Digital pathology matchmaking: people, pixels

Karen Titus

February 2019—Digital pathology is many things. One thing it's not is a one-night stand.

As laboratories contemplate using digital pathology for primary diagnosis in the wake of the FDA's approval nearly two years ago, it's become abundantly clear that while digital pathology might seem to promise easy pleasure, it's actually as complicated as keeping multiple spouses happy. Think Jacob, Rachel, and Leah. Think "Big Love."

Whatever your reference, you better (to quote the Queen of Soul) *think*.

Dr. Anil Parwani and Dr. Wendy Frankel at OSU Wexner Medical Center, where pathologists are using digital pathology at their own pace. "Technology should not be used as a reason to change people," Dr. Parwani says. "People should change themselves and use the technology they're most comfortable with." (Photo courtesy of Jodi Miller)

Think about the questions and worries of top executives. Think about pathologists and their workflow. Think about the influence of IT. And then keep thinking. As several experts recently told CAP TODAY, buy-in doesn't happen once, with one group of people. It is, instead, a perpetual wooing.

David McClintock, MD, associate chief medical information officer, Michigan Medicine, Ann Arbor, recalls being in meetings with pathologists who, "when push came to shove, went from, 'Yeah, we support this,' to 'Why are we doing this?' to 'We support it'—all at the same meeting. There's a real internal struggle with them," says Dr. McClintock, who is also director of digital pathology, associate director of pathology informatics, and associate professor of pathology, Department of Pathology. That's not to say Michigan isn't interested in digital pathology, including for primary diagnosis. "But," he cautions, "you shouldn't anticipate that everybody understands it" simply because they've been hearing about it.

Even when people come on board with little fuss, they may still want an escape hatch. The Ohio State University

Wexner Medical Center has taken a deep plunge into digital pathology—Anil Parwani, MD, PhD, MBA, vice chair of anatomic pathology and director of both digital pathology and pathology informatics, estimates that about 90 percent of the institution's pathologists use digital slides for some type of application, including primary diagnosis, research, education, or consults. Yet even now he hears their fears: of new technology; whether it will help them do their work; poor image quality; being slowed down; unease with looking at a monitor. It's as if they dread entering a bad, 1950s marriage, telling Dr. Parwani, "I'm going to be trapped forever."

Though they are divided by a state line (and a storied football rivalry), Drs. Parwani and McClintock have much in common as they shepherd their colleagues and institutions along the digital pathway. Both presented at the Association for Pathology Informatics workshop at OSU last December, and in follow-up interviews with CAP TODAY they spoke further on what makes the field both unnerving and exciting.

When Dr. Parwani, who is also professor of pathology and biomedical informatics, arrived at OSU in July 2015, the institution's leaders had already given their first, crucial blessing to build an expansive digital pathology program. Primary diagnosis was on the horizon, and the need for improved technology was obvious. Wendy Frankel, MD, the Kurtz chair and distinguished professor, and chair, Department of Pathology, laid the groundwork. One of her objectives (and likely a selling point) was in fact to hire someone with the expertise and knowledge to put the grand scheme into practice.

Enter Dr. Parwani.

Dr. Parwani's first step was to map out the expedition, so to speak. What was OSU doing digitally at the time, and what did it want to be doing in 2016, 2017, 2020, 2025? That led to a series of questions: What did they hope to accomplish by using digital? What clinical applications did they want to use? Did they want to pursue primary diagnosis? Or should they focus on other areas, such as consultations, image analysis, and/or artificial intelligence? What about remote frozen sections?

Once they put primary diagnosis in their sights, they had to look at the prerequisites. One was barcoding and tracking of glass slides, which OSU lacked. Dr. Parwani and his team spent some nine months setting this up.

At the same time, they planned simpler projects that would be steps along the primary diagnosis path. That included remote frozen section coverage. OSU has several off-site hospitals; in addition, frozens are done in the main on-site OR, but with pathologists working out of an office some 10 minutes away, "It's disruptive to their day to leave everything, go and do a specialty frozen, and go back to their office," Dr. Parwani says.

