Community hospitals keep time on tissue handling

Kevin B. O'Reilly

February 2016—The great promise of genomics and actionable cancer biomarkers relies on cancer tissues being handled in the right way so they are suitable for study. Reducing cold ischemia time and the total time that biospecimens spend in formalin is key to the process, say guidelines from the CAP and the American Society of Clinical Oncology on HER2 and on estrogen receptor and progesterone receptor testing in breast cancer specimens.

To hit the recommended times—less than an hour from excision to when the specimen is put in formalin, and between six and 72 hours of total formalin time—takes multidisciplinary coordination and reexamination of anatomic pathology processes. That was the experience of 30 community hospitals that took part in a seven-year National Cancer Institute project devoted to improving cancer care in the kinds of settings where most patients are diagnosed and treated.

By the time the project concluded, each of the participating hospitals was achieving the tissue handling goals for more than 90 percent of their breast biopsies, lumpectomies, or resections. And they reported the cold ischemia time (or time to formalin) and total time in formalin on each of their pathology reports. The hospitals then moved to a more ambitious goal of the NCI project—to achieve these biospecimen quality goals for all cancer tissues.

Dr. Robb

Meeting that goal proved more elusive, especially when it came to reporting the relevant times, says James Robb, MD, a consulting pathologist to the NCI who served as the lead of the pathology pillar of the National Cancer Institute Community Cancer Centers Program, or NCCCP. The major obstacle was and continues to be a lack of automation, Dr. Robb says.

"First, you have to know when the specimen comes out of the patient," he says. "Then you have to record the time when it's dropped into formalin. That colon can come into pathology and not be looked at until four hours later. So you first have to define that. When it comes out of the patient is pretty well defined in the anesthesia chart, but that's not available to the LIS in pathology. Then, in pathology you can put in exactly the second it was put in formalin. But, again, there's no field for that in the LIS, so you have to write it down manually. Then when it comes out of formalin, there's not a field so you have to write it down manually. It sounds very simple. It's three numbers, but trying to get them is not easy."

Coming up with a reliable way to calculate the elapsed times, especially for the total time in formalin, also proved to be a challenge. Not having a functionality to automatically calculate the time in their laboratory information systems, the participating hospitals turned to the Internet for help. A website called TimeandDate.com can perform the calculation but is vulnerable to manual input errors.

At one of the participating community cancer centers, Spartanburg Medical Center in South Carolina, the job had until recently been left to the laboratory's transcriptionists. The excision time, when the specimen was put in formalin, and the time when it was taken out of formalin were available to them. But they had to manually calculate the times and select which code to place in the pathology reports (for example, "preanalytic factors

within CAP/ASCO guidelines" or "preanalytic factors outside CAP/ASCO guidelines; cold ischemia time greater than one hour").

Dr. Lapham

"We're doing this on all specimens, except for specimens that have to be decalcified," says Spartanburg pathologist Rosanna Lapham, MD, giving a sense of the manual workload involved in recording, calculating, and reporting the tissue handling times. "We don't do this for placentas. We don't do it for specimens that are received fresh, like amputees—unless the amputation is for a tumor. Every other specimen, every biopsy, every resection specimen, greater than 95 percent of our specimens have it."

Why take on the job of improving tissue handling for all specimens?

"This is the future," Dr. Lapham says. "The future is now."

She says it is difficult to predict, given the rapid discovery of actionable cancer biomarkers and progress in genomics, when optimal tissue handling will prove critical to whether the biospecimen can be studied further in a way that affects the patient's diagnosis, prognosis, or treatment.

"This is something that most places think they're never going to do because it's such a pain," Dr. Lapham adds. "A lot of people would think it's an overwhelming task to get it on every single report. You need to work hand-in-hand with an LIS to do it. Now that we've put it out there and shown that it can be done, I would think other labs would probably follow suit, especially if you're going to be a hospital that's also submitting specimens for research."

Dr. Lapham says the struggle to work with information technology and vendors to automate the process became a do-or-die proposition.

"They [the transcriptionists] had the brunt of it," she says. "It was almost to the point where if they couldn't fix it, it had to stop."

The first step in automation was to add fields for the relevant time points in the computerized physician order entry system (excision time and time added to formalin, if done in the operating room) and in the LIS. In the CPOE, if the operating room staff does not specify when the tissue was removed from the patient, then no order for anatomic pathology work can be completed.

