Visualization Project Final Report:
Seeing is Understanding: COVID-19 Impact on the Lungs
CS 6635, Spring 2021

1. Group members

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2. Project title

Seeing is Understanding: COVID-19 Impact on the Lungs

3. Overview and Project Goals

In this project we examined CT scans of lungs from COVID-19 patients looking for features potentially unique to those afflicted with the virus. This entailed doing research into the various manifestations of COVID-19 in the lungs, what to look for in an afflicted patient's CT scans, and use of multiple visualization tools to identify the features of interest. One of our key hypotheses was that 3D rendering could offer additional insights into a patient's condition that might improve the speed and/or accuracy of diagnosis, reduce the incidence of false positives resulting from exclusive consideration of gray-scale axial 2D CT images, and effectively complement the RT-PCR (swab-/saliva-based) testing procedures in common use today.

We also explored ways to automatically zero in on the regions of interest, since one of the constraints that radiologists and other medical imaging specialists have is lack of time.

4. Important Definitions and Terms

The following terms are used frequently in this domain, so their meanings are explained here so the reader will understand explanations of phenomena that include them.

CT (Computed Tomography) – technique used to capture images of chest cavity providing a level of detail beyond traditional X-Ray radiography. Source of all the data used in this project.

Lung consolidation occurs when the air that usually fills the small airways in your lungs is replaced with something else. Depending on the cause, the air may be replaced with a fluid, such as pus, blood, or water. a solid, such as stomach contents or cells.

Ground-glass opacification/opacity (GGO) is a descriptive term referring to an area of increased attenuation in the lung on computed tomography (CT) with preserved bronchial and vascular markings. It is a non-specific sign with a wide etiology including infection, chronic interstitial disease and acute alveolar disease.

Ground glass opacification is also used in chest radiography to refer to a region of hazy lung radiopacity, often fairly diffuse, in which the edges of the pulmonary vessels may be difficult to appreciate.

RT-PCR (Reverse Transcription-Polymerase Chain Reaction) – predominant test for COVID-19

5. Background and Related Work

One of the most valuable resources we relied upon was of a decidedly non-digital nature, namely a radiologist colleague and friend (Dr. Stephen Smith) who has recently retired from a group supporting the Albany, NY hospital system. He pointed us to a set of articles that put our project objective in an unambiguous perspective. These included:

- "Chest CT and Coronavirus Disease (COVID-19): A Critical Review of the Literature to Date," Raptis, Hammer, et al.
- "Chest CT in COVID-19: What the Radiologist Needs to Know," Kwee, Kwee
- "Positive Chest CT Features in Patients With COVID-19 Pneumonia and Negative Real-Time Polymerase Chain Reaction Test," Pakdemirli, Mandalla, Monib

The first of these confirmed the relevance of our project in the Objective statement of the paper:

> "Coronavirus disease (COVID-19) is a global pandemic. Studies in the radiology literature have suggested that CT might be sufficiently sensitive and specific in diagnosing COVID-19 when used in lieu of a reverse transcription–polymerase chain reaction test; however, this suggestion runs counter to current society guidelines. The purpose of this article is to critically review some of the most frequently cited studies on the use of CT for detecting COVID-19."

The Conclusion section of the paper likewise highlighted the challenges faced in applying this technology, which we took more as motivation than critique:

> "To date, the studies reporting CT features of COVID-19 pneumonia have been retrospective reviews and case series…. Reports of the various CT features of COVID-19 pneumonia are an important first step in helping radiologists identify patients who may have COVID-19 pneumonia in the appropriate clinical environment. However, test performance and management issues arise when inappropriate and potentially overreaching conclusions regarding the diagnostic performance of CT for COVID-19 pneumonia are based on low-quality studies with biased cohorts, confounding variables, and faulty design characteristics."

Clearly more time and effort are needed to address the author's critique, and we believe our project represents a small but meaningful contribution to that end.

The second paper provided more practical value for the project, as it included actual 2D renderings of CT scans showing the most common COVID-19 manifestations in the lungs. In other words, it told us what we should be looking for. To indicate what the "state of the practice" is in 2D CT rendering and to serve as a foil for the techniques we explored in this project, we have included seven (7) of those captioned figures below. Note that we will refer back to these figure numbers as we identify comparable features in the project datasets.

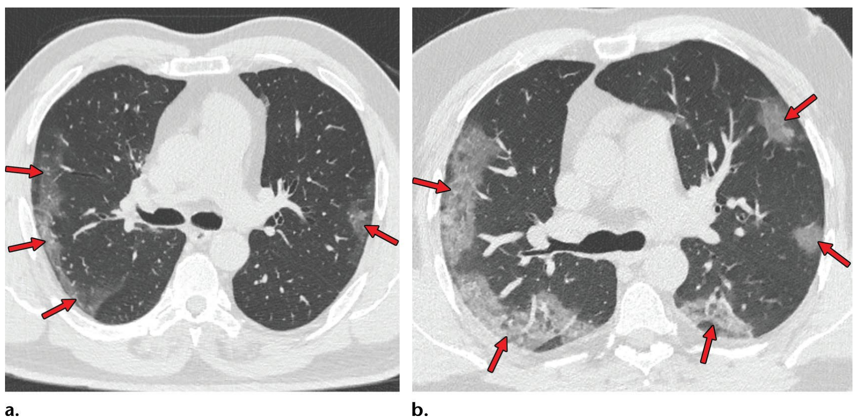


Figure 1. COVID-19 pneumonia with typical imaging features according to the Radiological Society of North America (RSNA) chest CT classification system (51). Axial nonenhanced chest CT images (lung window) in a 59-year-old man (a) and a 47-year-old man (b), each with positive RT-PCR test results for SARS-CoV-2, show bilateral areas of ground-glass opacities (arrows) in a peripheral distribution.

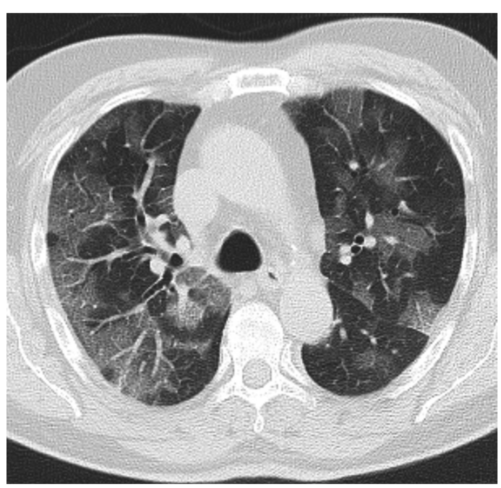


Figure 2. Chest CT abnormalities of relatively high prevalence in COVID-19. Axial nonenhanced chest CT image (lung window) shows bilateral ground-glass opacities and

dilated segmental and subsegmental vessels, mainly on the right, in a 70-year-old man with positive RT-PCR test results for SARS-CoV-2.

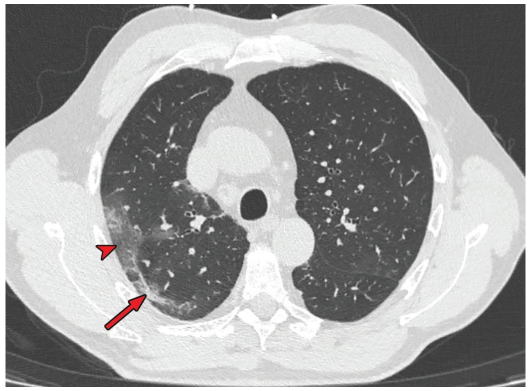


Figure 3. Chest CT abnormalities of relatively intermediate prevalence in COVID-19, shown in a 63-year-old man with positive RT-PCR test results for SARS-CoV-2. Axial non-enhanced chest CT image shows a subpleural curvilinear opacity (arrow) and an area of ground-glass opacity (arrowhead) in the right upper lobe.

