K-Track™: A Streamlined Personalized Assay to Detect Molecular Residual Desease in Solid Tumors

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Poster #407P

Nam H Vo[1], Van-Anh Nguyen Hoang[2], Anh-Tuan Nguyen[2], Hoang-Giang Vu[2], Lan N Tu[2]

[1]Department of Oncology, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh city, Vietnam

[2]Medical Genetics Institute, Ho Chi Minh city, Vietnam

MEDICAL GENETICS INSTITUTE HO CHI MINH CITY

GENE SOLUTIONS

BACKGROUND

- Minimal residual disease (MRD) refers to a small number of cancer cells that remain in the body after curative-intent treatment, causing relapse and metastasis. Current tumor biomarkers and imaging methods have limited sensitivity and specificity to monitor MRD for solid tumors.
- Circulating tumor DNA (ctDNA) in liquid biopsy has emerged as a promising biomarker to monitor MRD.
- ***Current MRD assays remain mostly inaccessible and unaffordable for patients in developing countries.***

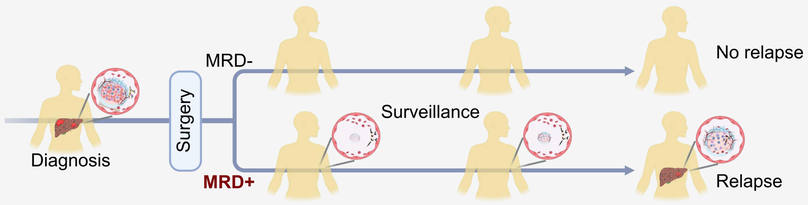


Figure 1. MRD in solid tumors. MRD, or the remaining cancer cells after curative-intent treatment, is the leading cause for relapse and metastasis.

METHOD

- Tumor-informed personalized ctDNA tracking assay
- Streamlined and cost-effective

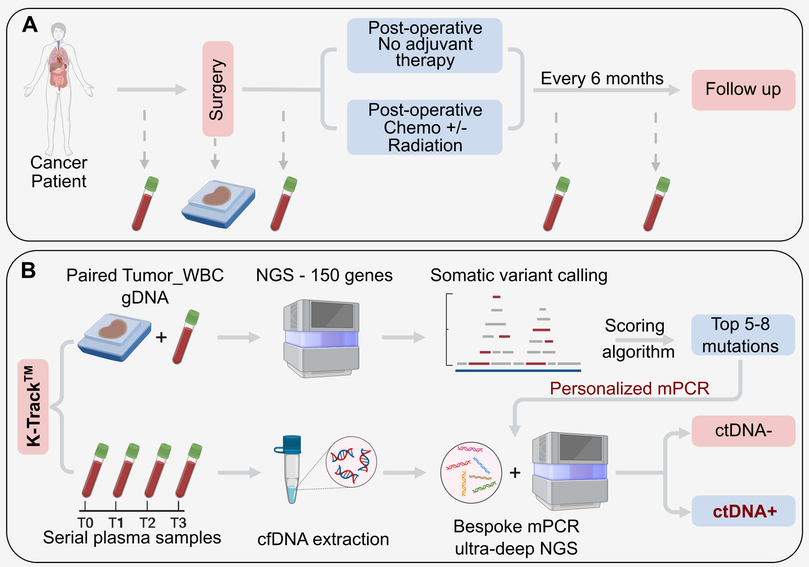


Figure 2. Study design and workflow of K-Track™ assay. (A) Cancer patients indicated for curative-intent surgery were enrolled. Serial plasma samples were collected before surgery and at scheduled visits. FFPE samples were also collected. **(B)** gDNA of paired FFPE and WBC samples were sequenced to identify all tumor-specific somatic mutations in 150 cancer-associated genes. Top 5-10 mutations were selected to monitor ctDNA presence in plasma samples by a multiplex PCR assay and ultra-deep sequencing at an average depth of 100,000X.

PRE-OPERATIVE DETECTION OF ctDNA

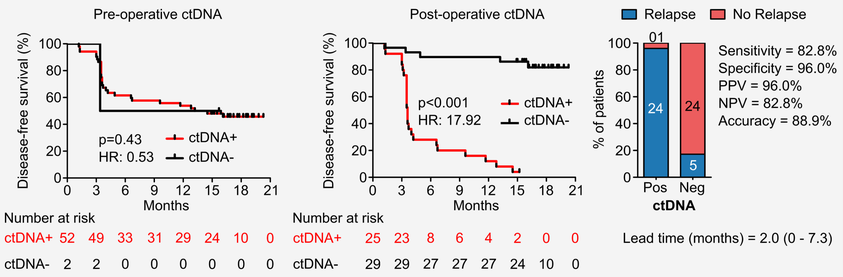
Table 1. Detection of ctDNA in plasma samples before radical surgery

Cancer type	Cohort (N)	Detection rate
Hepatocellular carcinoma (HCC)	60	96.6%
Colorectal Cancer (CRC)	115	85.2%
Breast Cancer (BC)	115	
HR(+), HER2(+/-), high risk*	70	40.0%
HR(-), HER2(+)	30	83.3%
HR(-), HER2(-)	15	80.0%
Non-small cell lung cancer (NSCLC)	55	62.0%
Gastric Cancer (GC)	94	45.7%
Ovarian Cancer (OC)	17	64.7%