Once barcoding was in place, they purchased a small scanner to facilitate digital remote frozens. The results have been striking—"It took off," Dr. Parwani says—with pathologists making fewer specimen identification errors. It also sharply reduced the need for travel. They then purchased another scanner for another hospital, where they started offering FNA services remotely.

These smaller steps set the stage for large-scale scanning protocols. Scanners would be crucial, of course, and Dr. Parwani and colleagues went through an RFP process to figure out the best choice for primary diagnosis. They also selected a workflow management system. "We actually looked at how much it would cost if we built some of the software ourselves," before deciding to use multiple vendors. "They have different applications," Dr. Parwani explains. "We also realized that not all vendors can provide hardware and software for everything. So we did a best-of-breed approach."

As things continued to unfold, he continues, "We spent a lot of time validating small scanners, training the technicians, training the pathologists. We expand the protocols when we buy a scanner, and we follow the CAP guidelines for validation."

Again, the small steps soon led to bigger ones. Because the only whole slide imaging system currently approved for primary diagnosis is a closed one (Philips IntelliSite Pathology Solution), that made it harder to integrate with the other pieces. "Throughout the whole process of implementing digital pathology, we worked closely with many,

many vendors on these issues [of] compatibility and interoperability," says Dr. Parwani.

Perhaps the biggest step of all was focusing on performance for pathologists. "You want the ability to review images in their office to be a very good experience," Dr. Parwani says. "It should not be an experience where the images are pixilated or out of focus—that would have killed things."

It turns out Dr. Parwani had smoothed the way by picking up small but crucial endorsements early on. Thanks to the success of those first, incremental steps, "We had some buy-in from a few pathologists who were willing to try primary diagnosis," which OSU went live with in March 2018.

As it embraced digital, OSU elevated the meaning of the word "multitasking." During the run-up to primary diagnosis, they were also scanning and archiving older slides—seven to eight years worth of all cancer cases. The goal was to barcode them, link them to the LIS, and make them available for clinical work, education, and research.

Dr. Parwani's excitement is palpable. "For the first time, we were able to see the value of not having to pull glass slides anymore."

The archive now contains 1 million digital slides. "Suddenly, the game has changed for us. We are connected to the information that's needed." Pathologists no longer need to wait for someone to pull slides from an archive, nor do they need to deal with slides that are, like Netflix DVDs, dusty, old, and possibly broken. This is particularly helpful for OSU's extensive clinical trial work. Transactions that once took hours if not days now occur within minutes, says Dr. Parwani. "We simply send an email with a link to the slide." He says that earlier in the day, in fact, he spent a mere five minutes accessing three cases from 2014, for patients who were now undergoing new treatments and molecular testing.

Dr. Parwani concedes he had mixed feelings when they began tackling the archive. "We thought this would happen, but I wasn't optimistic at the time that we would be able to scan so many slides and be able to have enough cases in the archive to implement this. I wasn't optimistic about performance at this scale." This was the rare public works project that went better than planned. "If I knew two years ago that we'd have a million cases scanned, and that the performance would be so good . . . ," he marvels. "But I didn't want to oversell it."

Before this, pathology was huddled in its own silo. Now, he says, "We are a clinical system." By that measure, it has also "become a system that cannot go down." They store every image in duplicate, at two different sites. Another backup can be created, if needed, within 30 minutes.
This big leap has made pathology the largest user of digital storage in the medical system. "We're not talking about terabytes anymore; we're talking about petabytes." In a sense, pathology is a campus giant, not unlike the Buckeyes football team. "Yes, yes we are," Dr. Parwani says with a laugh. "People know who we are now."

At Michigan, Dr. McClintock, who is API's immediate past president, is likewise working to raise the profile of digital pathology. For years the institution has used digital pathology in education. And its Kidney Precision Medicine Project, an NIH-funded endeavor, includes developing tools for digital analysis and slide viewers for digital pathology. "But this is on the research side," says Dr. McClintock.

If OSU has pursued a big bang approach to digital pathology, Michigan might be embarking on a Socratic stroll. As he and his colleagues consider clinical applications, including primary diagnosis, Dr. McClintock finds himself asking an increasingly complex series of questions to figure out next steps.
The lengthy courtship has been complicated by a reinvention of Michigan's Department of Pathology, which included moving all AP laboratories to an off-site facility. (See "For one laboratory, a workflow transformation," CAP TODAY, June 2018.) In the process, glass slide handling was made much more efficient, Dr. McClintock says. One example: While it used to take up to two hours to have slides delivered, it now happens in 15 minutes.