Several years ago, Dr. Lapham went to the Healthcare Information and Management Systems Society's annual meeting and, as a representative of the NCCCP, "talked to every single LIS vendor" about whether they had or could add the functionality to document and calculate the optimal tissue handling times. None offered it. Orchard Software, Spartanburg's vendor, promised to work on the issue as part of its Harvest LIS.

Jim Hannah, a systems analyst in Spartanburg's information services group, says the request was submitted to Orchard in 2013, and it wasn't until August 2015 that the functionality was fully implemented within Spartanburg's LIS.

"The initial problem was that they could not calculate times greater than 24 hours," Hannah says. "The fields they had developed initially didn't accommodate the time we might need. When you go from one day to the next, you're just taking the difference between the two times and not taking into consideration the elapse of more than 24 hours."

Nancy Stoker, director of product management at Orchard, describes that problem as “an early stumbling block” and emphasizes how the company accommodated Spartanburg’s request at no extra cost.

“We started completely from scratch and created another modality to do this calculation—when the tissue was removed from the body, the time into formalin, and then the end time out of formalin,” she says. “You just enter or scan those in and then our system automatically calculates the cold ischemic and total formalin times.”

Stoker

“We just needed to refine the methodology of calculating,” Stoker says. “Some things seem like they are relatively easy to do, and then it’s like peeling an onion and you find that it touches so many other things that it’s difficult to do…. There was a lot of data that touched a lot of pieces in the software, and we were able over time to get that resolved. We just kept plugging away on it, and tweaked and tweaked it until they got what they wanted.”

Stoker says Spartanburg’s work “in the trenches” will benefit other laboratories.

“A lot of this type of documentation was done offline,” she says. “Even today, we see a lot of that documentation being done offline [elsewhere]. Spartanburg just kept holding us to a higher standard to automate that process. Anybody who gets our pathology system now will reap the benefits of Spartanburg’s hard work.”
When the software is demonstrated to prospective clients, laboratory professionals will ask about the functionality to record, calculate, and report cold ischemia and total formalin times and “it gets positive reviews,” Stoker says.

The next step for Spartanburg, Hannah says, was to “set up rules on how long the elapsed time was and then drop the proper phrase [in or out of guideline and how long] on the report.”

Dr. Robb says laboratories using other laboratory information systems may have to play a waiting game before this kind of automation is available to them.
“It’s very clear that until there’s really a mandate for these kinds of extensive changes, they won’t happen,” he says. “You can do it manually for breast cancer because it’s relatively few cases. But when you do this for all cancer specimens, it’s incredibly difficult to do manually.”

While Spartanburg is ahead of the pack in automating the documentation of optimal tissue handling, that came only after years of working with other hospitals participating in the NCI project to share lessons learned on how to achieve the recommended times.

“We really had to change the whole process,” says Spartanburg histotechnologist Claudia Tirpak, HT(ASCP). “We were working with the OR pretty closely to make sure they were giving us all these times. And training the accessioning staff to put different specimens on different carts based on when they were collected, if they came in late in the day, for example. It was a huge undertaking.

“In the beginning, the OR staff didn’t even really understand why we were doing it,” Tirpak adds. “It interrupted their flow. They would collect the specimens, put them in the container, send it out of the room, and forget about it. We had to get the OR staff that was actually adding the formalin to start writing this on the specimen container label designed for this purpose. Getting them on board was probably one of the most difficult tasks—not that they weren’t cooperating, just that the OR’s a very busy place. Everybody’s trying to hurry and get so much done that they don’t have time to do this or that. But they were able to do that, and then it allowed us to do our part.”

For Corrado Minimo, MD, vice chair of pathology and chief of anatomic pathology at Philadelphia's Einstein Medical Center, gaining an in-depth understanding of his nonlaboratory colleagues' role in the process of optimal tissue handling was essential to meeting the NCI project's goals.

"The first thing was to recognize who were our stakeholders," Dr. Minimo says. "The nurses, first off, the manager of the OR, and the surgeons. One thing I knew is that ORs are very busy, busy places with lots of people, different heads with different sensitivities. The OR is a very complex organization and I knew I had to recognize that before making a request."

Using the imprimatur of the NCI project as his entree, Dr. Minimo spent months observing procedures in the OR and in meetings with surgeons and nurses. He explained to each group in early-morning meetings the science behind reducing cold ischemia time and the impact it could have on patient care.

