

Use of Telepathology to Facilitate COVID-19 Research and Education through an Online COVID-19 Autopsy Biorepository

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Abstract

Introduction: The coronavirus disease 2019 (COVID-19) pandemic has increased the use of technology for communication including departmental conferences, working remotely, and distance teaching. Methods to enable these activities should be developed and promulgated. **Objective:** To repurpose a preexisting educational website to enable the development of a COVID-19 autopsy biorepository to support distance teaching and COVID-19 research. **Methods:** After consent was obtained, autopsies were performed on patients with a confirmed positive severe acute respiratory syndrome coronavirus-2 reverse-transcriptase-polymerase-chain reaction test. Autopsies were performed according to a COVID-19 protocol, and all patients underwent both gross and microscopic examination. The H and E histology slides were scanned using a Leica Biosystems Aperio CS ScanScope whole slide scanner and the digital slide files were converted to deep zoom images that could be uploaded to the University of Alabama at Birmingham (UAB) Pathology Educational Instructional Resource website where virtual microscopy of the slides is available. **Results:** A total of 551 autopsy slides from 24 UAB COVID-19 cases, 1 influenza H1N1 case and 1 tuberculosis case were scanned and uploaded. Five separate COVID-19 research teams used the digital slides remotely with or without a pathologist on a Zoom call. The scanned slides were used to produce one published case report and one published research project. The digital COVID-19 autopsy biorepository was routinely used for educational conferences and research meetings locally, nationally and internationally. **Conclusion:** The repurposing of a pre-existing website enabled telepathology consultation for research and education purposes. Combined with other communication technology (Zoom) this achievement highlights what is possible using pre-existing technologies during a global pandemic.

Keywords: Autopsy, coronavirus disease-2019, research, severe acute respiratory syndrome coronavirus 2, telepathology

Key Points

1. Scanned microscope slides of COVID-19 autopsy cases with corresponding tissue blocks available for research applications were used to create an online COVID-19 autopsy histology biorepository with hi-resolution digital slides.
2. An online COVID-19 autopsy histology repository and hi-resolution digital slides were used remotely to facilitate COVID-19 research and education during the pandemic.

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- Continued autopsy examinations linked to telepathology systems that facilitate COVID-19 research are needed to further characterize this disease.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has led to multiple pathological case reports and case series that focuses on defining the pathology of COVID-19.^[1-4] The pandemic has also led to widespread remote work including teleconference, telemedicine, and recommendations to “explore options for remote research”.^[5] Whole slide imaging in pathology has been reported to allow pathologists to work remotely in regions with severe logistical constraints due to COVID-19.^[6] However, the use of whole slide imaging for distance teaching has been reported as “underutilized and not fully exploited”.^[7] This article describes the repurposing of the Pathology Education Instructional Resource website (PEIR) at the University of Alabama at Birmingham (UAB) (<https://peir.path.uab.edu/>) and its Aperio CS digital slide scanner to enable COVID-19 education and research via telepathology thus linking a virtual COVID-19 biorepository with a physical (tissue) COVID-19 biorepository.^[8]

MATERIALS AND METHODS

Included cases were either positive for SARS-CoV-2 by reverse transcriptase-polymerase chain reaction or included at the request of collaborating investigators. A case of influenza A H1N1 and a case of miliary tuberculosis were included at the request of collaborating investigators. One included case was co-infected with influenza A H1N1 and SARS-CoV-2 (case C). Autopsies were performed at the UAB, Birmingham, AL, USA after obtaining consent for diagnostic, teaching, and research use of the tissue from next-of-kin. Autopsies were performed according to a COVID-19 protocol in biosafety level-2+ conditions. A COVID-19 histology block key was developed with special emphasis on lung histology including a central and peripheral section from each lung lobe [Table 1]. The exception to the block key was that cases 1–6 did not include material from the gastrointestinal tract because the first COVID-19 autopsies at UAB were limited to the heart, lungs, liver, and kidneys. The gastrointestinal tissue was added later at the request of gastrointestinal pathologists. Tissues were fixed, embedded in paraffin, and 5 µm cuts were stained with hematoxylin and eosin (H&E) for microscopic evaluation. The de-identified H&E slides were scanned using an Aperio CS digital slide scanner (Leica Biosystems Division of Leica Microsystems Inc., Buffalo Grove, IL) and were reviewed for quality and image clarity using Aperio ImageScope [v.12.4.0.5043] (Leica Biosystems Division of Leica Microsystems Inc., Buffalo Grove, IL). These large SVS (SVS file is a digital slide image file created by an Aperio ScanScope slide scanner. It contains a series of TIFF images, and its ImageDescription tag starts with