Michigan's experience has shown an alternative to taking aim at glass houses. Why not pull a Philip Johnson and add *more* glass? Michigan's new setup includes multiple sign-out rooms whose construction allows for easy

collaboration, Dr. McClintock says. "There are glass walls in between these sign-out areas," which makes it easy to see nearby colleagues and request help. Consider it a triumph of person over pixel.

At Michigan, making it easier to use glass slides has made Dr. McClintock's job harder. "I have some work to do to figure out, what are those true-use cases" that justify a move to digital pathology? Moreover, the university is looking to build a new clinical tower, which means (among other things) belt-tightening overall. "You have to show how you can save money at the same time you're going digital, which is going to cost money and typically doesn't have an obvious return on investment."

'You can skip the FDA process if you want. But then you're putting risk on your institution.'
David McClintock, MD

Dr. McClintock, naturally, has kept abreast of what his counterparts are doing in Columbus. "They have a good plan—it made sense for OSU to do it in the way they're doing it." But the outcome has many sitting on the edge of their seats. "We're all waiting with bated breath to see how it works out for them. If it works: *What did you do and how can we do it?*" Dr. McClintock says with a laugh, before adding, "If it doesn't work: *Oh, wow, good thing we waited, because, God, look at what you did.*"

If you're a college football fan, it would be easy to put a competitive spin on matters—two great powerhouses going head to head, guided by different game plans. What will bring the goal closer: three yards and a cloud of dust, or a high-flying aerial game? Each has risks. "That's not to say Anil's doing anything wrong," Dr. McClintock says, thus scuttling any comparisons between Woody Hayes and Bo Schembechler. "But you don't know how it's going to play out."

The point is not to dismiss digital, nor to champion one scheme over another. Rather, Dr. McClintock's experience is a reminder that when it comes to adding digital pathology, each institution has to decide for itself what it needs.

While the growth in storage consumption is seen as a point of pride at OSU, Dr. McClintock thinks about storage and sees only questions. How long will digital slides need to be stored? The current thinking is 10 years, he says, unless the glass slide is retained. "But until you get that first court case" involving a discrepancy between glass and digital, and a crucial piece of information isn't available, that unknown is worrisome. "What's going to happen?" Dr. McClintock asks.

Dr. McClintock keeps up a steady stream of questions as he considers the wider field of digital pathology.

Even before asking if digital should replace glass, he says, it's important to make sure everyone understands what digital pathology is. Though it's commonly defined as virtual microscopy or WSI, he says it makes sense to think more broadly. "We'd be remiss not to include all our gross images, any microscopic images you take from the microscope itself, electron microscopy images, fluorescence imaging—anything that you do with imaging as part of

the pathology process, you should be capturing those and including them in your set."

Other questions to ponder:

- How will you obtain operational money for digital pathology?
- What will it mean for your FTE footprint?
- How will it affect human resources?
- How will it affect CLIA and HIPAA?

"Before, we didn't think about HIPAA much with glass," short of losing a set of slides, Dr. McClintock says. Digital pathology, on the other hand, presents cybersecurity issues.

- How do you integrate digital pathology with the LIS, specimen ID systems, the EHR?
- How much is this going to cost?

Dr. McClintock, comparing it to a home renovation, uses the adage, *double the cost, triple the time*. "We got this induction stove, and a washer—wait, you need a new water line? My *dryer* needs a water line? That kind of stuff."

- Do you want to validate your scanners as an LDT?

"You can skip the FDA process if you want," says Dr. McClintock. "But then you're putting risk on your institution. If something goes wrong, is your validation good enough to get you through a court case?"

- Where are the cost savings?

Asks Dr. McClintock: "Is saving pathologists time something you can prove? If you save two FTE pathologists by going digital, can you then cut two FTEs? Will you be allowed to do that? You need to think about numbers."

Like a bathing suit at the beach, certain numbers are gently creeping upward at OSU.

