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Cancer Screenings: The Impacts of Early Detection Technology

ReachMD Announcer:
Welcome to ReachMD. This medical industry feature, titled, *Cancer Screenings: The Impacts of Early Detection Technology,* is sponsored by GRAIL.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
According to the CDC, the number of patients in the United States who were diagnosed with cancer increased from 1.4 million[1] in 2009 to 1.7 million in 2019.[2] With cancer rates continuing to rise seemingly out of control, what impact could cancer screenings have on our patients?

This is ReachMD, and I'm your host, Dr. Jennifer Caudle, and joining me to discuss multi-cancer early detection technology and its implications is Dr. Sana Raoof, who's a physician scientist at Memorial Sloan Kettering Cancer Center. Dr. Raoof, it's great having you here today.

Dr. Raoof:
Thank you very much. I'm excited for our discussion.

Dr. Caudle:
I am as well. And let's dive right in, Dr. Raoof. Can you tell us about current cancer screening practices in the United States?

Dr. Raoof:
Absolutely. So in the United States, there is a handful of tests that are at our disposal to try and catch cancers at early stages. For women there is breast cancer screening with mammography, there's cervical cancer screening with pap smears, and then for both men and women, there's colon cancer screening—the gold standard of which is colonoscopy—and then there's a few other types of tests that are available.[3] PSA screening for prostate cancer is no longer recommended for average American men,[4] and then for high-risk smokers, low-dose chest CTs are available.[3] So, if you're an average American man today, you know, the only cancer that you have to be screened for is colorectal cancer, and for women, there's breast and cervical cancer screenings.[3] So, these are just a couple of the many different types of cancers that exist, and so one of the most important things to know about cancer screening tools currently is that roughly 70 to 75 percent of cancers that ultimately kill Americans are from cancers that we don't have recommended screening tests for, and so there's a huge unmet burden of cancer mortality that could be reduced if we had additional cancer screening tests to promote detection in early stages.[3]

Dr. Caudle:
Excellent. And as I understand it, we do have an alternative cancer screening tool that's emerged fairly recently, but before we dig into the science, what is this alternative screening tool? And how did it come about?

Dr. Raoof:
It's a really interesting history. So, you know, the tool that we're going to discuss today is a molecular cancer screening tool. This is meant to use in healthy, asymptomatic adults that have no sign or symptom of cancer.[5] So, several years ago, it was discovered that in pregnant women, you can actually find DNA from the fetus floating around in the mother's bloodstream, and, unfortunately, in some of these women, a second signal of DNA was discovered, not coming from the fetus, but coming from a cancer that wasn't diagnosed, and so that discovery in 2015 created the insight that even localized, early-stage cancers can shed their DNA into the peripheral blood, and

from this, oncologists and scientists swooped in and did a tremendous amount of research on circulating tumor DNA and started to create really exciting cancer screening tests that search for these early-stage cancers based on DNA that tumors shed into the peripheral blood.[6]

Now, if you want to know, sort of, what is the status of these cancer screening tests in clinic, there's a variety of tests like this that are in different stages of preclinical and clinical development.[7] There's only one, called Galleri, and it's made by the company Grail. There's only one so far that is prescribable and has a body of prospective clinical evidence on the basis of which you can actually get one of these tests today from a physician in any of the 50 states.[7] I expect in the next several years, we might get more evidence about other tests that are based on other types of science but for now, the most clinically relevant one is this test called Galleri.

Dr. Caudle:
And with that information in mind, Dr. Raoof, can you explain how Galleri works?