Aperio. SVS files are used for archiving and analyzing Aperio microscope images) format whole slide image files were converted to Deep Zoom Image (DZI) format and these DZI folders were uploaded to the PEIR website. The high-resolution DZI images can be viewed on the PEIR website using any web browser. This online virtual microscopy system uses technology similar to Google Earth with pan and zoom features. The original whole slide imaging SVS files were also archived on a Western Digital My Passport USB 2 terabyte hard drive (Western Digital, San Jose, CA). The files were saved as Aperio ScanScope Virtual Slide format in de-identified alphabetic sequence as Case-A.svs. The Aperio ImageScope viewer allowed magnifications of the tissue from 1× to 40× using digital zoom, the ability to take digital photomicrographs, and measuring and annotation capabilities. At the time of submission of this manuscript, 24 COVID-19 autopsy cases, 1 influenza autopsy case, and 1 tuberculosis autopsy case have been scanned consisting of a total of 551 slides. At the time of submission of this manuscript, 551 DZI files were uploaded to the PEIR website at: <https://peir-vm.path.uab.edu/specialcases.php>. The files on the USB hard drive ranged in size from 1.0 gigabytes up to 2.5 gigabytes. Because of the large file size, the SVS files on the USB hard drive were uploaded upon request to the UAB file share box (<https://www.uab.edu/it/home/tech-solutions/file-storage/box>) for investigators to download for their own research and education use after confirmation of their institutional review board (IRB) approval. In addition to viewing the slides on the PEIR website and downloading the SVS files, investigators used the virtual slides, in consultation with a pathologist, to select formalin-fixed paraffin embedded blocks to recut, thus linking the virtual biorepository with specific tissue blocks in physical COVID-19 biorepository.

The repurposing of the PEIR website and creation of an online COVID-19 autopsy biorepository was promulgated to investigators and educators through the UAB Center for Clinical and Translational Science Enterprise COVID-19 Research Initiative website.^[9] The UAB PEIR website including the COVID-19 autopsy virtual biorepository is freely available to the scientific and academic community for research, education, and training purposes. This study was approved by the UAB, Birmingham, AL, USA IRB (UAB NHSR Determination 300006364).

RESULTS

The creation of the UAB COVID-19 virtual biorepository has enabled research and education pursuits locally at UAB and internationally. The PEIR website provides a scrollable list of the autopsy slides [Figure 1]. Clicking on an autopsy slide opens a virtual microscope to view

Table 1: University of Alabama Birmingham COVID-19 histology block key

Slide 1	Trachea
Slide 2	Right and left mainstem bronchi
Slide 3	Subcarinal/ hilar lymph node
Slide 4	Lung, right upper lobe, central
Slide 5	Lung, right upper lobe, peripheral
Slide 6	Lung, right middle lobe, central
Slide 7	Lung, right middle lobe, peripheral
Slide 8	Lung, right lower lobe, central
Slide 9	Lung, right lower lobe, peripheral
Slide 10	Lung, left upper lobe, central
Slide 11	Lung, left upper lobe, peripheral
Slide 12	Lung, left lower lobe, central
Slide 13	Lung, left lower lobe, peripheral
Slide 14	Heart, anterior left ventricle and left anterior descending coronary artery
Slide 15	Heart, lateral left ventricle and left circumflex
Slide 16	Heart, posterior left ventricle and right coronary artery
Slide 17	Heart, interventricular septum and aorta
Slide 18	Right ventricle and pulmonary artery
Slide 19	Liver
Slide 20	Kidney
Slide 21	Stomach
Slide 22	Duodenum
Slide 23	Small intestine
Slide 24	Colon
Slide 25	Extra block if needed

the high-quality H&E stained image [Figure 2]. At the time of submission of this manuscript, four separate COVID-19 research teams were provided telepathology consultation via Zoom, and one investigator independently reviewed the digital slides on the PEIR website independently to select the best material for his study. The UAB COVID-19 virtual biorepository was used in several different ways to achieve this. Most commonly, the autopsy pathologist scheduled a Zoom conference with the interested investigators and discussed their aims of the research and which tissue would best meet their needs while reviewing the digital slides and their research plan during screen sharing. The number of physical formalin-fixed paraffin-embedded blocks that were recut per investigator are presented in [Table 2]. In addition to providing telepathology consultation to research teams, the digital slides were used to take photomicrographs for one published cardiology case report.^[4] Additionally, digital slides of the liver from five cases were shared via the UAB Box website for consultation with liver pathologists at UAB. Lastly, digital slides from COVID autopsies were reviewed on Aperio ImageScope via Zoom with a UAB collaborator at the African Health Research Institute (AHRI) in Durban, South Africa on five separate Zoom calls (6/4/2020, 6/15/2020, 6/24/2020, 7/17/2020, and 1/29/2021) in efforts to help educate the collaborators about the pathologic findings in COVID autopsies and

to foster ideas for an international COVID-19 research project. This approach has also been used to submit an R01-level grant application to the National Institute of Health for SARS-CoV-2 research and has resulted in one additional manuscript being published.^[10]

Out of five investigators who accessed the virtual biorepository for their research, 147 physical recut H&E stained or unstained slides were requested and distributed. Telepathology consultation was also enabled by uploading virtual slide files to the UAB file share website. In order for the investigators to view the SVS virtual slides locally, they needed to download the virtual slide viewer Aperio ImageScope [v.12.4.0.5043] to their own computer.