The several pathologists who began using digital pathology early on, for research endeavors, saw its value and have begun applying it elsewhere. When primary diagnosis became an option, "They were willing to look at it and see if it worked for them or not. I didn't have to convince them too much," Dr. Parwani says. The early adopters also served as almost casual ambassadors for the digital adoption. "When they do something, and show it to their colleagues, that improves visibility."

The next group of pathologists who agreed to try digital pathology came aboard when OSU began scanning all consult slides. Pathologists now have access to these images and can sign out digitally—about 15 are doing so. "Once that initial wave of consult slides were scanned, more people wanted to do it," Dr. Parwani says. OSU has also launched digital tumor boards, which has drawn in additional digital adherents.

In the past year, Dr. Parwani estimates, about 20 pathologists have begun using digital slides for some application; six to eight now also use it for primary diagnosis. (OSU has 36 anatomic pathologists among its 77 pathology faculty.)

"Everyone is taking their own journey," he says with the cheerful patience of a yoga instructor. "Some are far ahead; others are following. I don't have a single pathologist who says, 'I don't want to use digital slides.' Everyone is willing to try it for a different application."

Dr. Parwani sounds completely comfortable with this approach, noting that for its many successes, problems in the digital workflow remain, including scanner-related issues. "If everything was working 100 percent the way I think it

should," he says, "then I would go with the top-down approach. I would say, 'By July 2019 everybody has to sign out digitally.'" But since that's not the case, "I'm letting technology and adoption catch up together." At some point, he hopes, "These two tracks will merge."

Adds Dr. Parwani, "Technology should not be used as a reason to change people. People should change themselves and use the technology they're most comfortable with. That's when true adoption will occur."

Until then, he will continue asking his colleagues to renew their digital vows. Pathologists' early fears have been replaced by fresh ones. Now that the glass slides have been digitized, will they be expected to be online 24–7? Will they become slaves to the IT system, with cases constantly pushed into the queue? Will the demands of digital pathology kick teaching and research to the curb? Some even express skepticism at the amount of money being spent on digital pathology, Dr. Parwani says.

Dr. Parwani knows these fears because he actively solicits them. With the help of OSU epidemiologists, he did a baseline survey of pathologists' attitudes before primary diagnosis began, and he says he plans to repeat it annually. "Some of those things were valid," he says. "And some of those beliefs changed once they saw what we were doing."

They now send out digital controls, for instance. And in November he launched a digital case of the day, modeled after the CAP's case of the month. Every morning a new case is sent out to pathologists, residents, and medical students, with a link to the whole slide image. The answer to the previous day's case is also included. "We don't keep track of the answers or who's doing what," he says. "But we do know that more and more people are clicking on the link and going to the digital image," another step, he hopes, in encouraging adoption. It's already created a large educational archive, he says, and it's contributing to the organic growth of the program.

He's also added a monthly tech round, which focuses primarily on digital pathology or something related to it. "It helps us tremendously to have these sessions, because people are learning, asking questions, and seeing how it will help them in their world." One session dealt with creating high-resolution images from a digitally scanned slide for research, education, and publication. Another discussion focused on using an image analysis algorithm to look for very specific features in the digital image.

The potential uses keep piling up. With those million archived slides in their pocket, so to speak, Dr. Parwani and colleagues are trying to use the data sets and images to build algorithms for pathologists and researchers. "We want to help with very specific questions and applications," he says, including bladder cancer staging, prostate cancer diagnosis, and finding cancer in lymph nodes.

They're also partnering with OSU's computer science and bioinformatics departments to build a core group of imaging experts for research projects. "We have submitted grants already," he says. They've added a semester-long course for PhD students on pathology imaging and artificial intelligence. These "outside" groups bring their own buy-in, he says, and he's seen an uptick in interest in the last year.

Even though Dr. Parwani has plenty of numbers handy, he says he mostly relies on a less formal gauge of success. He contends it's not about the number of slides scanned, although given OSU's archive, that might be a little like Bill Gates saying money doesn't matter. But he persists, saying it's not about the number of cases signed out by primary diagnosis, either. Instead, he offers a hopeful, apt metaphor, likening real achievement to people at one political extreme or the other moving themselves to the middle. "The people whom I least expect to adopt, when they adopt, that to me is a milestone."

