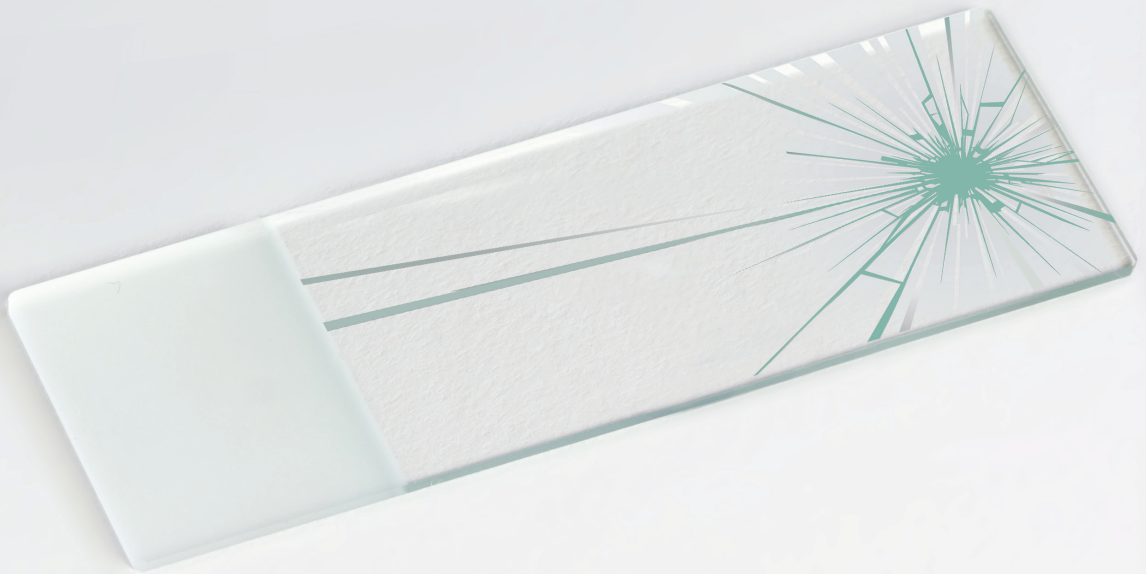


# BREAKING THE GLASS?

*Digital pathology making waves in dermatology*



BY **RUTH CAROL**, CONTRIBUTING WRITER

Digital pathology is the wave of the future, but that wave won't be crashing on shore any time soon. Although the technology is increasingly being used in teaching and some consulting scenarios, it must overcome some significant obstacles before making the leap to assisting in the diagnosis of patients in the office. When it does, how big of a splash digital pathology will make to referral relationships and payment models remains to be seen. It could be a ripple or a tidal wave.

In the meantime, those familiar with digital pathology praise the technology that involves using standard tissue processing with hematoxylin and eosin (H&E) stain on a glass slide, which is then scanned to produce a digital image. This digital slide can be read on a computer and scanned on low and high power.

"It's almost better than looking at the slide in a microscope, especially if it's scanned at high resolution," noted Clay Cockerell, MD, clinical professor in the Department of Dermatology and Pathology at the University of Texas Southwestern Medical Center in Dallas. >>



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There is a lot of data to show that the imaging on a digital slide read is the equivalent to that of a microscope, according to Thomas Olsen, MD, lab director of the Dermatopathology Laboratory of Central States (DLCS) in Dayton, Ohio, whose laboratory has a considerable investment in digital technology. Studies have been published by the Cleveland Clinic and University of Pittsburgh, among others, he said. Dr. Olsen reports that he can make a digital diagnosis approximately 95 percent of the time. For the remaining 5 percent, he has to review the glass slide under a microscope to identify with more certainty different nuances of the case.

On the downside, loading the digital slides takes longer than placing a glass slide under a microscope. “The technology is getting better and faster,” said Dirk Elston, MD, chair of the dermatology and dermatologic surgery department at the Medical University of South Carolina. “But it’s still nowhere near as fast and cheap as using a glass slide,” he said. “It’s not that I don’t think digital pathology is wonderful. It’s just not going to replace H&E slides, at least, any time soon.”

