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Beyond Single-Cancer Screens: Unveiling Progress in Early Detection Testing

ReachMD Announcer:
Welcome to ReachMD. This medical industry feature, titled “Beyond Single-Cancer Screens: Unveiling Progress in Early Detection Testing,” is sponsored by GRAIL. Here’s your host, Dr. Charles Turck.

Dr. Turck:
In the realm of cancer detection and management, addressing unmet needs associated with cancer screenings are pivotal. And as it turns out, we now have a tool to screen for multiple cancers before they become symptomatic, including those without recommended screening tests. Early detection may help to advance cancer care and improve patient outcomes.

This is ReachMD, and I’m Dr. Charles Turck. Joining me to discuss a compelling patient case that demonstrates how PCPs and oncologists can help improve early detection rates by using multicancer early detection screening are Drs. Jesse Hsieh and David Isaacson.

Not only is Dr. Hsieh an Adjunct Associate Teaching Professor for Notre Dame's MBA, E-MBA, and Executive Integral Leadership programs, but he’s also the Chairman of the Board of Beacon Health System in Indiana. Dr. Hsieh, welcome to the program.

Dr. Hsieh:
Please to be here.

Dr. Turck:
And Dr. Isaacson is an Assistant Professor of Otolaryngology at the Indiana University School of Medicine, as well as the Medical Director at Beacon ENT and Audiology in South Bend. Dr. Issacson, it’s great to have you with us as well.

Dr. Isaacson:
Thank you, happy to be here.

Dr. Turck:
So I’d like to start with you, Dr. Hsieh. Where do we currently stand with cancer survival rates in the United States?

Dr. Hsieh:
Well, we all know that diagnosing cancer early can dramatically improve cancer survival. In fact, in patients aged 50-79, when cancers are diagnosed early, say in stage one, the 5-year survival rate is 89 percent. But when it’s diagnosed later in stage three or four, survival rates drop to 21 percent.[1] So the difference really is dramatic.

And unfortunately, the status quo in cancer has largely remained bleak. In fact, about 70 percent of all cancer-related deaths are associated with cancers that don't have recommended USPSTF screening modalities, such as pancreatic, brain, kidney, and stomach cancers.[2]

So of course it’s really important to prevent cancer, but in the absence of great, effective preventative approaches, we have a huge gap to fill here. And to have a greater impact, we must do more to screen for cancer.

The good news here is that with the arrival of multi-cancer early detection testing, or MCED testing for short, we’re starting to see some positive impacts. To be a truly effective MCED test, it must meet the minimum criteria. It needs to detect many deadly cancers, including unscreened cancers, using a single blood sample. It has to predict the signal origin to help guide diagnostic workup. And it needs a high

positive predictive value and a low false-positive rate to limit unnecessary workups.[3-5]

Dr. Turck:
Thank you for that background, Dr. Hsieh. And if we stay with you for just another moment, do you have any experience with MCED testing?

Dr. Hsieh:
Yes. We actually implemented an MCED test called Galleri into our practice in 2021. And we were able to get some test cases by presenting Galleri as a screening option, along with standard screens, to 120 of our patients presenting for a physical exam. Of those patients, about 87 chose to proceed with Galleri testing. Four of the 87 screens came back with a positive cancer signal, or "cancer signal detected." And these were patients who really had no symptoms.

In two of the cases, head and neck cancer signal origin was predicted by Galleri. One of these is a 57-year-old male, whose experience we'll be talking about in-depth today. This patient presented for his annual physical but also opted for a Galleri test. He was in good health, had no family history of cancer, practiced healthy habits. But when test results came back with a positive signal, there was a strong predicted cancer signal origin for head and neck, but also a weaker prediction for the lung.

So for diagnostic evaluation, we did CT scans of the chest and neck, and referred him to Dr. Isaacson for a complete head and neck exam, including fiberoptic laryngoscopy. Now most squamous cell head and neck cancers may be located posterior behind the tonsils, but we found out that he'd undergone a tonsillectomy as a child.