Dr. Raoof:
Absolutely. So as I said, there's different tests that are in development that look for different types of molecules that cancers can shed into the bloodstream. These tests might look for DNA, proteins, they might look for the length of DNA fragments in the blood,[8] but what's exciting to me, at least, about the Galleri test is that it's looking for this epigenetic marker called methylation.[8] So, rather than looking at the sequence of DNA itself, it's looking at the pattern of this molecule called a methyl group that's stuck onto the DNA, and if you look at the pattern of DNA methylation, it can tell you two important things. One – aberrant methylation patterns can be analyzed with machine learning algorithms to predict which patient has cancer.[8]

Let's say you have a test that looks at DNA, the genetic sequence of DNA. Well, as many of our listeners know, you know, your DNA comes from your mom and your dad, and in all of the different cells in your body except for some of your lymphocytes, that DNA is the same. So, you might find some genetic mutations, but you're not going to be able to say, based on the background sequence, you know, is this coming from the eye, the brain, or the kidney. The important thing about looking at aberrant methylation as compared to aberrant genetics is that methylation is tissue specific.[8] So, as a clinician, I would say this is one of the most important considerations because at least I personally would not like to take a healthy asymptomatic person and then go on a wild goose chase through their body to try and localize a molecular cancer signal with imaging. It's certainly more convenient for the physician and the patient, as well as more practical, less radiation exposure, less expensive, etc., to be able to pursue a targeted work-up. So, you know, this is an important feature of Galleri.

The other important feature of Galleri that I would say is that because it's based on methylation, a peculiarity of methylation-based cancer screening tests becomes relevant, which is that it selectively picks up cancers that have a more aggressive course. So, as compared to other types of molecules, methylation specifically does not detect very indolent, slow-growing cancers,[9] and I would say that's a good thing. I don't want to start diagnosing millions of Gleason 6 prostate cancers and millions of papillary thyroid cancers that would have never killed anyone. I would like to catch cancers that, if you intercept them early, can actually bend mortality curves, and that is one of the other features of the Grail test that I find appealing.

Dr. Caudle:
You're listening to ReachMD, and I'm your host, Dr. Jennifer Caudle, and joining me to talk about the science behind multi-cancer early detection technology is Dr. Sana Raoof. So, now that we've examined Galleri and how it functions, Dr. Raoof, let's put this all together. What impact does this have on cancer screening for our patients?

Dr. Raoof:
I think it has a potentially very exciting impact. So as I said at the earlier part of our conversation, roughly 70 to 75 percent of cancers that kill Americans we don't have any screening tests for, [3] and how are we going to try and improve on that? I don't think that we have the option of trying to just come up with more single-cancer screens, which means just coming up with more targeted organ-by-organ screening. There's too many types of cancer, and it will just become impractical for patients and cause a lot of false positives and over-medicalization if we just keep adding tests one by one to screen the different types of tissues from our head to our toes.

So, I think the future for patients has to incorporate a shift to a multi-cancer screening paradigm, but where are we in evidence development for molecular cancer screening tests? Well, where we are for Galleri is, at this point, we have a good sense that they're working as described. So, we know from a prospective multi–centered study called PATHFINDER that if the test comes back positive, the chance that the patient actually has cancer is roughly 40 percent. So, this number is the positive predictive value.[10] What it means is possibly a cancer screening test with a very high positive predictive value,[8,9] which means a smaller chance of having a false positive and a smaller chance of having an unnecessary medical work-up.

The question you might be asking is – if it's so great, then what are we waiting for? And the answer to that is, you know, many physicians are not waiting. There's plenty of physicians who are ordering these tests now before there are guidelines on how to use them and before they're covered by insurance and before they're FDA-approved as cancer screening tests. About 100,000 of these tests have been ordered by physicians who are early adopters and are excited about molecular cancer screening, but, you know, what are other people waiting for before using these tests? You know, traditionally, people have waited in the field of cancer screening for very long randomized control trials with something like a survival or a mortality endpoint before they decide on the clinical utility of tests. If you're a very proactive patient and you have a resourceful PCP, they're available to you now. If you're more conservative and you are someone who likes to wait for gold-standard evidence and guidelines, then that information is forthcoming.

Dr. Caudle:
Thanks, Dr. Raoof. Now considering that this is a fairly new technology that's not yet seen full uptake with healthcare providers, is this difficult to incorporate into current clinical workflows?