DISCUSSION

An increased interest in autopsy pathology due to the COVID-19 pandemic is documented in the literature.^[11] Basic science and translational researchers need access to COVID-19 biospecimens, including autopsy specimens. The creation of this COVID-19 virtual biorepository makes this resource available to the global community for research, educational, and training purposes. Many of the investigators or basic scientists are translational clinician-scientists who lacked training in histopathology evaluation. Several investigators indicated that the availability of an autopsy pathologist to guide them through material selection and region of

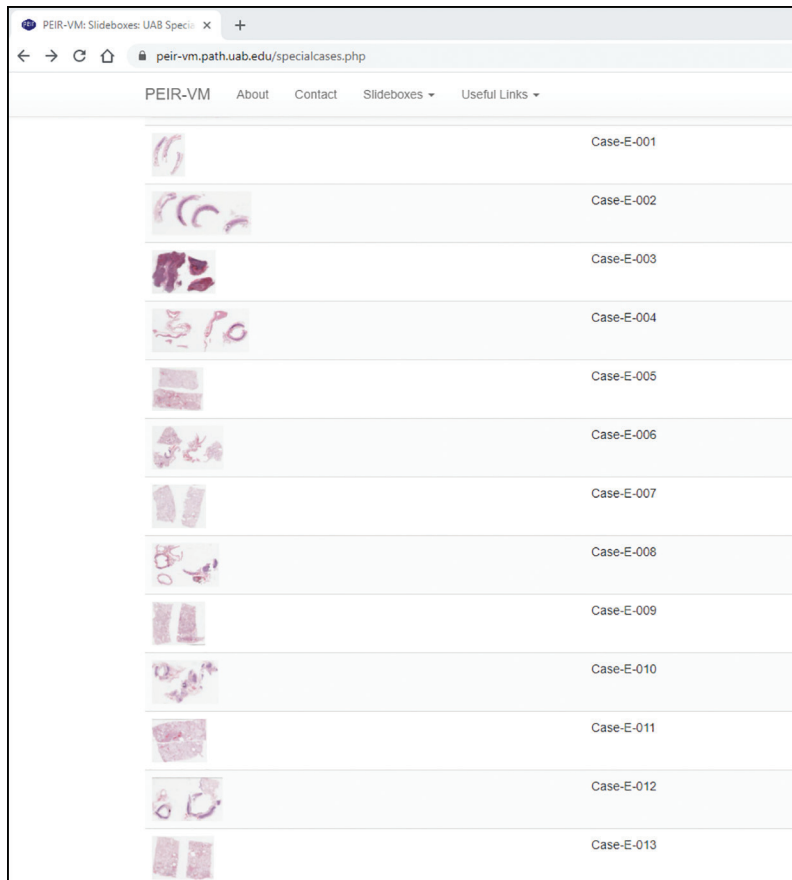


Figure 1: The University of Alabama Birmingham Pathology Educational Instructional Resource (PEIR) Coronavirus Disease 2019 (COVID-19) virtual biorepository scrollable list of slides available for online viewing. <https://peir-vm.path.uab.edu/specialcases.php>