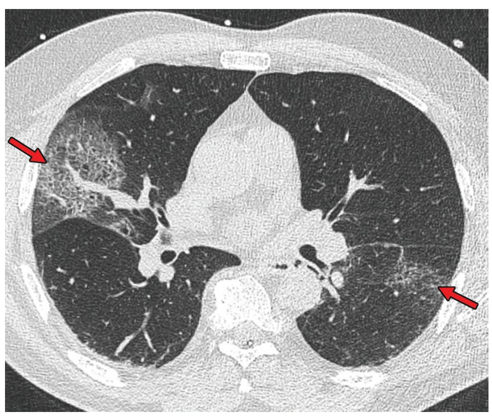
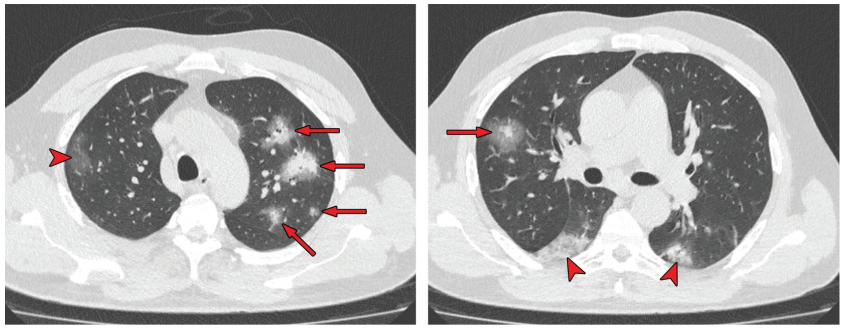


Figure 4. Crazy-paving pattern in a 66-year-old man with COVID-19. Axial nonenhanced chest CT image shows ground-glass opacities, with superimposed septal thickening (arrows) in the middle lobe and left lower lobe.



a. b.

Figure 5. Halo sign in a 55-year-old man with RT-PCR-test–proven COVID-19. Axial nonenhanced chest CT images show consolidations surrounded by ground-glass opacities (arrows) in both upper lobes, findings consistent with the halo sign. There is a ground-glass opacity in the right upper lobe (arrowhead in **a**) and consolidation in both lower lobes (arrowheads in **b**).

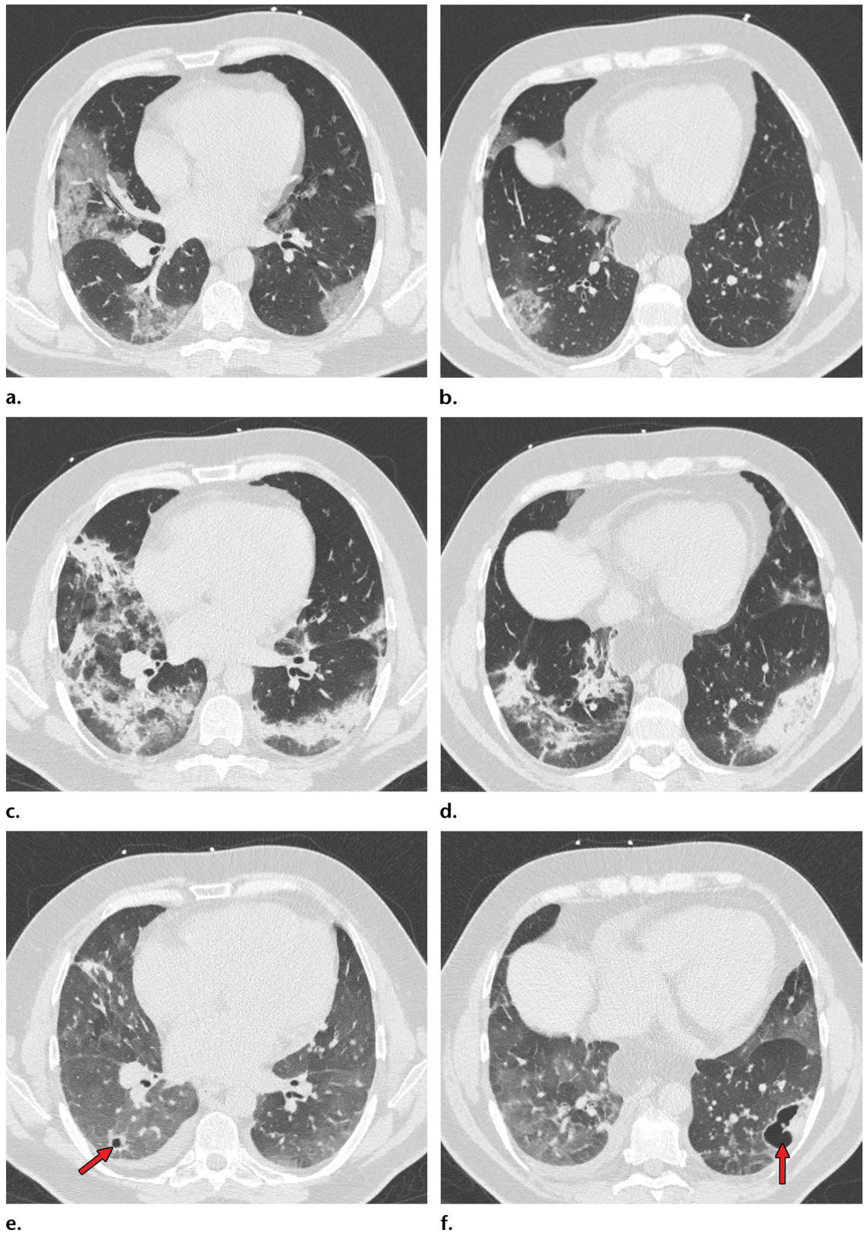
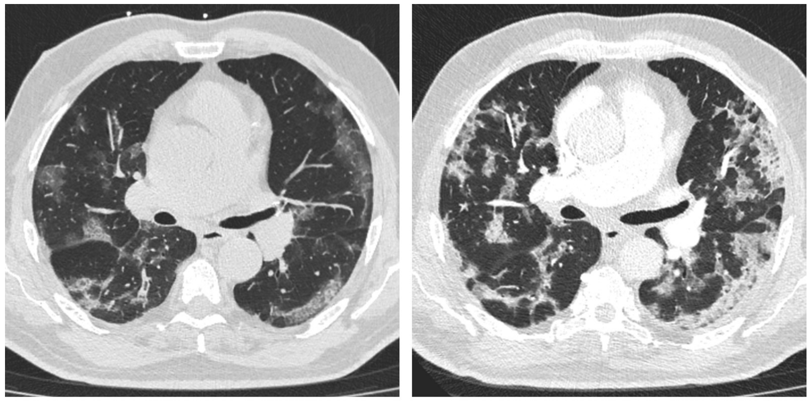


Figure 6. Development of cavitating lung lesions in a 47-year-old man with COVID-19. **(a, b)** Axial nonenhanced CT images (lung window) obtained at hospital admission show ground-glass opacities in both lungs (early progressive stage). **(c, d)** Axial nonenhanced CT images (lung window) obtained after 10 days show progressive organizing consolidation (peak stage). **(e, f)** Axial nonenhanced CT images (lung window) obtained 40 days after the baseline CT images **(a, b)** show cavitating lesions in both lower lobes (arrow) (late stage).



a. b.

Figure 7. Transition from progressive stage to peak stage in a 69-year-old man with COVID-19. **(a)** Axial nonenhanced chest CT image (lung window) obtained at hospital admission shows bilateral areas of ground-glass opacities and crazy-paving appearance. **(b)** Axial contrast-enhanced chest CT image (lung window) obtained after 7 days shows progression from ground-glass opacities to multifocal organizing consolidation.

