Comprehensive validation of a cell-free DNA-based assay for multi-cancer detection: A Vietnamese longitudinal prospective cohort study (K-DETEK)

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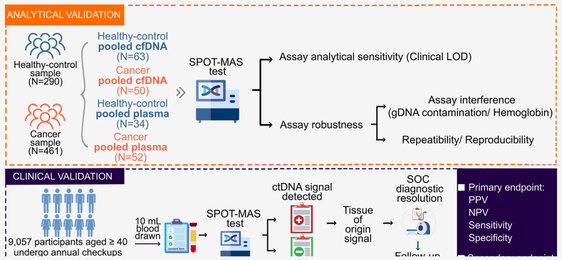
BACKGROUND

Blood-based multi-cancer early detection (MCED) has emerged as a promising method for enhancing early cancer detection efficiency and benefiting population health. However, the lack of evidence for their clinical utility across diverse populations has prevented their routine use. To address this, we conducted a comprehensive analytical and clinical validation of SPOT-MAS (Screening for the Presence Of Tumor by DNA Methylation And Size) - a non-invasive MCED test.

STUDY DESIGN

- Analytical validation was conducted on a retrospective cohort of healthy (n=290) and cancer-confirmed (n=461) individuals to determine the LOD, reproducibility, and potential interferents.
- K-DETEK (NCT05227261) is a multi-center prospective study to clinically validate diagnostic performance, recruiting 10,027 asymptomatic individuals aged 40 years or older from 75 major hospitals in Vietnam. Out of these, 9,024 eligible participants completed a follow-up period of 12 months.

Figure 1. Overview of Study



Clinical characteristics of 9,024 eligible participants

Risk classification		N = 9,024	%
High risk		3,814	42.27
Moderate risk		5,210	57.73
Age	Median	50	
	Min	40	
	Max	79	
Gender	Female	4,933	54.67
	Male	4,091	45.33
Liver infection (HBV/HCV)	Yes	1,478	16.38
	No	7,546	83.62
Alcohol consumptions	Yes	1,453	16.10
	No	7,571	83.90
Heavy smoking	Yes	1,466	16.25
	No	7,558	83.75
Diabetes	Yes	517	5.73
	No	8,507	94.27
Family history of cancer*	Yes	1,350	14.96
	No	7,674	85.04

* Participants who have first-degree relatives (FDR) diagnosed with two types of cancer at an age younger than 45, or being identified as carriers of mutations

LIMIT OF DETECTION OF SPOT-MAS ASSAY

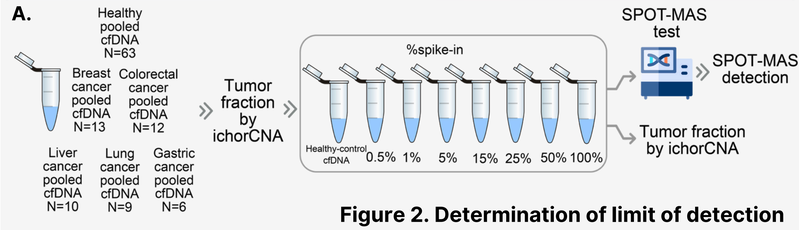
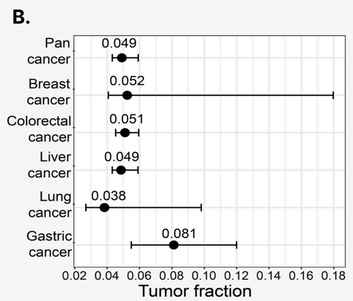


Figure 2. Determination of limit of detection



A. The workflow involves measuring tumor fraction using ichorCNA and determining the limit of detection (LOD) with SPOT-MAS test
B. LOD values based on TF of five cancer types. Error bars denote 95% confidence intervals.

SPOT-MAS demonstrates the capability to detect at least 50% of cancer samples with a specificity of 98% when the tumor fraction was 0.049 (95% CI: 0.043-0.059).