Per the NCI project's emphasis, Dr. Minimo and his colleagues also sought optimal tissue handling for all cancer tissues, not just those from breast cancer cases.

"If you don't do it for all the cases, then you'll forget," he says. Dr. Minimo asked nurses for their ideas on how they could reliably accomplish the goals. At the start, OR staff noted the times (out of body, into formalin) on paper. About a year ago, the ordering system was computerized and now the times must be entered for the testing order to be completed. As part of its standard operating procedures, all specimens have a total formalin time of more than six hours and less than 72 hours, Dr. Minimo says. For all malignancies, they indicate the actual time in formalin through a manual process.

"We'd like one day for this to be a value that's automatically produced," he says. "In the meantime, we feel it's important—knowing these cases may be subject to molecular investigation one day—to take the little extra effort to give the patients the right information that they deserve."

Hartford Hospital, in Connecticut, also took part in the NCCCP project. Richard Cartun, PhD, directs biospecimen collection programs at the hospital, and says that in the early going it took some reminding to get the OR staff to reliably note the relevant times.
"Early on, we were making frequent phone calls and sending a lot of emails," says Dr. Cartun, director of histology and morphologic proteomics and assistant director of anatomic pathology. "But after getting the message out, things got better. We did that by meeting with the OR staff, the managers, the nurses in the OR, so then they could communicate with their staffs. I can always tell when I have a new surgeon or interventional radiologist here because I start seeing cases with no time in formalin. And after a friendly call or email I get them on board with the importance of this. We have to follow this all the time."

Dr. Cartun says that tracking total formalin time will be made easier by a barcoding system that will be implemented this summer. But his primary concern is not that specimens will stay in formalin too long but that the formalin will not penetrate sufficiently.

"You have to ensure adequate fixation," he notes. "And part of that is making sure the specimen doesn't dry out. A lot of times specimens are transferred from the OR suite to the pathology frozen section room or the grossing station on another floor and there's a delay there that affects not only the cold ischemia time but also may allow the specimen to dry out. When it dries out, it's very difficult to get formalin into it unless it's sectioned. You want to make sure the specimen is transferred on a saline-soaked gauze, OR towel, or in a specimen container."

Hartford, which handles more than 50,000 AP specimens annually, has received high marks for the quality of its specimens. The hospital was one of 17 hospitals participating in a cancer research project with the Moffitt Cancer Center in Tampa, Fla.

"Of the 17 institutions, our specimens were ranked at the top of the pyramid in terms of quality for DNA/RNA extraction and also proteomic study," Dr. Cartun says. The Hartford HealthCare Cancer Institute also is part of an

alliance with New York's Memorial Sloan Kettering Cancer Center that will allow Hartford patients the opportunity to enroll in MSK-conducted clinical trials.

"I don't think Memorial would want to partner with anyone who did not provide state-of-the-art care or quality biospecimens through their pathology department," he says.

Several other hospitals that won the competitive process to take part in the NCCCP project—each getting $500,000 annually and asked to make good on 80 deliverables—have gone on to form similar partnerships that give their patients greater access to cutting-edge care. Spartanburg, for example, formed the Guardian Research Network with four other health systems representing nearly 80 hospitals to aggregate hundreds of thousands of patient profiles for a molecular big-data project designed to identify patients who might benefit from clinical trials and targeted therapies.

"The government, through the NCI, was a catalyst in really positioning these organizations to develop new skills, and take those skills and get very innovative," says Donna O'Brien, who served as special advisor to the director of the NCI for the NCCCP and is president of Strategic Visions in Healthcare.

O'Brien

Dr. Robb says the idea of tracking, improving, and reporting cold ischemia and total formalin times for all cancer specimens is starting to take root in hospitals across the country.

"Everyone's doing it for breast cancer now," he says. "And as we start seeing biomarkers for lung cancer, colon cancer, and kidney cancer that are detected with immunohistochemistry and in situ hybridization in formalin-fixed, paraffin-embedded tissue specimens, we are realizing that we have to treat these specimens the same way as we treat breast cancer specimens. I think a large majority of the pathology departments are trying to move to processing all cancer specimens as they do with their breast cases.

"You can't have two ways to do it," he adds. "You can only have one process in your laboratory or you go crazy."
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