Other sources of COVID imaging information included:

- “Photo Gallery of how COVID-19 appears on Medical Imaging,” Fornell (Editor) https://www.itnonline.com/content/photo-gallery-how-covid-19-appears-medical-imaging

- Video: “How to Image COVID-19 and Radiological Presentations of the Virus,” Revzin https://www.itnonline.com/videos/video-how-image-covid-19-and-radiological-presentations-virus

Sources of technical information about the visualization software used included their web sites and references therein:

- https://slicer.readthedocs.io/en/latest/
- http://www.itksnap.org/pmwiki/pmwiki.php?n=Documentation.SNAP3
- https://kitware.github.io/paraview-glance/app/
- https://www.paraview.org/Wiki/The_ParaView_Tutorial

6. Project Description

5.1 Data used

We primarily used the following datasets in this project:

- COVID-19 dataset at the Cancer Imaging Archive https://wiki.cancerimagingarchive.net/display/Public/CT+Images+in+COVID-19

- Lung CT images from OsiriX DICOM Image Library https://www.osirix-viewer.com/resources/dicom-image-library/

- Lung CT images from embodi3D biomedical 3d printing company
  https://www.embodi3d.com/

- Other one-off instances from various sites

5.2 Software used

- ITK-SNAP – ideal for quick visualization, also able to export datasets in a variety of formats
- 3D Slicer -- best tool for 2D analysis; also, good preset transfer functions for volume rendering
- ParaView – most flexible tool for precise volume rendering
- Paraview Glance – holds promise for future cloud-based analysis

5.3 Software developed

- Python utility to convert .nii.gz files to .nrrd format for ease of visualization in ParaView
- Script to automatically load .nrrd CT dataset into ParaView, perform volume rendering, and apply COVID-19 lung transfer function

5.4 Creative backlog

- Python script to slide and scale transfer function across a Color Map in Paraview as is done in 3D Slicer and ParaView Glance. This would make it very easy to adjust a "standard" COVID transfer function to the data distribution of a particular CT scan rather than adjusting each point as one must do presently

5.5 Questions answered

During the project we answered many of the key questions posed in the Project Design Report, including:

- Does COVID-19 affect a patient's lungs in ways that are visible on medical imaging datasets, such as X-Rays, CT scans, and MRIs?
    - The answer is a resounding "Yes," which can be seen in the Implementation Details portion (section 6) of this report.

- What visualization techniques will be most useful in isolating these features?
    - A combination of 2D rendering with multiple views and 3D (volume) rendering with carefully designed transfer functions was the most useful for quickly identifying regions of interest and then more fully characterizing their shape and location

- Are there a ways to partially automate the rendering process to speed the diagnostic process?

  - Yes. The key word in the question is “partially” because differences in CT equipment brands and instances as well as physiological differences in patients precluded the definition of a single, “one size fits all” transfer function. More on this in the Implementation Details section.

- What improvements in the visualization process could help heath care professionals in diagnosing COVID-19 and other pulmonary diseases?

  - We demonstrate several improvements to the COVID-19 CT visualization process in this report and identify future work that could be done to build on this foundation.

5.6 New questions that arose during the project

As we got into the domain, the biggest question that arose was “How could we make the results of this effort truly meaningful, given the global spread and serious nature of this pandemic?” and the related question “What expert resources could we tap to generate a robust requirements document to guide further development?”

The answers to these could consume a development team for some time…

7. Implementation Details and Process

The quickest way to get an idea of what we implemented is to view the 3-minute video at this link: https://youtu.be/PR1aX7U2ZNc. The first minute shows how we used the 3D Slicer software to volume render infected lungs from several patients in the Cancer Imaging Archive dataset and adjust the transfer preset CT-Lung transfer function to highlight the regions of interest.

The next section (beginning at 1:03) focuses on 2D rendering in 3D Slicer and the selection and adjustment of high-contrast transfer functions that enhance these images and help the user identify features that may otherwise be overlooked.

The next section (beginning at 1:40) demonstrates a python script that automates the data loading, volume rendering, and transfer function application in ParaView. It them shows how a Slice filter can be used select a 2D slice anywhere in lung for further inspection.

The final section (beginning at 2:35) briefly introduces ParaView Glance and shows how to load an image, navigate its library of predefined transfer functions, select and easily adjust the appropriate one to perform 2D and 3D rendering.

Needless to say, we didn’t get here overnight. We experimented with a variety of software tools to see which ones were best suited for quick evaluation of the files in the COVID-19 dataset (which has images for 698 patients), conversion of the file formats for use with other software tools, selection of preset transfer functions to focus on the lungs, adjustment of these functions to zero in on the COVID-related features, and overall ease of use for generating compelling images.

The rough sequence of activities in our implementation process follows:

- Reviewed literature to understand characteristics of COVID effects as they appear in lung CT images

- Used ITK-SNAP to quickly visualize 2D rendering COVID patients to get an idea of the overall dataset contents and to look for “interesting” cases; also used its export capabilities to generate datasets in other formats for input to other software tools

- Used 3D Slicer to do volume rendering of COVID patients’ CT scans of their lungs and applied additional cropping to focus on the infected areas

- Used 3D Slicer to compare 3D volume of COVID patients against the 2D rendering of their CT scans

- Reviewed many lung CT images from available datasets with a variety of software tools to find examples of specific conditions identified in the literature

- Looked at Paraview Glance to get ideas for “ease of use” capabilities for rapid visualization; specifically used it to render 3D images and shift transfer function for better visualization of COVID symptoms area

- Looked at the data distribution (Data Histogram function in ParaView) across many scans in the COVID-19 datasets to understand the challenge of developing common transfer function(s) for isolating COVID-specific pathologies

- Developed multiple transfer functions to quickly render lung conditions from chest CT scans; however, all required some adjustment per patient to achieve consistent results

- Automated the initial application of these transfer functions in ParaView and used it to render .nrrd image files into 3D images

The rest of this section is devoted to showing representative images (CT renderings and related screenshots) from the above activities.

Before evaluating images of the lungs of COVID-infected patients, it is useful to know what the lungs of a normal person look like. To this end, we found a CT dataset from such a patient and rendered it in Figure 8 below.

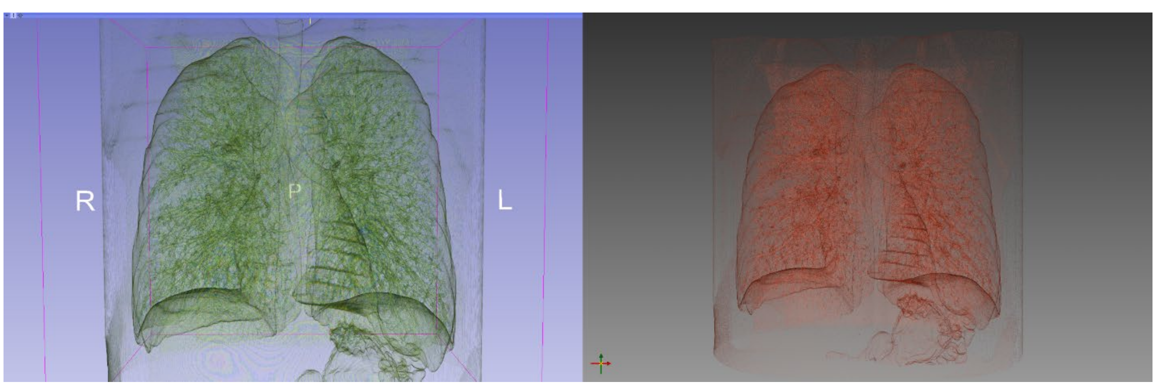


Figure 8 - by Hazme El Halabi – Left: Normal Lung 3D rendered in Slicer 3D
Right: 3D rendered in Paraview Glance