ROBUSTNESS OF SPOT-MAS ASSAY

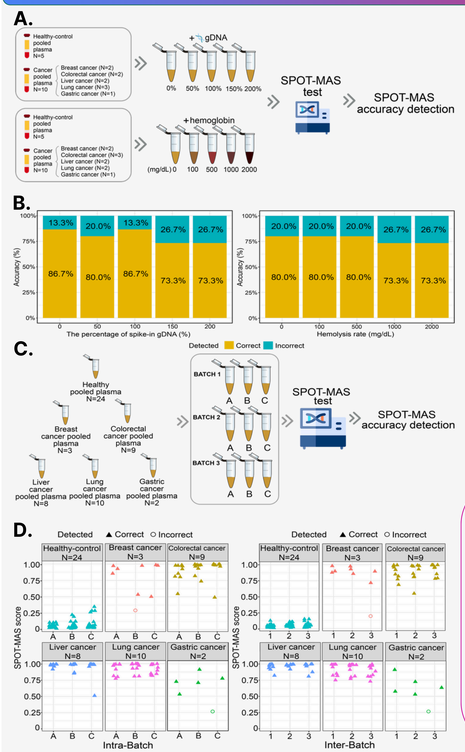


Figure 3: Impact of potential interferents & reproducibility – repeatability

A. Workflow describes the preparation of potential interferent study
B. Charts show the accuracy (%) in detecting cancer and healthy-control samples spiked with 5 different concentrations of genomic DNA (top) or hemoglobin (below)
C. Workflow examines reproducibility and repeatability of SPOT-MAS test
D. SPOT-MAS scores from intra-batch (left) and inter-batch (right)

- SPOT-MAS test remained robust even with hemoglobin contamination up to 500 mg/dL and genomic DNA contamination up to 100%
- Consistency in SPOT-MAS results was observed across both intra- and inter-batch analyses

EVALUATION OF CLINICAL PERFORMANCE OF SPOT-MAS TEST

Analysis of 9,024 eligible participants across a 12-month follow-up period demonstrated SPOT-MAS' ability to detect cancers in asymptomatic individuals with:

- **Positive Predictive Value (PPV) of 58.14%** (95%CI: 43.33- 71.62)
- **Tumor Origin Prediction Accuracy of 84.00%** (95%CI: 65.35-93.60)
- **Negative Predictive Value (NPV) of 99.92%** (95%CI: 99.83-99.96)

	N = 9,024 – n (%)
Cancer signal detected	43 (**0.48%**)
True positive	25 (**0.28%**)
Precancerous stage	08 (**0.09%**)
Early stage & non-metastatic stage	12 (**0.13%**)
Late stage	05 (**0.06%**)
False positive	18 (**0.20%**)
Cancer signal not detected	8,981 (**99.52%**)
True negative	8,974 (**99.44%**)
False negative	07 (**0.08%**)
Specificity	**99.80%** (**8,974/8,992**)
PPV for Cancer Signal Detection	**58.14%** (**25/43**)
NPV for Cancer Signal Detection	**99.92%** (**8,974/8,981**)
Tumor origin prediction accuracy	**84.00%** (**21/25**)

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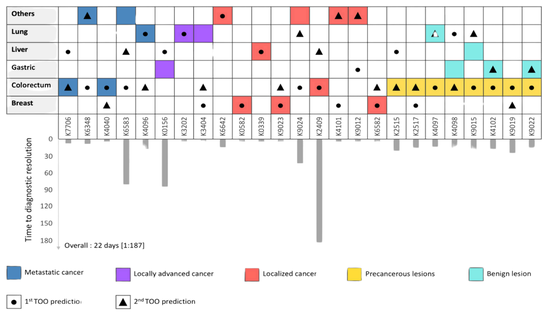
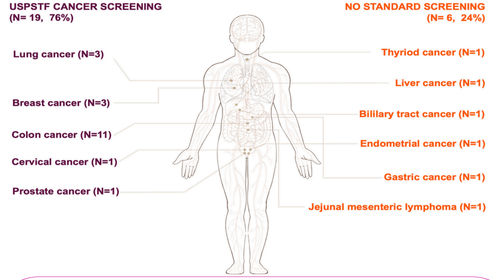
Figure 4: Analysis of diagnostic results of 25 true positive participants

Colored squares show the lesion-specific origin of 25 true positive cases, while circles and triangles denote the 1st and 2nd TOO prediction by SPOT-MAS. The intersections between colored squares and circles or triangles indicate the correct prediction of TOO by SPOT-MAS. The bar charts show the observed time from receipt of positive ctDNA results to final diagnosis confirmation.

Figure 4. Diagnostic Analysis of 25 true positive cases





SPOT-MAS can detect a wide range of early-stage cancers, including those lacking SOC screen

CONCLUSION

K-DETEK represents the most comprehensive and largest validation study of non-invasive multi-cancer early detection test in Asia to date with 10,027 asymptomatic participants. The study supports the utility of SPOT-MAS as a multi-cancer blood test for early cancer detection, particularly in low- and middle-income countries lacking nationwide cancer screening programs

FUTURE DIRECTION

Future randomized trial studies may further demonstrate the effectiveness of the test and impact on patient outcomes.