So this presented a really interesting mystery because we couldn't easily pinpoint where the cancer signal was coming from. We were able to conduct a second Galleri test 6 months later, for which GRAIL—Galleri's manufacturer—covered at no cost. This second test also came back positive, but this time the predicted cancer signal origin was solely head and neck cancer with no prediction for lung cancer.

Dr. Turck:
Interesting. So if we turn to you now, Dr. Isaacson, what were your next steps for this patient?

Dr. Isaacson:
Well, I have to say that this test was brand new to me, and it was an unusual request to do a consultation for a cancer that was completely asymptomatic and without any physical findings. But regardless, after another CT scan of the neck came back completely unremarkable 7 months after his first CT scan, this gentleman underwent PET imaging, which identified a very small right level 2A lymph node of about 11.4 millimeters. This is really just outside of normal size, so it's not something that you would really notice clinically. And interestingly, no primary tumor site was identified.

So I reexamined our patient with fiberoptic laryngoscopy and ordered an ultrasound-guided needle biopsy that demonstrated squamous cell carcinoma from this lymph node, which was p16 positive and incidentally, an increasing demographic of head and neck cancer. So now at this point, 9 months had gone by from the initial positive Galleri test, and I decided to do a very thorough head and neck exam again using fiberoptic laryngoscopy. I found some subtle asymmetry in the right base of tongue, but again, no definitive primary tumor site absent his tonsils.

At 10 months post-initial Galleri test, my next step was to perform a direct laryngoscopy and biopsies under general anesthesia, which is the standard of care for working up this type of cancer. And this time, I found a miniscule remnant of the tonsils that hadn't been removed earlier in life, and it was at this area that had developed a p16-positive squamous cell carcinoma. So even though this gentleman had undergone tonsillectomy as a child, he still developed a primary carcinoma in that small tonsillar remnant.

So now that we'd identified a primary tumor site, we then explored treatment options. I considered performing robotic resection of this tonsillar carcinoma, but unfortunately, the anatomy of the oral cavity was such that it made this option less favorable. Instead, we recommended radiation and chemotherapy, with five cycles of cisplatin and 6,000 centigray radiation delivered in 35 fractions.

And I'm happy to report that our patient had complete normalization of his PET positivity at 14 months after his first Galleri test. His recent PET imaging shows no evidence of recurrence, and he continues to show that he's in a durable remission.

Dr. Turck:
That's great news, Dr. Isaacson, thank you for sharing those details with us. And for those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck and joining me today to discuss a case review using an MCED test called Galleri are Drs. Jesse Hsieh and David Isaacson.

So, Dr. Isaacson, if we keep this case review in mind, what's the best way to apply this technology into practice, particularly in the

otolaryngology space?

Dr. Isaacson:
So from a head-and-neck-surgeon standpoint, there are some questions that need to be answered as to how best to apply the technology because we're seeing asymptomatic patients without any physical findings. And in this case, we saw cancer signal detection precede detection by some types of diagnostic imaging.

So that's pretty significant because we'd always thought that PET imaging was one of our most sensitive modalities. So my suggestion for those in the head-and-neck field who may find themselves in a similar situation would be to perform a comprehensive head and neck exam as well as a contrast-enhanced CT scan. And if no primary tumor site is identified, then I would recommend periodic follow up, probably every 2 months, until a primary site is identified. If one isn't found by 6 months, then I would recommend PET imaging to be performed.

The reason I'm suggesting waiting on PET scans is because I'd like to avoid any false negative PET imaging results that could misdirect my attention away from the primary site. And although this protocol is anecdotal, it'll probably be fleshed out over the coming years to hopefully become more evidence-based.

Dr. Turck:
Thanks, Dr. Isaacson. And coming back to you, Dr. Hsieh, what strikes you as you look back on this case?

Dr. Hsieh:
Well from my vantage point, I'm really fascinated about this new world we're entering. This is a new paradigm in terms of cancer screening, and not everyone's heard of MCED testing or Galleri, especially PCPs and ENTs. And typically, when an oncologist receives normal, negative results using standard testing, and especially when a patient is asymptomatic, there probably isn't much incentive to dig any deeper.