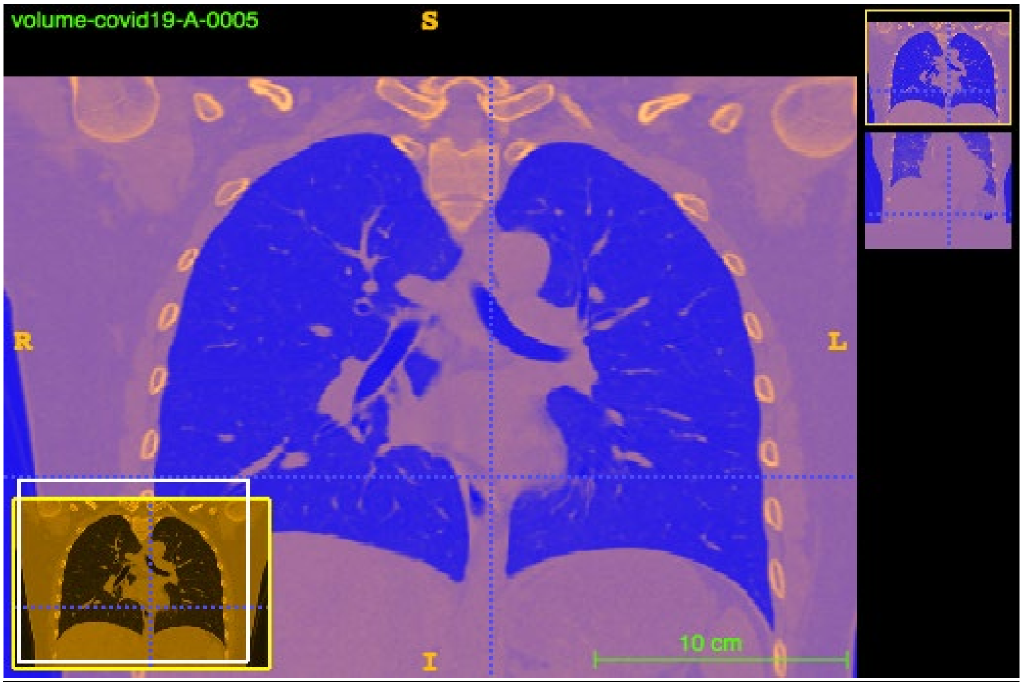


Figure 9 - COVID Patient 5 Lung CT Scan: 2D Coronal rendering using ITK-SNAP

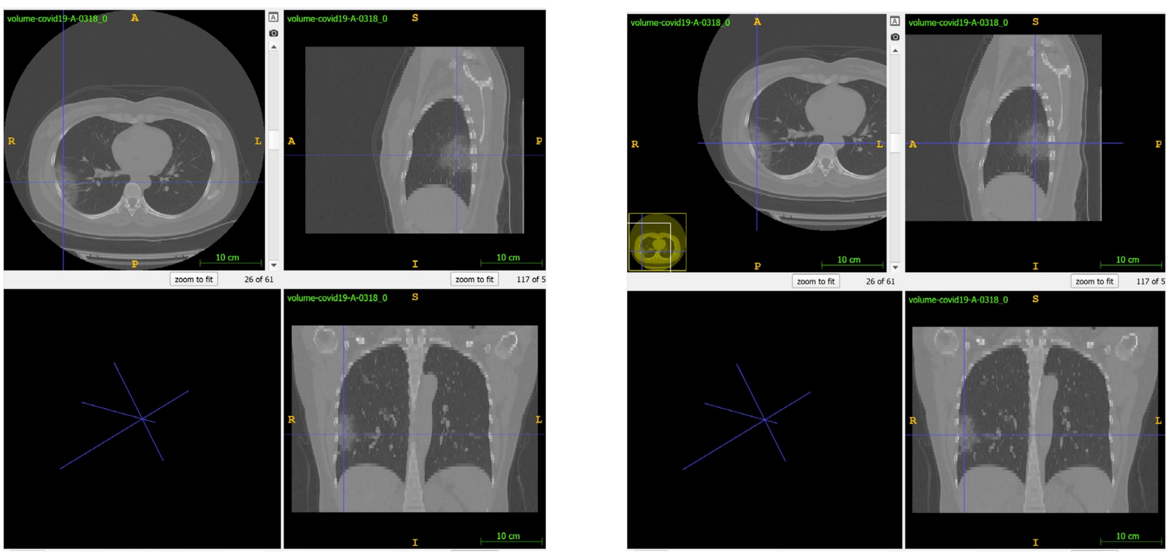


Figure 10 - COVID patient #318 with ITK_SNAP 2D slice rendering
(Overall, then centered/zoomed on infection)

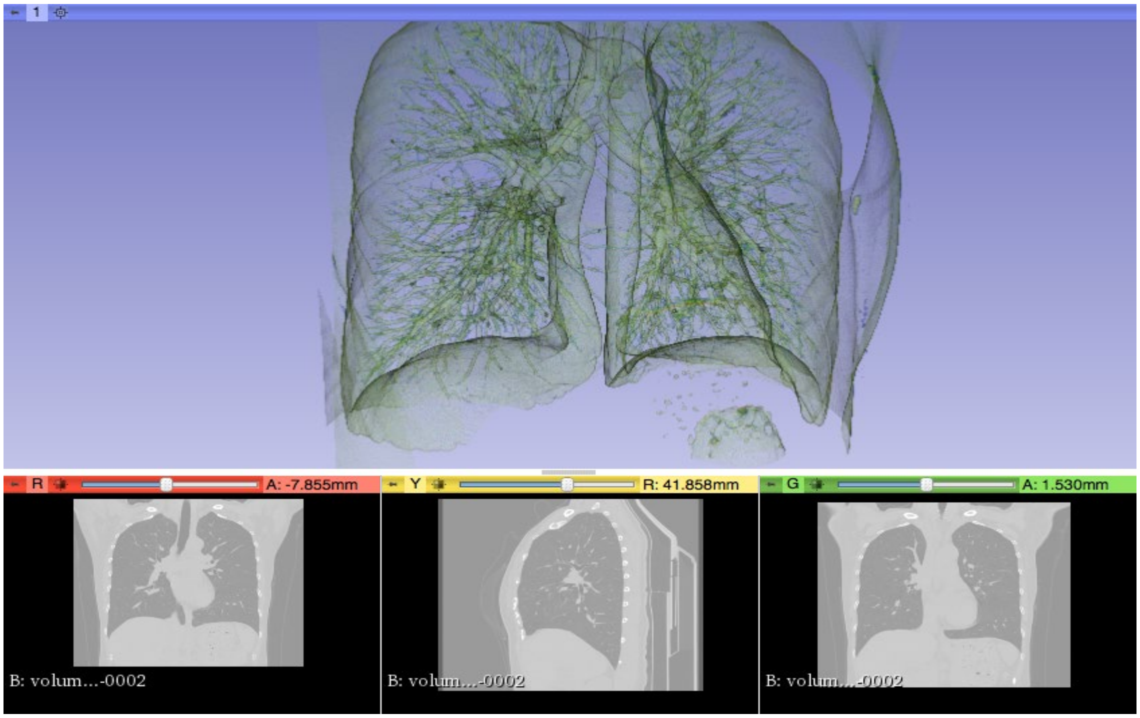


Figure 11 - Covid Patient#02 Lung CT Scan: 3D rending alongside 2D view of the patient lungs using 3D Slicer

