Newsbytes

COVID-19 digital pathology repository picking up steam

September 2021—When Stephen Hewitt, MD, PhD, went down the COVID-19 rabbit hole in early 2020, little did he know about the long-term value of a comprehensive COVID-19 digital pathology repository—and how such a project would come to fill his days and, occasionally, nights.

But fill his time it has. Since the early days of the pandemic, Dr. Hewitt has been working diligently on behalf of the National Institutes of Health to make the repository more than its original offering of a "flat file dump of cases with a little bit of metadata so you could find an individual patient or an individual organ."

To understand the future of the NIH's COVID-19 Digital Pathology Repository requires cognizance of its past. "We needed a better understanding of the pathophysiology of SARS-CoV-2 if we were to treat patients effectively," recalls Dr. Hewitt, head of the Experimental Pathology Laboratory, Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, and captain, U.S. Public Health Service. To that end, he and collaborators from the NIH, in partnership with Indica Labs and Octo, launched the COVID-DPR—a centralized, cloud-based whole slide image library of tissue from those with SARS-CoV-2.

The repository, which went live in April 2020, is hosted by the NIH and underpinned by Indica Labs' Halo Link platform, a Web-based collaborative slide-management and slide-sharing platform. The overarching goal for the COVID-DPR, says Dr. Hewitt, is to have it serve as a reference data set of COVID-19–related pathology for the greater biomedical community that, among other functions, helps inform immune response to SARS-CoV-2.

Dr. Hewitt

As of CAP TODAY press time, the COVID-DPR housed more than 2,300 whole slide images representing over 100 autopsies, as well as surgical specimens, cytology specimens, blood smears, and a comparator case of H1N1 influenza. The site also contains placental images because the placental pathology for pregnant women infected with SARS-CoV-2 is complex, Dr. Hewitt says. The autopsy images are arranged by organ and patient, with all patient information deidentified. But because the Halo platform is highly flexible, it easily could allow for other organizational schemas, Dr. Hewitt says, such as categorization by disease process "if we chose to break it down to patients with diffuse alveolar damage, thromboemboli, or pulmonary edema, with reference to lungs."

Though many of the autopsy cases in the repository were donated by Dr. Hewitt's pathologist colleagues at other institutions, the NIH has contributed 44 autopsies from its COVID-19 autopsy consortium, 15 of which had been uploaded by CAP TODAY press time. After uploading the NIH autopsies, which are comprehensive across organ systems, with multiple sections per site, Dr. Hewitt plans to add more autopsies from external collaborators. (Cases can be submitted via the COVID-DPR website, at covid19pathology.nih.gov.)

As they address a number of roadblocks—staffing and remote work issues chief among them, in addition to competing institutional goals—Dr. Hewitt and his colleagues are preparing to substantially expand and overhaul the repository. The project has obtained funding for the next four to five years, he says. "It doesn't sound earth-shattering, but it's important."

Among the efforts underway are curating and annotating the whole slide images already in the repository to add

metadata and simple histopathologic interpretations; uploading the remainder of the NIH consortium's autopsies, along with associated immunohistochemical images, RNA in situ results, and EHR-derived data; and expanding the repository to support other NIH-funded COVID-19 studies.

Dr. Hewitt and his collaborators also hope to expand the site by adding more comparators, such as a nonhuman primate model of SARS-CoV-2 infection. Such comparators would allow investigators to contrast the pathophysiology of the virus among different organisms, thereby obtaining a better understanding of host response, Dr. Hewitt says. "We used to believe the pathophysiology and the spread of virus was more related to virus type than anything else." But the study of Ebola and Zika precipitated a shift in thought, he says, leading pathologists who study virology to focus more on host response, such as how host response is inadequate or modified between the viral processes, than the virus itself. In addition, Dr. Hewitt and his team are working to obtain cases from the outbreak of SARS in the early 21st century, as well as historical images of the 1918 H1N1 influenza and examples of other strains of influenza, which too cause pulmonary damage.

Also in the works is a plan to host whole slide and associated images from SARS-CoV-2–related manuscripts. The manuscripts' PubMed unique identifiers, or PMID, will be linked to the COVID-DPR, Dr. Hewitt says, allowing users to read a study and at the same time peruse the related whole slide images. The repository will only host images from NIH manuscripts initially but eventually will also display images from external studies.

The COVID-DPR "is the first instance, of which we're aware, where authors will be able to host whole slide images on servers unrelated to the publishers, as well as have a direct link to PubMed," Dr. Hewitt says. In the past, he explains, efforts to host whole side images associated with manuscripts were undertaken by the journal publishers themselves. However, "they found this was a complicated process for which sustainability was problematic," he adds, noting that most of those attempts have fallen by the wayside. "It's still not in the mindset of investigators to post their images."