## Interactive medium for education

What it is replacing is the traditional teaching methods in residency programs. “The days of 12 to 15 resident physicians crowded around a multi-headed microscope may soon be gone,” noted Robert T. Brodell, MD, professor and chair of the department of dermatology and professor of pathology (dermatopathology) at the University of Mississippi Medical Center. Nowadays, the professor can “tour” the digital slide with students watching television monitors, while hundreds or thousands of individuals around the world could listen and learn simultaneously or at a later time and date.

At the University of Connecticut School of Medicine, digital pathology is presently only being used for teaching and medical student testing, said Jane Grant-Kels, MD, founding chair emeritus of the department of dermatology; professor of dermatology, pediatrics, and pathology; and director of the Cutaneous Oncology Center and Melanoma Program at UConn Health. Currently all of the teaching slides are being digitized. “I was recently giving a lecture to medical students who joked that they don’t even

know what a microscope looks like anymore,” said Dr. Grant-Kels, who is also chair of the AAD’s Dermatopathology Rapid Response Committee.

Dr. Elston started using digital slides for teaching four years ago. He typically trains numerous groups of residents during a single conference. “They all want the same box of unknown slides to look at a week before the conference,” he said. “They can’t have the same piece of glass, but they all can have the same digital slide.” If the residents can’t attend the real-time conference, they can go online and view a video of it, Dr. Cockerell said. “That way, we can reach out to residency programs that don’t have a dermatopathologist.”

Another advantage to using digital slides is that they don’t require recuts. Sometimes it’s hard to get as many slices out of a tissue specimen necessary to make optimal glass slides, Dr. Cockerell added. With digital slides, only one section of a specimen is enough. “And you don’t have to worry about making recuts that may not show the same diagnostic features,” he added.

The use of digital slides reduces both the wear and tear on glass slides as well as the physical obstacles of transporting them, noted Murad Alam, MD, vice chair and professor of dermatology at Northwestern University in Chicago. Because the speed of processing and memory has improved so dramatically in recent years, digital slides can be stored quickly and easily without taking up any physical space. “By uploading them at high resolution, they are preserved in perpetuity,” he said. With this technology, sharing interesting cases is no longer limited to the individuals in possession of the glass slide, added Dr. Alam, who is also former chair of the AAD’s Dermatopathology Rapid Response Committee.

## Uses beyond teaching

Digital pathology slides have made inroads in dermatology beyond teaching. As an example, the American Board of Dermatology (ABD) began using digital slides for a small percentage of the pathology questions on its board certification examination several years ago, said ABD Executive Director Thomas Horn, MD. Each year, the ABD completes an analysis to determine how the candidates perform using digital slides versus

glass slides. There's no statistical difference, he said, but many candidates are anxious about using the technology in an exam setting. That and a slight delay that sometimes occurs when uploading the digital slides are the only downsides of the technology. The delay will not persist in the next software iteration.

"The advantage to virtual pathology is significant," he added. Transitioning to virtual pathology would eliminate the need for candidates to travel to the testing center in Tampa, Florida, where 60 microscopes are set up. In addition, the ABD is limited by the number of cases from which a large number of glass slides can be made; virtual pathology requires only one case. "It would really expand our ability to test a wider range of dermatopathology," said Dr. Horn, a dermatologist and dermatopathologist who described the quality of digital imaging as "stellar."

Dr. Horn believes that the software anxiety will decrease as more computer-savvy individuals sit for the exam. He notes that digital pathology is very popular in the Harvard Combined Dermatology Residency Training Program, for which he is on faculty, and at Massachusetts General Hospital, where he is vice chair for academic affairs. "We're living in an increasingly digital world and to think we're not headed there eventually is naïve," Dr. Horn said. He expects that within three to five years all of the slides being used for the ABD exam will be digitized. In fact, the ABD is in the process of digitizing all of its slides now.

Similarly, the American Society of Dermatopathology (ASDP) is digitizing its entire teaching library, noted Dr. Elston, who is also president of the ASDP. Once the ASDP completes the task, which is expected to take three to five years, the library will be available online.