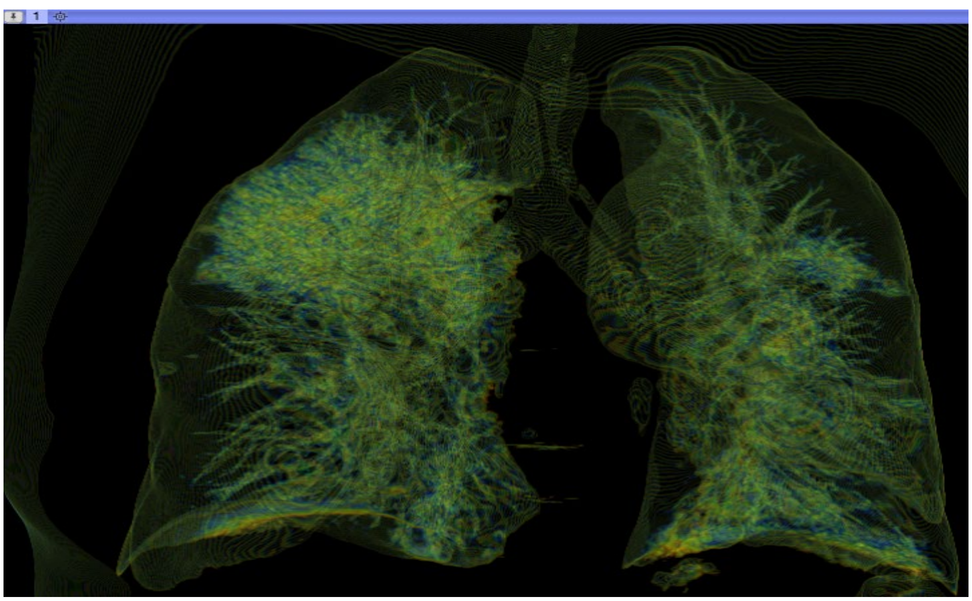


Figure 12 - COVID Patient 19 Lung CT Scan: 3D volume rendering with cropped ROI using 3D Slicer (Example of “Crazy paving” feature from Figure 4)

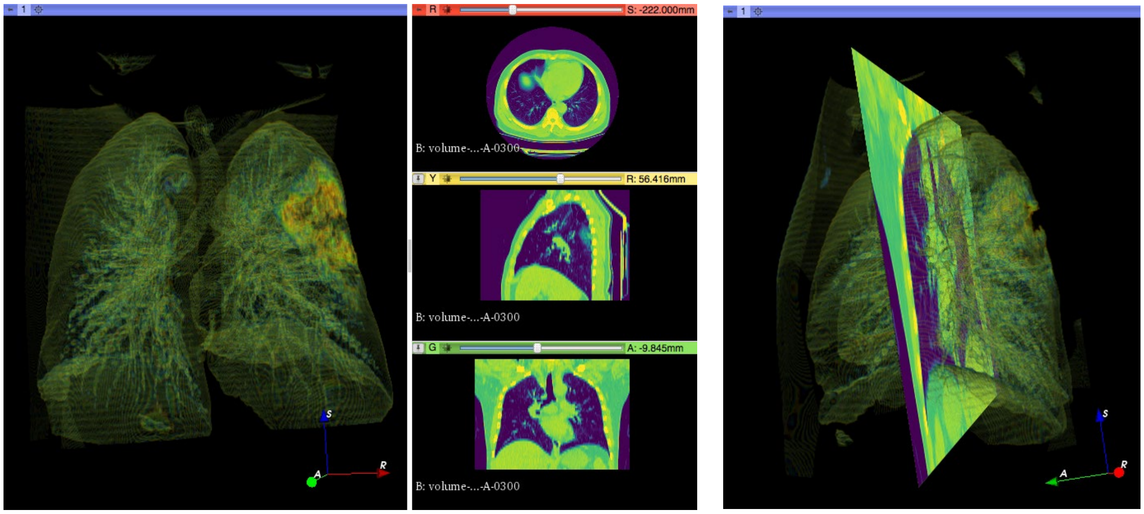


Figure 13 - COVID Patient 300 Lung CT Scan: 2D, 3D, and Sliced Rendering Using 3D Slicer
(Another example of “Crazy paving” feature from Figure 4)

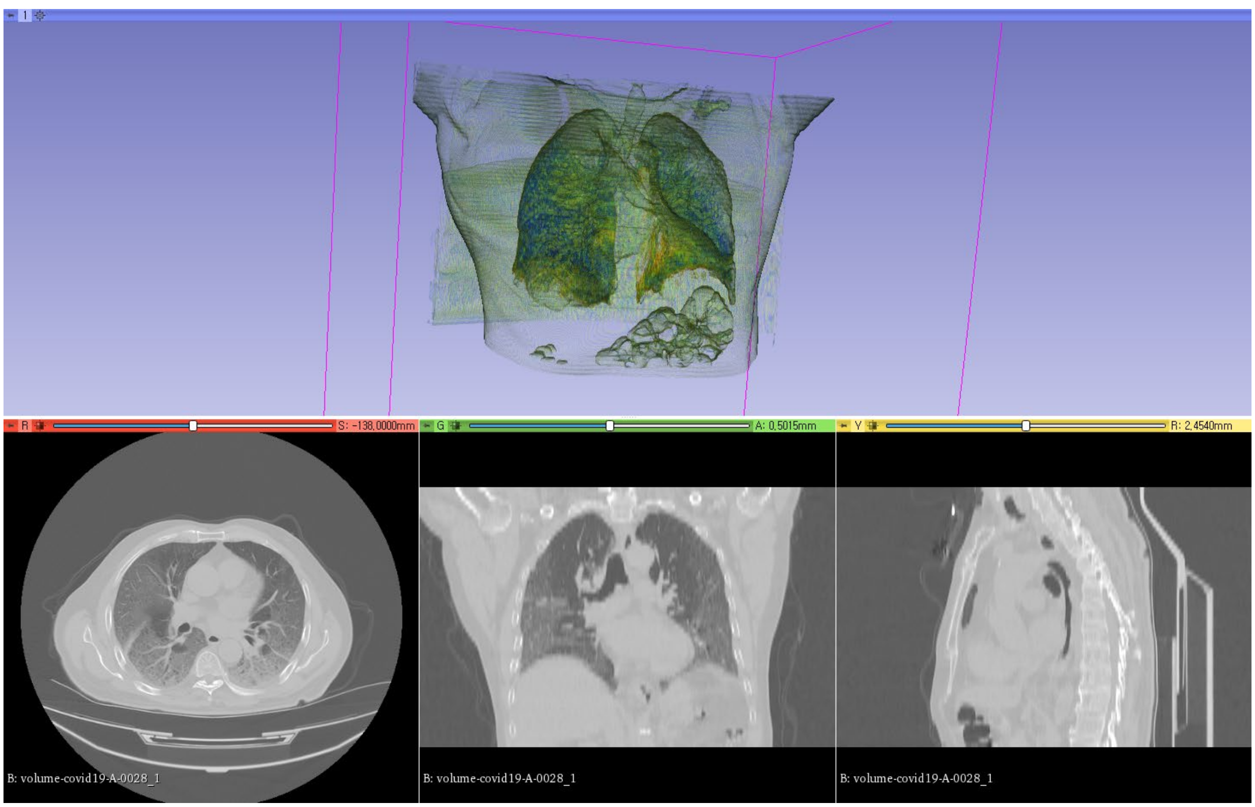


Figure 14 - COVID Patient 28 Lung CT Scan: 2D and 3D Rendering Using 3D Slicer
(Another example of “Crazy paving” feature from Figure 4)

