A liquid-biopsy-based multicancer early detection test may detect early-stage disease and low DNA-shedding cancers

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A liquid biopsy-based multicancer early detection (MCED) test could detect 12 types of cancers, including low DNA-shedding cancers and

early-stage cancers, according to data from a retrospective study presented at the [AACR Annual Meeting 2023](link), held April 14–19.

"Detection of cancer in early stages through screening programs has been demonstrated to save lives. However, only a few [cancer types](link) have screenings available today, and the majority of cancer deaths are from cancers for which there are no screening methods," said presenter Ben Ho Park, MD, Ph.D., Benjamin F. Byrd Jr. Professor of Oncology, director of the Vanderbilt-Ingram Cancer Center, and professor of medicine in the Division of Hematology and Oncology at Vanderbilt University Medical Center.

Blood-based MCED tests are under development for the early detection of multiple cancer types in the same [blood sample](link). However, detection of early-stage disease and cancers that shed small amounts of cfDNA into the blood is still challenging. "To achieve the greatest impact on patient outcomes, MCED tests will need to demonstrate strong detection of early-stage cancers and the ability to detect a wide range of cancers," Park added.

Aberrant DNA methylation is a key driver of cancer development, Park explained. "Different methylation patterns exist between cancerous and non-cancerous cells. In addition, there are shared methylation patterns across cancer types, as well as differentially methylated regions that are tissue specific. Therefore, MCED approaches based on methylation are suitable to both detect cancer and predict the tissue of origin of that cancer," Park said.

Park and colleagues are evaluating a novel genome-wide methylome enrichment platform that captures methylated cell-free DNA (cfDNA) molecules circulating in the bloodstream without chemical or enzymatic treatment, enabling sequencing of the whole methylome without the need to sequence the whole genome, thus making it cost-effective and

preserving the quality of the cfDNA.

The authors conducted a retrospective case-control study to assess the ability of this platform to detect 12 cancer types in a cohort of approximately 4,000 people that included individuals with newly diagnosed, treatment-naïve cancer and age- and gender-matched non-cancer controls. Approximately 50% of the cancer cases were early stage (stage I and II). For this initial analysis, the researchers reported findings from cross-validation within a subset of 1,903 samples in the training cohort to assess the performance of a machine learning algorithm designed to distinguish cases from controls, using 80% and 20% of the samples for training and testing, respectively.

Performance was assessed by a measure called the area under the curve (AUC), which estimated how accurately the test was able to differentiate cancer from non-cancer, with a score of 1 representing perfect discrimination.

In this initial development study, the test could detect cancer with an AUC of 0.94 for all cancer types and stages. Notably, the performance of the MCED platform to distinguish stage I and II cancers from controls remained high, with an AUC of 0.92 and 0.95, respectively.

The AUCs for detection of individual cancer types ranged from 0.89 to 0.99. Performance was also high for low-shedding cancers (including bladder, breast, renal, prostate, and endometrial cancer), which, combined, were distinguished with an AUC of 0.91.

"This platform allowed for a higher signal-to-noise ratio and led to increased performance in the more challenging applications where the cfDNA burden is the lowest. Cancers that shed a high amount of cfDNA had the best performance, but even cancers that are typically difficult to detect with cfDNA assays were detected with high performance in this

interim readout," Park said. "At this early stage in development, the robust detection of early-stage and low-shedding cancers with this genome-wide methylome enrichment platform is very promising."

According to the author, the key limitation of this study is that it utilized samples obtained from multiple biobanks. "There may be some confounding factors by biobank or population that may limit the performance of the test in this study," said Park. He also pointed out that this is an early development study, and additional studies will be needed to confirm these findings and before the blood test is ready for use in a clinical setting.

In addition, the performance of the platform was evaluated retrospectively in individuals with newly diagnosed cancer and matched non-cancer controls. "The findings will need to be validated in prospective studies," Park said.

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