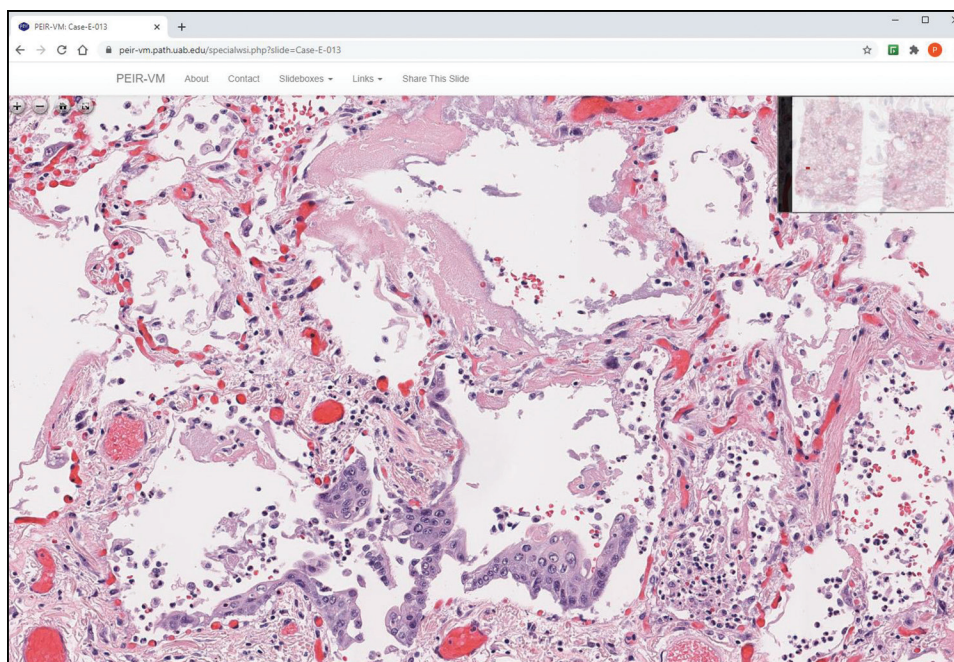


Figure 2: Low power (approximately 1×) (inset) and higher power (approximately 20×) images from University of Alabama Birmingham (UAB) Pathology Educational Instructional Resource (PEIR)-virtual microscopy of Coronavirus Disease 2019 (COVID-19) infected autopsy lung via the UAB PEIR website shows hyaline membranes, interstitial lymphocytic infiltration and squamous metaplasia of type II pneumocytes

Table 2: Number of cases and slides provided through use of the University of Alabama Birmingham Pathology Educational Instructional Resource COVID-19 online biorepository

Investigator	Number of cases	Number of blocks	Number of slides per block	Number of slides recut
A	8	9	3	27
B	2	2	7	14
C	1	2	8	16
D	4	6	5	30
E	10	10	6	60
			Total	147

interest selection was crucial to their investigations. The availability of the virtual biorepository alone or combined with consultation by a pathologist could be very important for resource-poor countries or other underserved areas. It is important to note that an adequate internet connection is necessary for smooth slide viewing at distant locations such as South Africa. All images hosted on an online platform are subject to the speed at which the end-user is connecting and downloading these images. The physical location, around the world, of both the server and the end-user, is less likely to be a deciding factor of the performance of viewing the images if both sides have an adequate connection to the internet. AHRI has very high bandwidth internet capabilities coming into Durban and regularly moves very large datasets around, nationally and internationally. It is for this reason that the South African collaborator (A.S.) reported clear slide viewing, smooth image scrolling, and magnification changes at the African Health Research Institute. The scanning and uploading of additional cases to the virtual biorepository are ongoing. As new COVID-19 positive autopsies are performed, the slides will be scanned and added to the biorepository thus expanding the available cases increasing the investigative value.

National and international autopsy registries are being created to enable COVID-19 research.^[12] We believe the successful creation of the UAB PEIR COVID-19 online biorepository is important to report because this project demonstrates linking the virtual resource with a physical biorepository of COVID-19 autopsy biospecimens. This report demonstrates the successful implementation of this system to produce collaborations resulting in the publication of new knowledge during a global pandemic. Resources similar to the UAB PEIR COVID-19 virtual biorepository could be developed at other universities to enable multiinstitutional collaborations.

The methods described in this article could be expanded to include autopsy cases other than COVID-19 and would be useful for enabling other types of autopsy research such as cardiovascular and oncology research.

This study is limited by not including COVID-19 autopsy neuropathology. Although the current website does not include brain slides, neuropathology slides from

COVID-19 autopsy brains should be included in the future by collaborating with the UAB Division of Neuropathology.

Another limitation may be the lack of annotation of the PEIR slides. Although the PEIR website does allow for annotation of slides, we chose to not annotate the slides to preserve patient anonymity and promote collaboration with the UAB pathologists when educators or researchers want to use the biorepository. With approved IRB documents the UAB pathologist would provide corresponding clinical phenotype data to investigators and educators on a case-by-case basis. De-identified slide annotations may be considered in the future.

CONCLUSION

The repurposing of the PEIR at the UAB and its Aperio CS digital slide scanner successfully enabled telepathology consulting for COVID-19 research investigations at UAB and enabled international collaboration. Adding more autopsy cases in the future will provide additional study material for research and education. The described methods can enable non-COVID-19 research in the future. Further development and promulgation of the PEIR COVID-19 webpage may be useful for expanding the number of users.

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Conflicts of interest

There are no conflicts of interest.

Ethics

The authors confirm they are in compliance with national and institutional ethical standards.

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