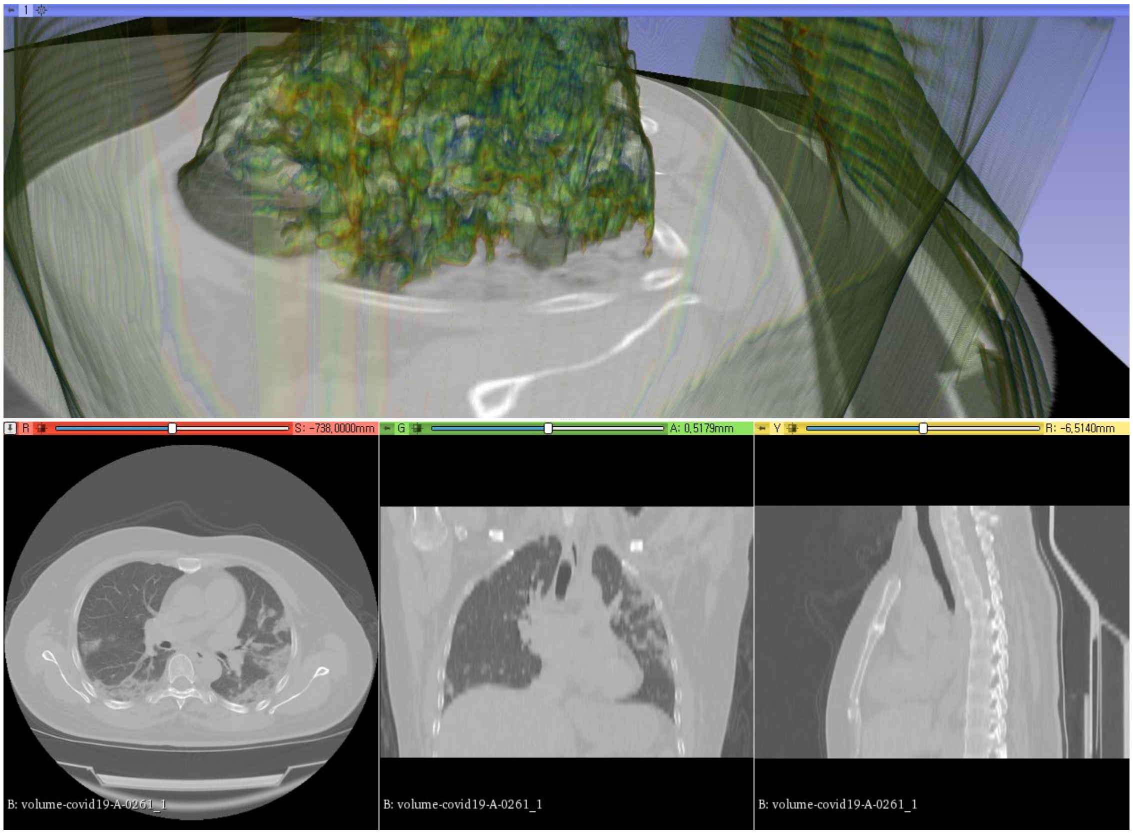


Figure 15 - COVID Patient 261 Lung CT Scan: 2D and 3D Rendering Using 3D Slicer
(Example of "ground glass opacity" feature from Figure 1)

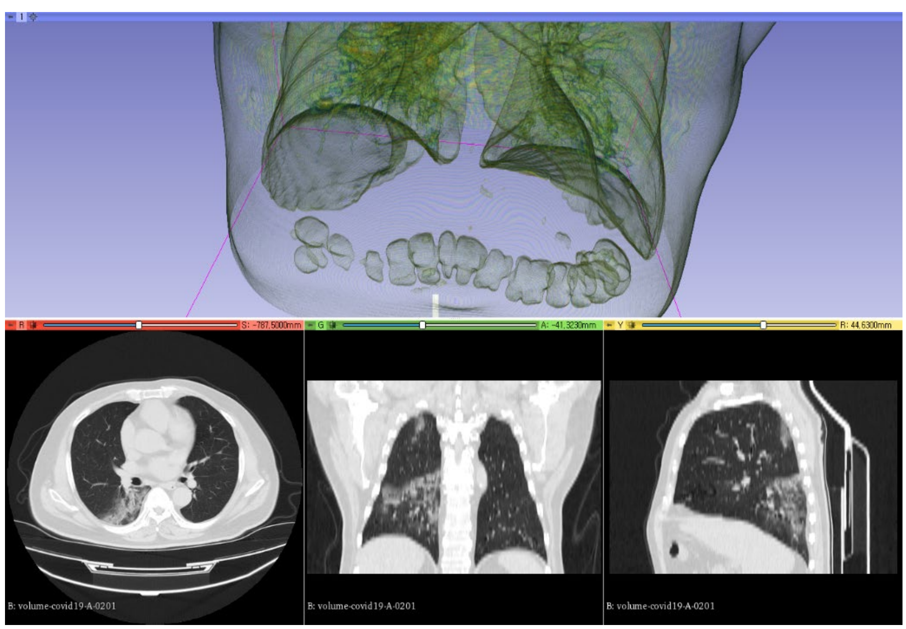


Figure 16a - COVID Patient 201: 2D and 3D Rendering Using 3D Slicer Default Rendering

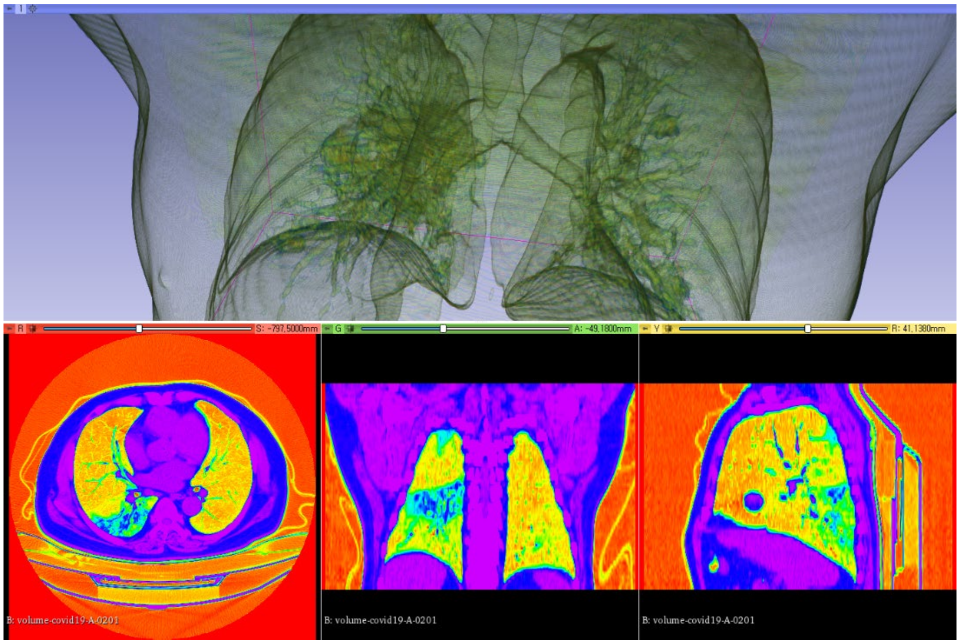


Figure 16b - COVID Patient 201: 2D and 3D Rendering Using 3D Slicer Enhanced with Colorful 2D Transfer Function