Additionally, digital pathology has created opportunities in global pathology, enabling dermatopathologists in the U.S. to read cases for practitioners in developing countries who lack access to dermatopathologists. For one focus of the Africa Teledermatology Project, glass slides are processed at a pathology lab in Botswana. Then they are read by dermatopathologists in the U.S. using a live telepathology microscope. Currently, the entire slide can't be digitized and transmitted because the file is too large, explained Carrie Kovarik, MD, associate professor in the department of dermatology at the University



## Current use of digital pathology requires validation studies

Currently, dermatologists can use digital pathology for primary diagnosis, despite its lack of FDA approval, as long as they perform validation studies under the "laboratory developed test umbrella" following the guidelines published by the College of American Pathologists in 2014, noted Thomas Olsen, MD.

Through the Clinical Laboratories Improvement Act (CLIA), the Centers for Medicare and Medicaid Services oversee laboratory practices. When a technology that is not FDA approved is used to perform testing, CLIA requires the lab to perform a rigorous validation of the laboratory-developed test before putting it into use. The dermatologist would take 60 of his/her cases and give an interpretation under the microscope. There would then be at least a two-week washout period before the same cases would be interpreted on the tablet device or computer screen and the results compared.

Dr. Olsen hopes to be using the technology for primary diagnosis at DLCS in 2016. He has performed a validation study that demonstrated 95 percent agreement between glass slide and digital read out among four dermatopathologists. A 47 percent efficiency gain also was documented. Dr. Olsen presented the results at the ASDP 2014 annual meeting.



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of Pennsylvania, and one of the volunteer dermatologists who reads the slides. While the lack of bandwidth and Internet server speed still present some obstacles, such as requiring the files to be sent overnight, the technology continues to evolve at a rapid pace, she said. In addition to offering store-and-forward teledermatology consultation services for clinical cases, the dermatologists stateside provide discussion pertaining to histologic findings in the biopsies submitted, diagnosis and management of patients with skin disease, links to educational resources, and access to a dermatologic curriculum created specifically for African sites.

## Making the transition to clinical care

While many see digital pathology's role in teaching and consulting continuing to grow, they are uncertain about its role in clinical care. "It's too early to say exactly how it will be rolled out as a routine patient care service," Dr. Alam said. When it does get incorporated into clinical practice, the benefits of the technology would likely carry over.

Digital pathology offers tremendous opportunities to enhance efficiencies, reduce errors, and facilitate communication between the pathologist and clinician, Dr. Olsen said. At DLCS, he and his colleagues have developed a proprietary workflow software program that enables the physician to read the slides digitally on a tablet and if uncertain of the diagnosis, to request that the same image be read by a dermatopathologist, and the results integrated to the dermatologist's electronic medical record. Dr. Olsen believes that this interfacing and software linkage will more closely tie the dermatology practice and referring lab, resulting in better patient care. He maintains that this technology will reduce the turnaround time for reading slides by at least 24 to 48 hours.

Dr. Brodell suggests that the turnaround time could be even quicker. "Clinical-pathological correlation could be rendered by the referring dermatologist and dermatopathologist looking at the same histopathologic and clinical images together in real time," he said. The same holds true when a dermatopathologist wants a consultation with a trusted colleague.

Dr. Alam agrees that the technology will make obtaining second opinions more efficient, particularly for dermatologists practicing in rural environments who lack access to

dermatopathologists. If the dermatologist reads his or her own slides, then timeliness is a moot point. "Our lab down the hall is already very timely," said Dr. Alam, who acknowledges that he practices in a large, metropolitan city.

In addition, attending an out-of-town meeting will no longer prevent providers from reading slides without significant delay as long as they have access to a computer or tablet, Dr. Cockerell said. Locating slides will no longer require searching the lab, he added.

## Referral relationships on the line

But the technology also has the potential to change referral relationships. While Drs. Cockerell and Elston don't see digital pathology as a driving factor in changing referral relationships, especially longstanding ones, others are more concerned about that possibility.

In a worst-case scenario, large commercial labs, which are the only ones that could afford the approximately \$250,000 price tag of a high-resolution digital slide scanner, could undercut the small and academic labs when negotiating with insurance companies to gain the business, Dr. Grant-Kels said. The large labs will make up for the lower payment on the volume. "If the payment model changes so that insurers force dermatologists to send slides to the cheaper lab, a lot of these small boutique labs that provide outstanding service because of their alignment, proximity, and knowledge of individual practitioners might not be able to compete," Dr. Alam added. Although he pointed out that this is already happening with glass slides, it could be exacerbated with digital slides because of how quickly and easily they can be sent.