But in this particular patient case, we really had to dig. As I mentioned earlier, GRAIL worked with us to offer that second test. The retest program supports providers with further insight to support patient care, and in our case, to retest our patient to see if that signal was repeated and to rule out a false positive. And when the second test came back with a cancer signal detected, and head and neck as the predicted cancer signal origin, that told us that our initial diagnostic workup was insufficient to detect cancer.

So I'm here to say that Galleri and MCED testing is valid, and it's here to stay. And that's why it's critical that PCPs work very closely with oncology specialists and surgeons to do these workups and take the time necessary to pinpoint a primary tumor site so that patients can get the treatment they need as early as possible.

And I believe that this technology will become a normal practice in health care and we'll look back on this years from now and say hey, we were on the cutting edge.

Dr. Turck:
Now we're almost out of time, but before we close, I'd like to hear from you, Dr. Isaacson, one last time. Do you have any final thoughts you'd like to leave with our audience today?

Dr. Isaacson:
Yes, so after being introduced to Galleri with this case, I've been very impressed with it and the breadth of screening possibilities. Like me, my colleagues are just learning about it, but I think over the next few years, it'll become much more prevalent as Dr. Hsieh has already mentioned.

And I feel like in our ENT specialty, specifically, we'll begin to develop our algorithms to determine where primary tumor sites are located. Not having laterality is tough for us now, but I think it's doable once we have evidence-based protocols in place.

Dr. Turck:
Thank you, those are some great key takeaways to consider as we end today's program. And I want to thank my guests, Drs. Jesse Hsieh and David Isaacson, for helping us see the potential of MCED testing through this patient case. Dr. Hsieh, Dr. Isaacson, it was great speaking with you both today.

Dr. Hsieh:
Thank you for having me.

Dr. Isaacson:
Thank you, very much.

Dr. Turck:
And before we go, let's take a moment to review the sensitivity information for this type of cancer and Important Safety Information.

ReachMD Announcer:
Sensitivity Information
Based on a clinical study of people ages 50 to 79, around one percent are expected to receive a cancer signal detected result. After diagnostic evaluation, around 40 percent of these people are expected to have a confirmed cancer diagnosis. The overall sensitivity in study participants with head and neck cancer was 85.7 percent, 63.2 percent for stage one, 82.4 percent for stage two, 84.2 percent for stage three, and 96.0 percent for stage four.

Important Safety Information
The Galleri test is recommended for use in adults with an elevated risk for cancer, such as those aged 50 or older. The Galleri test does not detect all cancers and should be used in addition to routine cancer screening tests recommended by a healthcare provider. Galleri is intended to detect cancer signals and predict where in the body the cancer signal is located. Use of Galleri is not recommended in individuals who are pregnant, 21 years old or younger, or undergoing active cancer treatment.

Results should be interpreted by a healthcare provider in the context of medical history, clinical signs and symptoms. A test result of "No Cancer Signal Detected" does not rule out cancer. A test result of "Cancer Signal Detected" requires confirmatory diagnostic evaluation by medically established procedures (e.g. imaging) to confirm cancer.

If cancer is not confirmed with further testing, it could mean that cancer is not present or testing was insufficient to detect cancer, including due to the cancer being located in a different part of the body. False-positive (a cancer signal detected when cancer is not present) and false-negative (a cancer signal not detected when cancer is present) test results do occur. Rx only.

Laboratory/test Information
GRAIL's clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and accredited by the College of American Pathologists. The Galleri test was developed, and its performance characteristics were determined by GRAIL. The Galleri test has not been cleared or approved by the Food and Drug Administration. GRAIL's clinical laboratory is regulated under CLIA to perform high-complexity testing. The Galleri test is intended for clinical purposes.

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This program was sponsored by GRAIL. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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   *Assumes screening is available for all prostate, breast, cervical, and colorectal cancer cases and 43% of lung cancer cases (based on estimated proportion of lung cancers that occur in screen-eligible individuals older than 40 years)
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