COVID Challenges, Digital Solutions

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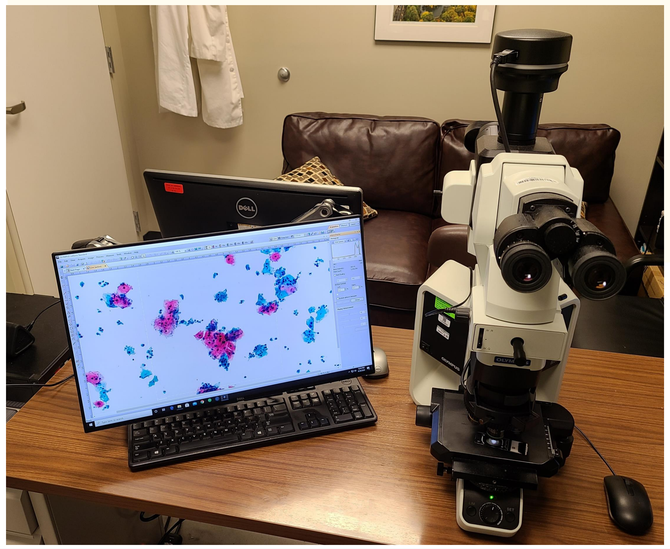
Background

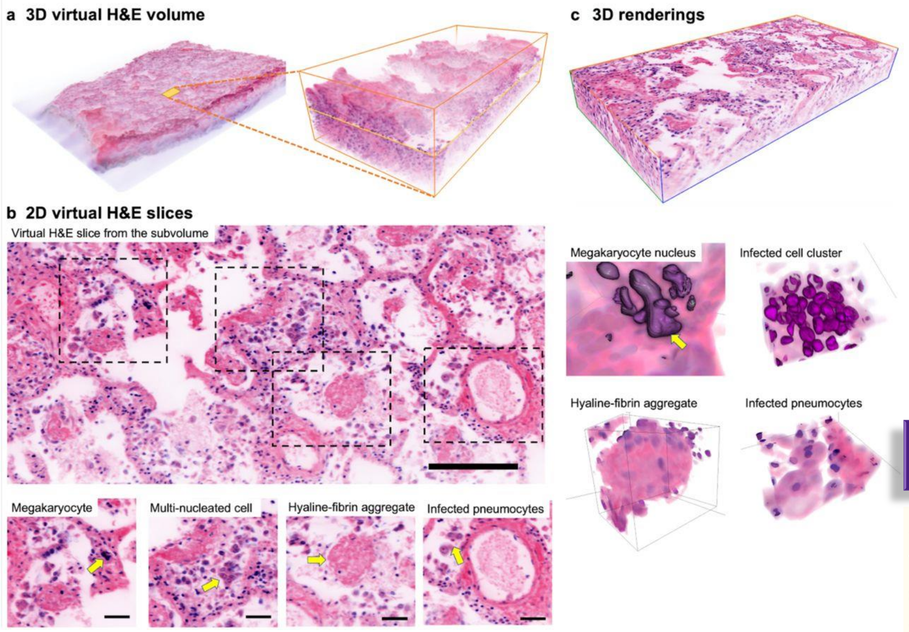
The COVID-19 pandemic has presented many challenges to pathologists, but has also become an impetus for innovation in the use of digital pathology tools. The benefits of digital pathology for distance education are tremendous, and such tools have additionally improved upon our reporting capabilities on over 30 autopsy cases of deaths due to COVID-19 infection – thus modernizing one of the oldest methods of analyzing the pathologic basis of disease.

Methods

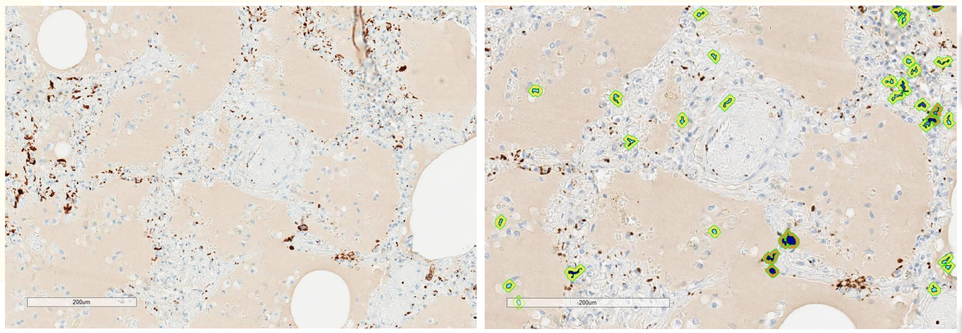
Digital pathology was applied to three domains of the anatomic pathology services at the onset of the COVID-19 pandemic shutdown at our institutions in New Orleans: 1) pathology education, 2) surgical pathology signout, and 3) COVID-19 related autopsy research. Implementations included the use of whole-slide scanners (Leica) and online repositories, along with PathPresenter for conferences. Live signout services adopted the Olympus CellSens software with Zoom conferencing. Existing image analysis algorithms, as well as multiscale microscopy using tissue clearing methods were employed to study the nature of SARS-CoV-2 infection at autopsy.