Dr. Raoof:
I think, you know, to answer is it difficult to incorporate into current clinical workflows, I would say it's not difficult. It just requires a little bit of initiative on the part of the physician and education for the patient. So, let's say that you're someone who would like to get molecular cancer screening in the short term. You can ask your PCP to order the test in any one of the 50 states. If your PCP is not comfortable, you can go onto the Galleri website and have a telemedicine physician have a virtual consult with you, speak to you about your history, assess you, and then consider ordering a test for you.

Your primary care doctor could pursue that work-up themself if they feel comfortable, or they could use a variety of clinical resources offered by Grail. So, you know, this is a new technology, and, therefore, the workflow is something that you sort of need to be proactive about creating for yourself in a way that makes sense in your own practice and in your own life, but the resources certainly exist.

Dr. Caudle:
Excellent. Now, unfortunately, we're almost out of time, but before we end our discussion today, are there any closing thoughts you'd like to leave with our audience?

Dr. Raoof:
I think an issue that's often not discussed in this field is, you know, the longer that we wait for randomized control trials or higher and higher levels of evidence about the functioning of these tests, you know, that does kind of prolong a period of disparity between those who can pay out of pocket for these tests and those who cannot. So, until these tests are FDA approved, CMS covered, covered by insurance, they are an out-of-pocket expense, and so, you know, on one hand as physicians, we want to use evidence-based medicine, and often we will wait decades before that evidence is generated.

On the other hand, as physicians, we also want to make use of important new scientific discoveries, and some of the patients that probably have the most to gain are disadvantaged patients. Many of the patients that have the most to gain potentially from these tests are the ones that can't pay for them, and so I would urge the community to think hard about what level of evidence would we accept before we start translating these tests into clinical practice and to simply be mindful of the cost of time. This is just an important discussion not only in the field of cancer screening, but I would say in many different fields of medicine.

Dr. Caudle:
Thank you. Those are great final takeaways to consider as we end today's program. I'd like to thank my guest, Dr. Sana Raoof, for helping us better understand the impact multi-cancer early detection technology could have for our patients. Dr. Raoof, it was great speaking with you today.

Dr. Raoof:
You, too. Thank you so much.

Dr. Caudle:
And before we go, let's take a moment to review some important safety information.

ReachMD Announcer:
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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References:

1. Centers for Disease Control and Prevention. Invasive cancer incidence — United States, 2009. *MMWR* 2013;62(07);113-118.
2. Cancer data and statistics. Centers for Disease Control and Prevention. Updated June 8, 2023. Accessed August 4, 2023. https://www.cdc.gov/cancer/dcpc/data.
3. American Cancer Society guidelines for the early detection of cancer. American Cancer Society. Updated February 24, 2023. Accessed August 3, 2023. https://www.cancer.org/cancer/screening/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html
4. American Cancer Society recommendations for prostate cancer early detection. American Cancer Society. Updated February 24, 2023. Accessed August 3, 2023. https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/acs-recommendations.html
5. Loomans-Kropp HA. Multicancer early detection tests: where are we?. *JNCI Cancer Spectr*. 2023;7(1):pkac084. doi:10.1093/jncics/pkac084
6. Bianchi DW, Chudova D, Sehnert AJ, et al. Noninvasive prenatal testing and incidental detection of occult maternal malignancies. *JAMA*. 2015;314(2):162-169. doi:10.1001/jama.2015.7120
7. American Cancer Society. Multi-cancer early detection (MCED) tests. Updated June 30, 2022. Accessed September 22, 2023. https://www.cancer.org/cancer/screening/multi-cancer-early-detection-tests.html
8. Liu MC, Oxnard GR, Klein EA, Swanton C, Seiden MV; CCGA Consortium. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. *Ann Oncol*. 2020;31(6):745-759. doi:10.1016/j.annonc.2020.02.011
9. Klein EA, Richards D, Cohn A, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. *Ann Oncol*. 2021;32(9):1167-1177. doi:10.1016/j.annonc.2021.05.806
10. Schrag D, Beer TM, McDonnell CH, et al. Bloodbased tests for multi-cancer early detection(PATHFINDER): a prospective cohort study. *Lancet*. 2023;402:1251-1260. doi: 10.1016/S0140- 6736(23)01700-2.