Perhaps because of its ambitious objectives, the repository project hasn't been without technical challenges—among them, incorporating into the platform the clinical metadata from the NIH autopsies. This has posed difficulties "both in presenting the data and using it analytically," Dr. Hewitt says. A potential solution to this problem involves building an interlinked search engine that would allow users to search for specific data and thereby access the related images. An alternative, he says, is to add new data fields and bring the clinical metadata directly into the site. How the data will be incorporated and the timeline are uncertain, he adds.

Integrating such data into the study of whole slide images is a challenge for the digital pathology space at large, Dr. Hewitt says, noting that data sets often are discontinuous and that the systems used to display whole slide images aren't designed to handle quantitative data queries. Though image analysis and analytics are routinely performed on whole slide images, "only when we include the metadata in those analytics do we accomplish substantial gains," he says. "I think the COVID-DPR will evolve so that in the future, researchers will be able to perform analyses on these images, but right now it's very much 'come and view.'" Furthermore, the version of Halo used for the repository doesn't include the full analytics package offered by Indica Labs, though it may be added later. "That doesn't mean we're not taking the images—especially the NIH images—and running them through advanced analytics, but that's happening on our internal platforms," Dr. Hewitt says.

Using artificial intelligence to analyze images in the COVID-DPR too has been challenging, though the repository was conceived with an eye toward AI applications. Early in the pandemic, Dr. Hewitt says, researchers assumed that SARS-CoV-2 infection gave "a consistent and static histopathology. We didn't know what it looked like, so everybody assumed it was unique and somewhat fixed." But the autopsies that emerged in the initial weeks of the outbreak demonstrated an inconsistent histopathology, particularly pertaining to the lungs. For example, time of infection to time of death was a significant vector with regard to lung injury. Furthermore, several patterns of lung injury were observed, including thromboemboli, pulmonary edema, and progressive acute respiratory distress syndrome with diffuse alveolar damage.

Preanalytic variables involving the patient's course of infection, as well as specimen handling, also complicated the

potential for AI analysis. For instance, the CDC requires 72 hours of fixation for autopsy tissue specimens, Dr. Hewitt says, “which is a major preanalytic variable impacting quality.”

“Now, if you have a small or large fixed set of organs handled with a very tight protocol, such as a 24-hour postmortem protocol,” he explains, “AI may be more interesting to do. We’re pursuing that now, looking at hearts, kidneys, livers, and eventually lungs. One of the questions we’re more interested in today—compared to what people thought they were going to focus on at the beginning of the pandemic—is not, ‘Is this SARS or not?’ but ‘What is the contribution of comorbidities to the pathology that we see?’ We’re saying, ‘Is it COVID related, or is it hypertension, diabetes, or obesity?’ So we’re using AI to try to understand the intersection of the comorbidities with SARS-CoV-2.”

As Dr. Hewitt tackles these and other COVID-related issues, he acknowledges the irony that the subject of his investigation is the very thing that slows his efforts to enhance the repository. “If I had more hands in the laboratory,” he says, “I could better utilize my virtual collaborators.”
—*Charna Albert*

PathAI purchases Poplar Healthcare Management

The digital pathology and artificial intelligence firm PathAI has acquired Poplar Healthcare Management, the management service organization for the anatomic pathology laboratory services provider Poplar Healthcare PLLC.

Under terms of the transaction, Poplar’s facilities and approximately 350 employees now compose PathAI’s diagnostics division. Poplar Healthcare supports a nationwide client base of gastroenterologists, dermatologists, oncologists, urologists, and gynecologists, and their patients.

PathAI and Poplar will focus on further digitizing the Poplar laboratory workflow and leveraging PathAI’s image-analysis and algorithm-development capabilities to develop new clinical applications, according to a joint press release from the companies.

PathAI, 617-500-8457

LigoLab offers TestDirectly for at-home specimen collection

LigoLab Information Systems’ TestDirectly patient-engagement platform supports at-home specimen self-collection for diagnostic testing and preventative screening.

Patients can place orders online for test kits from pathology laboratories throughout the United States that are featured in TestDirectly’s platform. Via interfaces to national shipping services, TestDirectly provides laboratories with backend support for shipping test kits to patients and tracks the delivery of kits to patients and the resulting specimens to laboratories. The platform also tracks laboratory processing of specimens.

The TestDirectly portal uses email and SMS notifications for automated delivery of test results to patients. LigoLab most recently added functionality that allows patients to participate in videoconferencing and schedule consultations via the platform.

TestDirectly is an agnostic, cloud-based solution that can be integrated with laboratory information systems and revenue cycle management solutions to simplify the ordering, collection, and testing of specimen samples and provide patient reporting.

LigoLab Information Systems, 818-395-4659

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