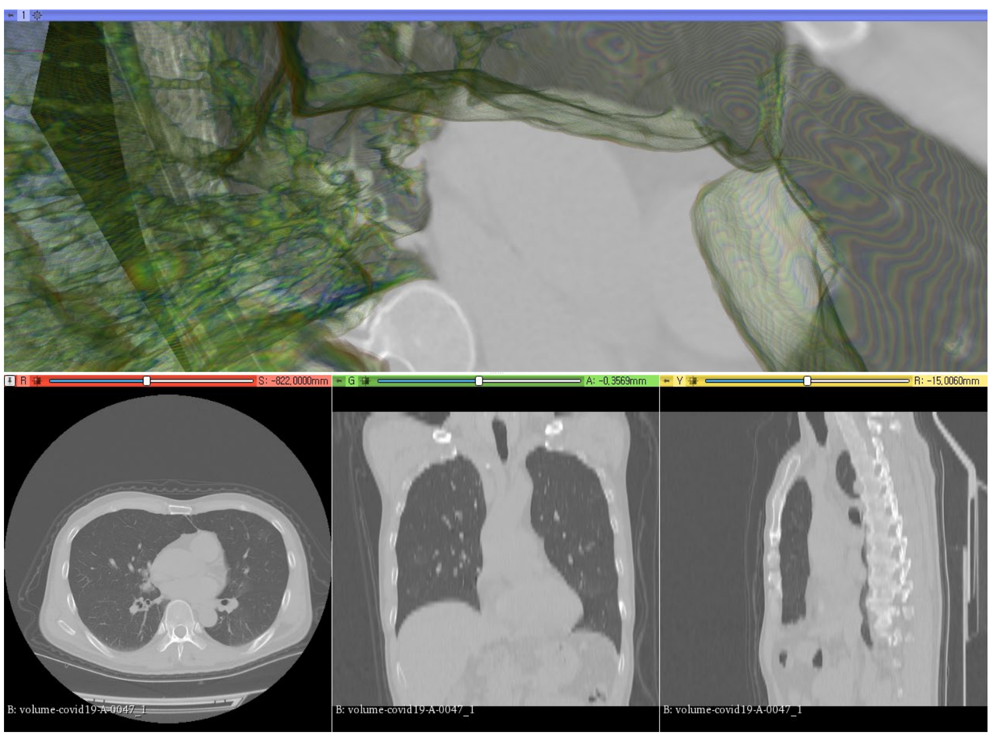


Figure 17 - COVID Patient 347 Lung CT Scan: 2D and 3D Rendering Using 3D Slicer (Example of false positive for “cavitating lesion” (leftmost 2D image above) referenced in Figure 6e but shown to be permanent physical feature in 3D view)

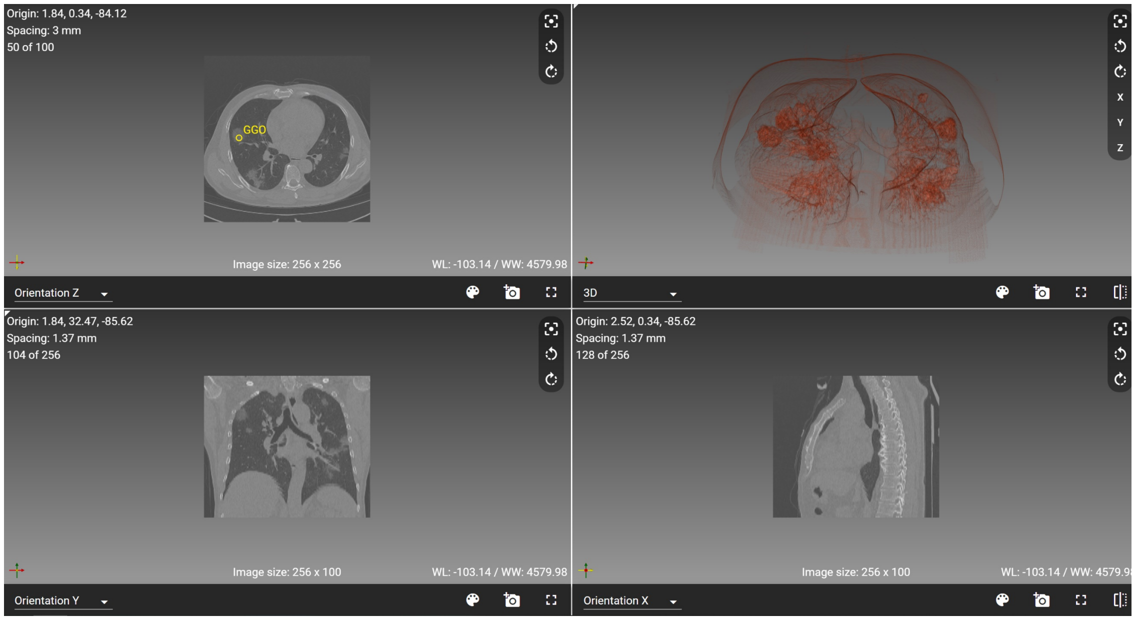


Figure 18 - Sample COVID patient 2D and 3D rendering using Paraview Glance and its built-in CT-Lung transfer function

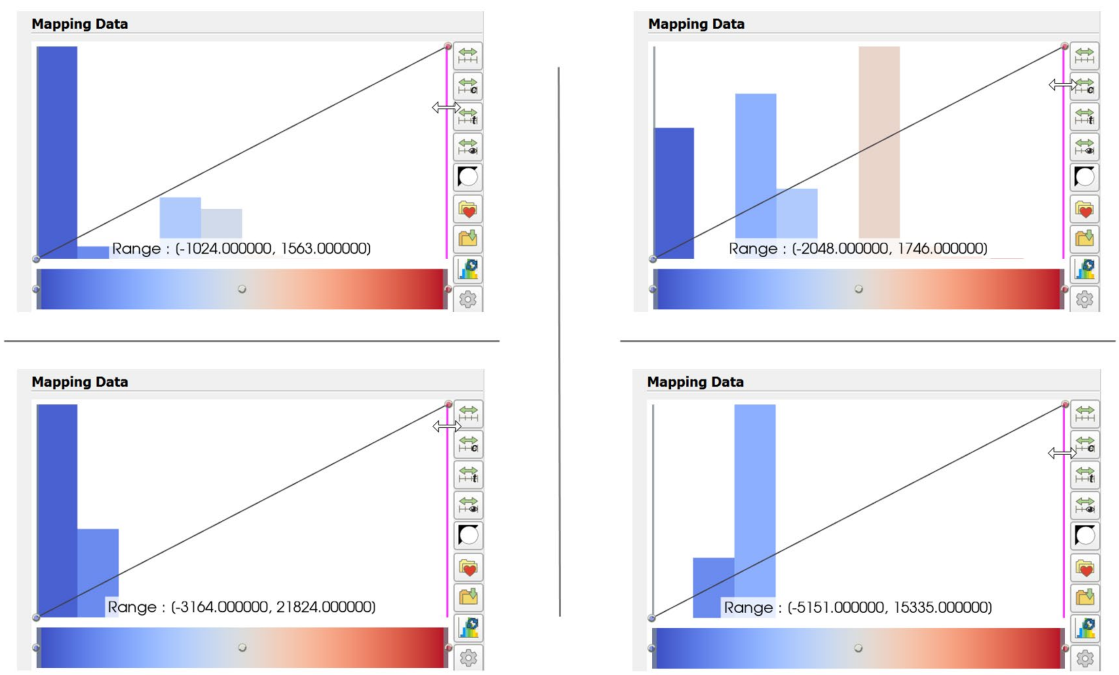


Figure 19 – Data Histograms and Associated Data Ranges from Selected COVID-19 Patient CT Image Data (This is what complicates creation of “standard” transfer function for all CT scans)