Analysis Tools for Autopsy Tissues



Multiscale 3-dimensional imaging of lung tissue demonstrating viral cytopathic changes, diffuse alveolar damage, and microangiopathy. (see citation section)
a) Full 3-dimensional virtual H&E volume of a single gross slice of optically-cleared and fluorescently-stained lung tissue, measuring 7.8 mm × 5.9 mm × 0.9 mm and comprising 0.832 teravoxels at full resolution. A smaller volume (1.2 mm × 0.6 mm × 0.3 mm comprising 4.5 gigavoxels) was selected for detailed analysis (right inset). b) 2-dimensional virtual H&E sections of the smaller volume from (a). Megakaryocyte in the capillaries, infected cell clusters and infected pneumocytes in the alveolar spaces, and hyaline-fibrin aggregates in the alveoli are apparent (yellow arrows). c) Selected 3-dimensional renderings corresponding to structures identified by yellow arrows in (b). 3D renderings of the tissue reveal nuclear, cellular, and tissue morphology in 3D.



Above: Megakaryocytes identified on scanned CD61 immunostain slides (above left: Leica Aperio AT2 scanner), using modification of existing image analysis algorithms. Cells with dark blue labeling of nuclei and orange labeling of cytoplasm (above right) were most likely to represent megakaryocytes. This method allows for rapid quantification of these cells in the lungs of decedents with COVID-19 as compared to lung specimens without COVID-19.

Left: Olympus CellSens software with a cytologic Papanicolau-stained cervical smear.

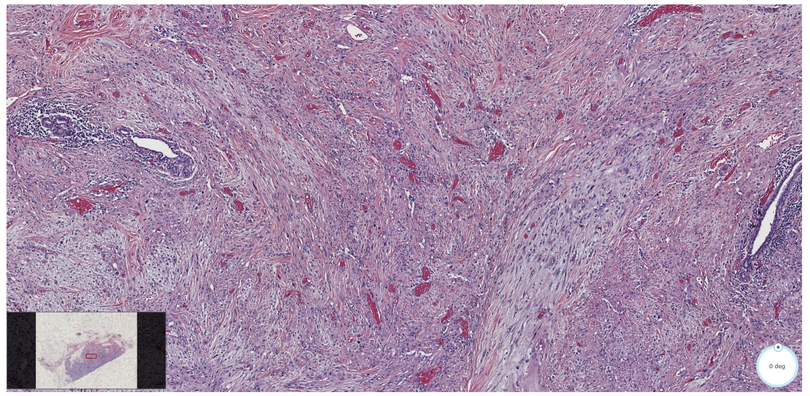


Image from digital residency morning conference at the Louisiana State University Health Sciences Center – New Orleans Department of Pathology residency program. Image scanned by Leica Aperio LV1 slide scanner and presented with PathPresenter.

Results and Conclusions

Safe distance learning objectives were achieved without disruption to resident education due to the implementation and adaptation of digital solutions. Existing image algorithms were tuned to analyze data from COVID-19 tissue samples, and the first 3-dimensional images of unsectioned lung from a COVID-19 patient were obtained, providing unique insights into the disease process. Conclusions: Digital pathology tools have been rapidly adopted for both routine and academic use during the COVID-19 pandemic. These methods offer practical solutions to both the altered workflow, and the study of SARS-CoV-2 infection by pathologists.

Acknowledgements

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Citations

Top middle image from bioRxiv pre-print:
Multiscale 3-dimensional pathology findings of COVID-19 diseased lung using high-resolution cleared tissue microscopy
Guang Li, Sharon E. Fox, Brian Summa, Bihe Hu, Carola Wenk, Aibek Akmatbekov, Jack L. Harbert, Richard S. Vander Heide, J. Quincy Brown
bioRxiv 2020.04.11.037473; doi: https://doi.org/10.1101/2020.04.11.037473