Dr. McClintock also takes the personal, well, professionally.

"We started by engaging the pathologists directly," he says. Though Michigan has a separate pathology informatics division, he says he wanted the initiative to be sparked by AP. "So I've engaged the director of AP; I've engaged the director of surg path." He's also spoken with several of the department's more active pathologists, and he encouraged them to attend the API meeting "so they could see what OSU is doing."

Dr. McClintock says an early goal is to understand what makes pathologists hesitant. "What I've learned is that they don't understand what it means to do digital pathology. So I'm going to do more education." A key message will be: *I'm not replacing your microscope. I'm not going to get rid of you.* Instead, he wants to convey the message: *We're trying to build tools that will help you. How do you want to help us do that?*

He also plans to work closely with vendors to identify products that will be mutually beneficial. And certainly there are business cases to be built.

"Are there ways for us to use whole slide imaging to generate more revenue or open up new business practices, besides just replacing what we're doing now with glass?" he asks. He and his colleagues would like to build a good case for ROI, "though once you start moving forward and it becomes standard technology that everyone agrees is needed, it becomes more of an institutional mandate than a pathology informatics ask."

Beyond the nitty-gritty lies an eternal challenge: It's human nature to abhor change. "Your old system is the worst in the world," Dr. McClintock says, until it's changed. "And then everybody talks about what a great system it was. Change is hard." With digital, it's not a matter of merely swapping glass for pixels. "It's changing the whole experience."

As OSU pathologists continue to take their tentative steps to adoption, so have the institution's leaders.

Those in the C-suite and IT were interested but cautious at first. They wanted to do it on a small scale, Dr. Parwani says, perhaps as a pilot project. Daniel Burnham they were not.

Interestingly, once executive leaders agreed to something more—more money, more capital, more people—that created more buy-in from pathologists. Little plans are more likely to fail, Dr. Parwani suggests. "Even if you have buy-in from the trenches, you are not going to move the rock. Let's say I had 10 pathologists who wanted to do it. And then I go to the administration and ask for money, and they don't approve it." Pathologists might then feel betrayed, he says: *You promised us something and didn't deliver.* But with an obvious commitment, "You've created the resource. Now it's easier to convince people—they can touch it, they can feel it, they can see it."

Dr. Parwani adds that he's used this approach successfully throughout his career. "I don't want to promise there will be something under the Christmas tree, and then it's not there," he jokes. "I always go out and get the toy first and show it to the kids."

Dr. Frankel, as noted, secured initial C-suite buy-in before Dr. Parwani arrived, but as scope and specifics emerged and Dr. Parwani had to nail down funding, timelines, ROI, and the like, the higher-ups needed to be courted all over again.

"When you project something without specifics, the ask is very different," he says. "So we had to fine-tune the proposal, put it in black and white, give them very detailed descriptions of the project"—not atypical of academic institutions, he notes, with their capital cycles and stringent application requirements. "You have to show what the clinical need is, and how it's going to help the department and the institution."

Looking back, he says he wishes he had done at least one thing differently. "The biggest thing I've learned is to engage IT from the beginning," he says. If IT doesn't "see the vision, or they don't see exact infrastructure and details, they may not play ball with you," he says. He calls this realization "eye-opening." IT is no longer a cost center, he says; rather, it's part of the strategic growth when designing information systems. If the digital pathology project did not meet the strategic growth plans of IT (as well as other affected departments), "it would not get the traction it needed."

He learned this the hard way, saying he took IT buy-in for granted. "We had the money—why wouldn't they agree with us that this was good?" he says with a laugh. Pathology and IT are now strong partners, he says, but the mistake (his word) brought delays.

For all the careful planning, Dr. Parwani says he continues to be surprised "every day" by how the system evolves

and as new uses appear. They are now using digital pathology for QA reviews. Previously, at the end of the month, a technician would pull hundreds of slides, match the paperwork, make and send folders for pathologists, and compile the information—but this has decreased significantly. Now, several pathologists review QA cases simply by clicking on a link to the slides.

"I still have a microscope in my office," he says. "But probably very soon it will be gone."

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