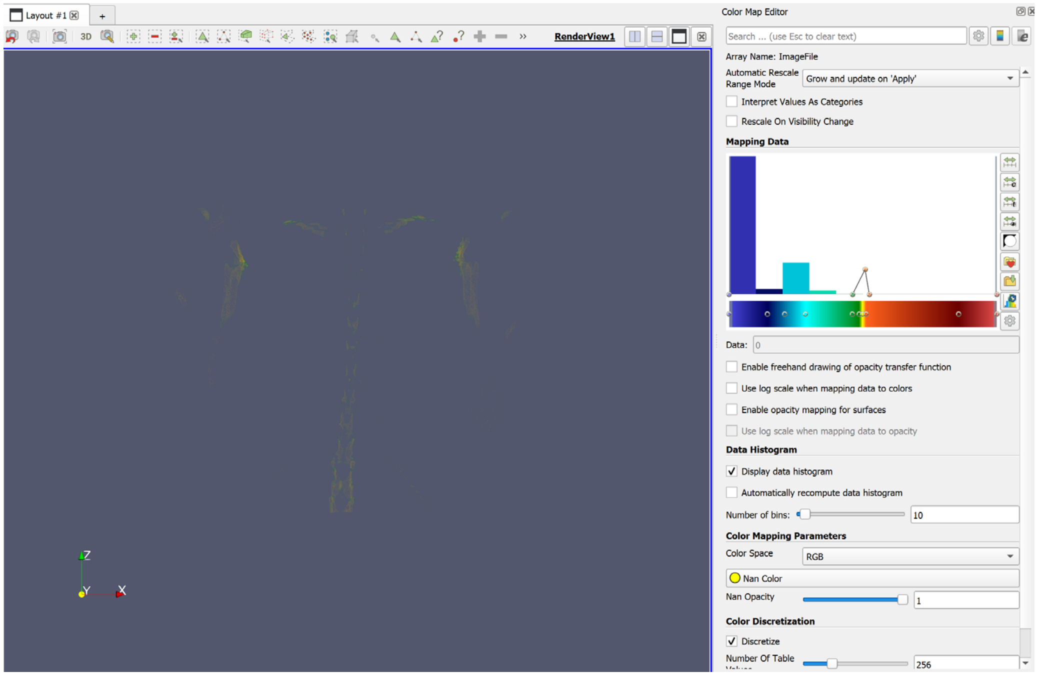


Figure 20 - COVID Patient 402 Volume Rendering using Paraview
With COVID Feature Transfer Function (note misalignment of Data Histogram)

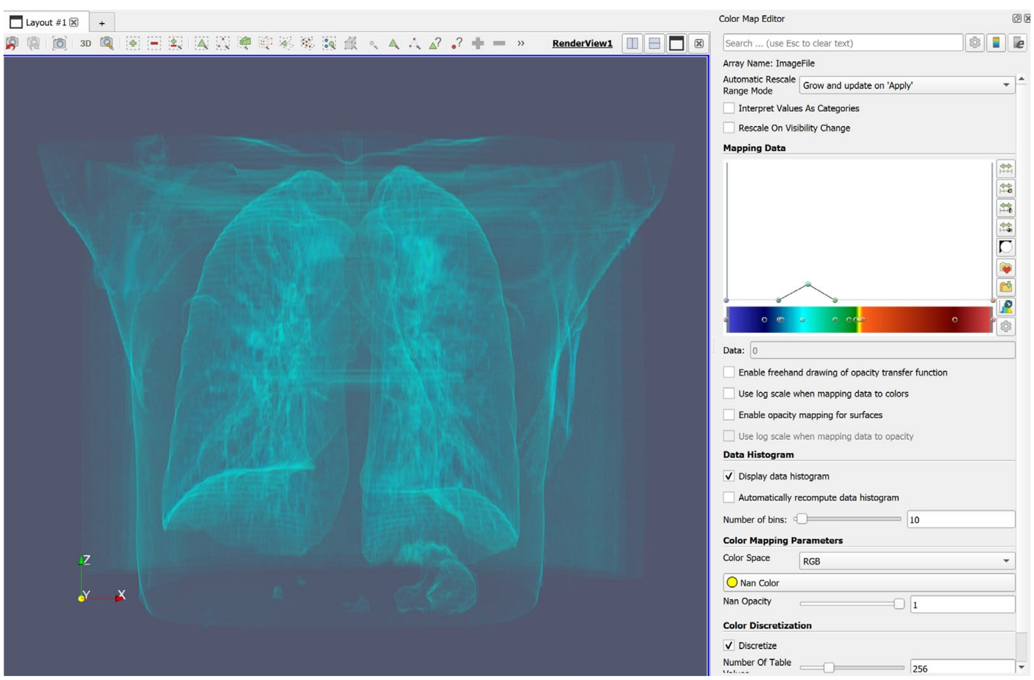


Figure 21 - COVID Patient 402 Volume Rendering using Paraview
after Adjusting COVID Transfer Function

8. What We Learned

Covid19 does impact lungs in ways that are clearly visible on 2D and 3D volume renderings of the CT scan. Moreover, there are many powerful software tools for visualizing the volume of a CT dataset, and we have become proficient in using several of them learned how to use a few of them in this pr oject, notably ITK-SNAP, 3D Slicer, and ParaView. Specifically,

- ITK-SNAP is a great tool for 2D visualization of CT scans. It is also great if you are looking for a quick way to convert files from Nifti format to NRRD.
- 3D Slicer is an excellent tool for visualizing medical imaging datasets, especially because it gives the users the ability to interact and compare and contrast 2D slices and 3D volumes.
- ParaView is the most powerful tool we evaluated because it supports a broad range of filters and rendering options to highlight specific features in the region of interest once a well targeted transfer function has been implemented

We also learned that fully automating the transfer function tuning process requires deeper analysis of the raw data from many CT scans to characterize the distribution and identify the relevant boundaries across varying equipment brands/models, settings, and patients

Finally, there is a genuine opportunity to improve the speed and accuracy of COVID diagnosis using CT scans to complement RT-PCR testing.

9. Accomplishments vs. Expectations

Our principal accomplishment was developing the ability to effectively use 3D Slicer and ParaView do 3D volume rendering of CT scans of COVID-infected lungs, and to compare this representation with 2D slice renderings these same datasets to improve the fidelity of the COVID feature identification process.

We were also able to develop a transfer function that could be applied to ParaView and automate the application of transfer function, even though it did require minor adjustment in many cases to isolate the COVID features.

The key difference in this accomplishment from our original expectation was the difficulty of writing software that could reliably automate this process for the range of available datasets, and we now realize that a deeper analysis of these data distributions is required to achieve this objective.

10. Project Self-evaluation

We believe we did very well in the time available for this project, accomplishing most of our stated goals and gaining valuable insights into the use of CT scans in diagnosing COVID-19 conditions.

As the project unfolded, we realized that one of the original ideas of finding evidence of COVID presence in the lung CT scans of non-symptomatic patients was unrealistic due to the time and data available and the learning curve for the project participants, so this is a topic for further investigation; likewise for comparison of COVID effects and those of other abnormal pulmonary conditions.

11. Future Work

As with all projects of this type, we thought of many things we could have accomplished if we had had another 3-6 months to work on it. For example, it would be instructive to interview actual practitioners about improving the discrimination in their published articles by using color transfer functions that highlight the COVID features.

The ParaView transfer function automation script has minor bugs that should be addressed: 1) some .nrrd files does not appear when script is used; and 2) some volume rendered by transfer function changes its value and changes its transfer function value by itself and needs shifting when another filter is applied.

Since the CT data ranges vary a great deal, we should also build a ParaView GUI plug-in for shifting the transfer function à la ParaView Glance.

It would be useful to create a 3D Slicer plugin to automatically crop chest CT scan which removes noise from the image. There is also room for improvement in determining the best transfer functions for 2D rendering in 3D Slicer.

We would also investigate the use of machine learning on the enhanced volume rendering of the CT scans to automate the detection of COVID via these images. This technique has proven to be very effective in diagnosing breast cancer from imaging data and radiologists rely on this technology as a matter of course.