The insurance company's pathologist of choice could be a dermatopathologist on another continent who outbid dermatopathologists across America, even those operating national labs, Dr. Brodell cautioned. "That pathologist would most likely not be able to provide a scientific article supporting an opinion, discuss cases at Grand Rounds, or provide a verbal consultation like the dermatopathologist down the street." The verbiage used to describe subtle features overseas might not be the same as that used by a community-based dermatopathologist, he added.

"I don't want the next available dermatopathologist in another state or country

reading my slides just because he or she happens to be online at that moment,” Dr. Alam said. “Payers don’t always understand that a dermatopathologist’s interpretation is not the same as spinning down a complete blood count. The process of successive approximation applies; the more slides you read, the better you get at providing an expert opinion.”

As the founder and former director of the dermatopathology lab at UConn, Dr. Grant-Kels is concerned that the loss of academic labs will negatively impact the training for dermatology residents. “You can’t have a good dermatology program without a robust dermatopathology lab,” she said.

“The AAD and others will have to make sure that improving technology and patient access, and increasing efficiency, are not used as a pretext to run small labs out of business or result in fewer dermatologists doing dermatopathology and more general pathologists doing dermatopathology,” Dr. Alam said. “It’s not a matter of protecting our turf; we have a special expertise in the skin and our clinical-pathological correlation allows us to provide really good care to our patients.” There should be a mechanism in place during the transition phase to protect the smaller labs, he said. Longer term, every lab can adopt the same technology.

Dr. Brodell agrees. “It is critical that the AAD develop clearly stated ethical constructs that reflect the highest ideals of our profession as we harness this technology,” he said. Patients, whose interest must always come first, should be permitted to choose their physician and physicians should be permitted to refer to the dermatopathologist and other specialists of their choice. Additionally, state medical boards should carefully monitor the corporate practice of medicine with an eye toward guarding the safety of patients, Dr. Brodell said. Whether or not dermatopathologists becoming employees of large national or multi-national corporations would improve the quality or cost of dermatopathology services is anyone’s guess. “The consolidation of pharmaceutical companies has certainly not led to reductions in the cost of drugs. Quite the opposite is true,” he noted.

### Other hurdles to overcome

How this technology would change payment models is even less clear. The professional

component would remain the same. However, costs could increase with the investment in software/hardware as well as computer processing and memory. Early adopters would most likely have to absorb those additional expenses. A new CPT code could be created or a re-evaluation of the practice expense component could occur in the future, Dr. Olsen suggested. Dr. Alam noted that the dermatologist would no longer have to pay to mail slides to the dermatopathologist and over time, memory and transmission costs would likely come down. So while start-up costs would be much higher, over time the practice expense may not be.

Aside from the cost, the Food and Drug Administration (FDA) has not yet approved digital pathology scanners for patient use or approved whole-slide imaging for primary diagnosis. “The FDA will approve them, it’s just a matter of time,” said Dr. Alam, noting that the agency has approved similar devices for radiology. “For the FDA, the issue is what sort of parameters the agency will set for the technology and if the technology is up to the task for meeting those parameters,” he said.

Currently, the scanner is a Class III medical device for primary diagnostic uses. However, many radiological imaging devices are either Class I or II, Dr. Olsen said. According to a spokesperson for the Digital Pathology Association, the association and the FDA are “working collaboratively to explore the feasibility of down-regulating the device to Class II, while still keeping patient safety paramount.”

The FDA published draft industry guidelines in February 2015. Additionally, the agency is conducting studies to determine how well pathologists perform when using a digital whole slide imaging system, according to Deborah Kotz, an FDA spokesperson, who would not comment on a timeframe for approving the device.

In the meantime, the technology will continue to improve. “There’s no question it will get better. There’s no question it will get incorporated,” Dr. Elston said. “It’s just a question of how. But I don’t think glass slides are going away any time soon.”

Dr. Olsen concurs. “I’d like digital pathology to be revolutionary, but it’s evolutionary,” he said. “It’s going to happen, but it’s not going to happen quickly.” *dw*