Multiple clinical sites in Europe, Canada, USA                           |
| Sex                  | Female: 3966, Male: 4570, Unknown: 687                                   | Female: 71, Male: 112, Unknown: 17                                     |
| Age                  | Median: 57 years, IQR: 45-66 years, Unknown: 5126                       | Median: 61 years, IQR: 56-62.5, Unknown: 64                            |
| Manufacturer         | Siemens: 4719, GE: 3406, Philips: 528, Toshiba: 2, Other/Unknown: 568    | Siemens: 62, GE: 68, Philips: 24, Toshiba: 28, Other/Unknown: 18        |
| Slice Thickness [mm] | ≤ 1.5: 8674; (1.5,3.0]: 395; > 3.0: 154                                  | ≤ 1.5: 56; (1.5,3.0]: 124; > 3.0: 20                                    |
| Reconstruction kernel| Soft: 8393; Hard: 179; Unknown: 651                                     | Soft: 119; Hard: 81, Unknown: 0                                        |
Table 2: Properties of training and testing data used for the segmentation of abnormalities associated with COVID-19. IQR: Interquartile rage.

|                      | Training                                                                 | Testing                                                                 |
|----------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|
| # Data Sets          | Total: 901, COVID-19: 431, Viral Pneumonia: 174, ILD: 296, Unknown: 0   | Total: 200, COVID-19: 100, Normal: 100                                   |
| Data Origin          | Multiple clinical sites in Europe, Canada, USA                            | Multiple clinical sites in Europe, Canada, USA                           |
| Sex                  | Female: 247, Male: 300, Unknown: 354                                    | Female: 71, Male: 112, Unknown: 17                                     |
| Age                  | Median: 60 years, IQR: 51-68, Unknown: 533                              | Median: 61 years, IQR: 56-62.5, Unknown: 64                             |
| Manufacturer         | Siemens: 485, GE: 201, Philips: 34, Toshiba: 17, Other/Unknown: 164      | Siemens: 62, GE: 68, Philips: 24, Toshiba: 28, Other/Unknown: 18        |
| Slice Thickness [mm]  | $\leq 1.5$: 533; $(1.5,3.0]$: 285; $>3.0$: Unknown: 83                 | $\leq 1.5$: 56; $(1.5,3.0]$: 124; $>3.0$: 20.                           |
| Reconstruction kernel| Soft: 111; Hard: 489; Unknown: 301                                      | Soft: 119; Hard: 81; Unknown: 0                                         |
Table 3: Pearson’s Correlation Coefficient between predicted disease severity measures and measures derived from ground truth for 100 COVID-19 positive and 100 control test cases.

| Metric | Pearson’s Correlation (COVID-19) | Kendall’s Rank Correlation (COVID-19) |
|--------|---------------------------------|--------------------------------------|
|        | Co-efficient | p-value | Co-efficient | p-value | Tau | p-value |
| PO     | 0.95          | 5.57e-106 | 0.92          | 9.92-43 | 0.77 | 3.63e-30 |
| PHO    | 0.98          | 1.73e-139 | 0.97          | 8.88e-65 | 0.86 | 3.52e-37 |
| LSS    | 0.96          | 1.98e-111 | 0.91          | 3.33e-38 | 0.83 | 3.41e-29 |
| LHOS   | 0.96          | 2.74e-111 | 0.9           | 3.93e-37 | 0.83 | 2.91e-26 |

Table 4: Model fitting parameters for predicted disease severity measures and measures derived from ground truth for 100 COVID-19 positive and 100 control test cases.

| Metric | Model Fit |
|--------|-----------|
|        | R² | Standard Error |
| PO     | 0.91 | 5.25 |
| PHO    | 0.96 | 0.86 |
| LSS    | 0.92 | 1.24 |
| LHOS   | 0.92 | 0.55 |
Fig. 1: Our system takes as input a non-contrasted chest CT and 3D segments the lesions, lungs and lobes. It outputs two combined measures of the severity of lung/lobe involvement, quantifying both the extent of COVID-19 abnormalities and presence of high opacities. The first measure (Percentage of Opacity, Percentage of High Opacity) or (PO, PHO) is global, while the second (Lung Severity Score, Lung High Opacity Score) or (LSS, LHOS) is lobe-wise (see section COVID-19 Severity Metrics).
Fig. 2: Overview of the deep learning system implemented in this work.
Fig. 3 Scatter plots for the four metrics computed on 100 COVID-19 cases and 100 controls. (a) Ground truth vs. predicted Percentage of Opacity (PO). (b) Ground truth vs. predicted Lung Severity Score (LSS). (c) Ground truth vs. predicted Percentage of High Opacity (PHO). (d) Ground Truth vs. predicted Lung High Opacity Score (LHOS). Note that a small jitter (0.2%) is added for the purpose of visualization to represent overlapping points.
Fig 4. Combined severity measures (PO, PHO) - right, and (LSS, LHOS) - left, computed on 100 COVID-19 cases and 100 controls. PO gives the extent of opacity and PHO gives the extent of the abnormality that has a high opacity, corresponding to consolidation regions. On the left, the diagonal line indicates PO and PHO are equal, i.e., that the abnormalities have 100% consolidation. The closer a marker is to the diagonal, the higher the relative percentage of consolidation in that subject. On the right, the diagonal indicates that all the lobes that are affected have a high percentage of consolidation as well. The points below the diagonal indicate that some of the lobes affected do not have as severe consolidation as the others. (see section COVID-19 Severity Metrics). Note that a small jitter (0.2%) is added for the purpose of visualization to represent overlapping points.
Fig. 5: Visualization of segmented abnormality regions. (a) We show the combined severity measures (PO, PHO) and (LSS, LHOS) computed for six successful cases. (b) Shows the same result side by side for abnormality segmentation, and just the high opacity segmentation. (c) Shows some of the outliers of the system.
Fig. 6: The training and testing set composition in terms of country of origin and pathology.