Transcript Details
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GEP Testing in Surgical Oncology

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I'm J. Michael Guenther, MD. I'm a surgical oncologist based in Northern Kentucky at the St. Elizabeth Hospitals. I first became aware of gene expression testing for melanoma about eight or nine years ago, and it's been a labor of love since then. I certainly learned to be a better physician through use of some of these gene expression products, both for melanoma and for the original one was for breast cancer. From the days of medical school, melanoma was fascinating because it could do almost anything. It could lay dormant for years and reactivate, it could spontaneously disappear, and there just were no rules about melanoma. That was the one rule about melanoma is that there were no rules and it was highly unpredictable.

And so the first run through on this, the first assay that we got was really the first test that ever gave us any prognostic information at all. And it basically gave patients recurrence risks and if you will, into a zip code or a bucket of risk. That was an approximation that was very helpful for predicting good from bad. But really the second iteration of this came when the integrated form of the gene expression came where the original assay was combined with some clinical pathologic factors and it really gave us two precise pieces of information. The first one, which we've used since 1991 when Don Morton essentially revitalized or popularized the concept of sentinel node biopsy for melanoma, was to predict exactly a patient's risk of sentinel node positivity.

Now through the years using our conventional staging, we've run a 12% node positive rate, which that's fine, but that's an 88% rate of nodes being removed that did not help patients. And there was a cost with that and there's a morbidity and there's potentially even an immunologic cost there. So we wanted to do a far better job at reducing the number of negative sentinel node biopsies. So one of the real uses of this has been to show us if we have patients with a less than a 5% risk of node positivity, then there was no purpose to looking for nodes. That was the error rate of the procedure from MSLT-1. MSLT-1 randomized patients to wide excision or wide excision and sentinel node biopsy. And that test had a 1% per year false negative rate. Patient failed in the base and then was dissected in a 1% per year rate. So it made no sense to look for something with a less than 5% yield.

So that 12% number was what pathology gave us. So any test that was worth anything really should reduce the number of negative nodes that we did. The DECIDE study that we participated in and that just got published as a second iteration of that, using that integrated gene expression. And its main purpose was to look at comparing the decision-making process between the patient and the physician and a comparison of patients who did not have that data. And it was a substantial reduction. We looked at, it was almost a 19% reduction in the number of sentinel node biopsies done when patients had this information made available to them before they had surgery.

So in conjunction with the patient and the surgeon, we would decide whether or not to remove nodes. So that was pretty nice. But within that study, we had 35 patients who said, "I'm not down for this. I want my nodes looked at anyway, even though I'm predicted not to have a positive node." And all 35 of them were negative. So if we took those 35 off of the original rate, we're getting down to somewhere under 30% now needing a sentinel node biopsy. So we found a safe group of patients who could forego a node biopsy.

The second piece of information that came out of DECIDE was there was a two-year follow-up in which no one recurred if they had a low-risk lesion. So we were able to identify a population of patients who, if they had a node biopsy, they did not have a recurrence, and if they didn't have a node biopsy, they were very safe to not have a recurrence. So we were able to substantially reduce the number of patients having unnecessary node biopsies. Now that in and of itself was the goal of the study was to identify that tool and see if it worked. But from the surgical oncology point of view, there's another goal to these and that is there are a certain number of patients with shallow lesions that are also going to have positive nodes, and somewhere around 10% under a millimeter are metastasizing lesions.

And those, in a weird way, are the most important ones to find because that's how we as surgeons can potentially save lives. So we also want to look at not just the negative predictive value of this test, but the positive predictive value. We want to identify patients who are likely to have positive nodes that we might not have thought of otherwise. So this is a very specific test, but it's also a very high negative predictive value. So in my practice, I order this on almost everybody who's got a lesion over 0.3 millimeters. Under 0.3 millimeters, the yield is very low unless it's a transplant patient or your partner's wife or a nursing student or something. The yield will be very low and the anxiety relief is great, but the yield for that is going to be low. Of course, it's not for patients with end-stage dementia and end-stage medical problems. But for someone who is otherwise a medical candidate, this very substantially helps me predict who's going to need node biopsies and who doesn't.

So that answers that question. I think we're getting ready to move away from looking at the lymph node as the most important part of this because it's a staging procedure. It helps us decide who's high risk and who isn't. It helps us guide systemic therapies. But the most important part of this is now we get a risk of recurrence. It's individualized to every patient, whether the node is negative or node is positive. And that's really where the rubber hits the road for melanoma. We've gotten data over the past couple of years where the real mosaic of melanoma care is being filled in and we're starting to see that early diagnosis of recurrence translates into high salvage rates. My own patient experience has been that somewhere almost two-thirds of our patients who recur are salvaged by a combination of therapies. And the data is telling us that if those people are watched closely, and closely being clinical follow-up, as well as cross-sectional imaging, maybe potentially even blood work in the future, that we have a high salvage rate.

So the recurrence risk of a patient is also a precious piece of information because it guides their follow-up. If they have low risk, which many of them do, praise God, they go back to their dermatologist for a routine follow-up. They don't need to see surgical oncologists and they don't need expensive testing and time away from work and copays and that kind of thing. And the anxiety relief is palpable. Having said that, patients who have higher risk lesions, they stay in the fold and they stay close to the doctors in follow-up. And if we have a problem, we tend to find it early where it's salvageable. So the two principal uses in my practice are if we have low risk disease, de-escalation, potentially avoiding node biopsies, back to dermatology for observation for their second lesion or their basal cell or whatever.

But the flip side is if we have high risk disease, whether it's node positive or high risk of recurrence, we have places to park them. We have evidence of adjuvant therapy that works. We have evidence that close follow-up translates into high survival rates. And we can give a patient what they need. So it's matching their care to the risk that they have. And I think that's a very efficient way to practice medicine, especially with melanoma. It's a very humbling disease and if you accept the limitations, I mean, when we were in medical school, we had a professor, he was a deaf cardiologist, and that's not like a punchline to a joke. He could bend your hand back and tell you your hematocrit. He could tell a jaundice patient's bilirubin level by looking under their tongue and he made a stethoscope out of a tongue depressor to tell you what rhythm you were in. He wrote a whole book on clinical diagnosis. He was a wizard.

But he can't tell you anything about melanoma because it's so variable. And it's incredibly humbling when you see things that you'd expect to behave one way and they don't; it can be very frustrating. This opens the jar or opens the top off, if you will, an understanding of a disease that really was so variable that if you guessed melanoma when you were asked a question, you had a fighting chance of being right almost no matter what the scenario was because melanoma could do anything. And so in a weird way, I wish my old chairman, Dr. Morton, was still alive today because he was like Moses, he saw the Promised Land, but he never got across the Jordan River.

He dreamed of this. He basically revolutionized and popularized sentinel node biopsy and his whole career was spent on immunotherapy vaccines and things. He just didn't get to the point where we saw the real technical breakthroughs for immunotherapy. So it's a great time to do melanoma work, but I'd also add, it's not the last gene expression test we're going to see for either skin cancers or other things. This is something for people to get used to because the time has come where we can get information that predicts the future. When I explain this test to patients, I say, "How would you like to know what the weather was going to be like in six months for planning a vacation?" Or, "How would you like to know what the traffic was like leaving here?" Or, "Your stock markets or your local sports teams, how they were going to do?"

Everyone says, "Yeah, that'd be great." Well, I have a test that tells me what your melanoma is going to do as far as node positivity and its chance of recurrence, and I've got tools to treat both of those. So people understand that. They like the idea of doctors not guessing at things like weathermen. No, it's no offense to weathermen.