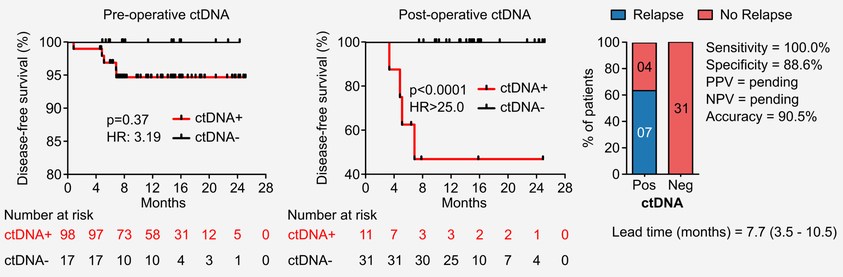
(*) High risk: ≥ 15% predicted risk of death within 10 years using ePREDICT V2.1, or tumor size T>5 cm, or N≥4 nodes, or N=1-3 nodes and at least one of the following: T>3 cm, grade 3, high genomic risk defined as Oncotype Dx Recurrence Score >26

PROGNOSTIC VALUE OF POST-OPERATIVE ctDNA

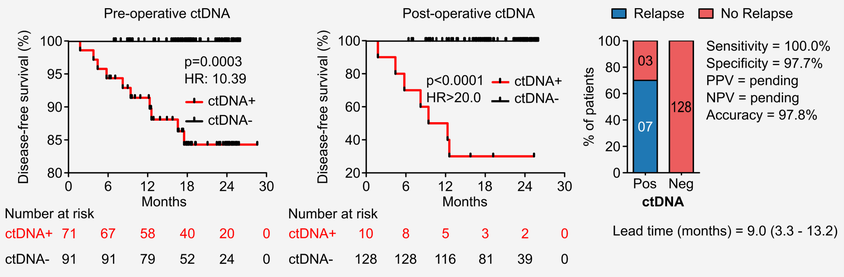
A – Hepatocellular carcinoma (HCC)



B – Colorectal Cancer (CRC)



C – Breast Cancer (BC)



D – Gastric Cancer (GC)

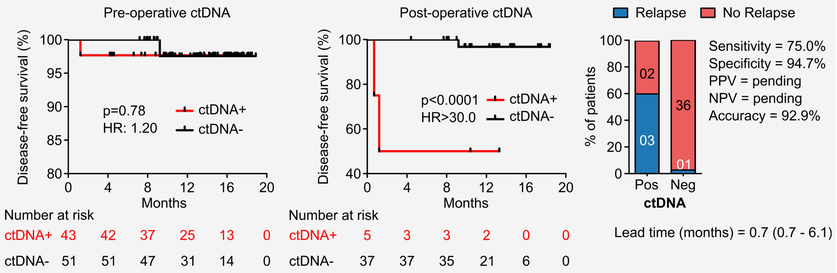


Figure 3. Prognostic value of post-operative ctDNA. (A-D) Kaplan-Meier plots showed that patients with ctDNA(+) after surgery were more likely to relapse than those with ctDNA(-). The sensitivity and specificity of ctDNA to detect relapse were shown in individual graph. This is an interim analysis as the study is ongoing.

ANALYTICAL VALIDATION

- Limit of detection at VAF ≥ 0.05%
- A sample is defined as ctDNA(+) if one of the mutations has VAF ≥ 0.05%

Standard samples — ■ Positive □ Negative

Gene	Mutations	0.50%	0.25%	0.10%	0.05%	0.00%
AKT1	E17K	■	■	□	□	□
BRAF	V600E	■	■	□	□	□
EGFR	L858R	■	■	□	□	□
KIT	D816V	■	■	□	□	□
KRAS	G12C	■	■	■	□	□
KRAS	G12D	■	■	■	□	□
KRAS	Q61H	■	■	■	□	□
NRAS	Q61R	■	■	■	■	□
PIK3CA	H1047R	■	■	■	■	□
EGFR	Del19	■	■	■	■	□
Variant-level Sensitivity (%)		100.0%	100.0%	80.0%	42.5%	0.83% Specificity: 99.17%
Sample-level Sensitivity (%)		100.0%	100.0%	100.0%	100.0%	0.83% Specificity: 99.17%

Figure 4. Analytical validation of K-Track™ assay. Sensitivity and specificity at variant-level and sample-level were determined by using Seraseq® ctDNA MRD Panel Mix (SeraCare, USA).

Ethical approval The study was approved by the institutional ethics committees of the University of Medicine and Pharmacy (#300/HDDD, #81/GCN-HDDD, #14/GCN-HDDD, and 164/HDDD), Thu Duc city Hospital (#17/HDDD), and Cho Ray hospital (# 1183/GCN-HDDD).

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CONCLUSION

- K-Track™ assay is streamlined and affordable with dual clinical utilities in residual cancer surveillance and actionable mutation profiling.
- The assay could lay foundation to empower precision cancer medicine in Vietnam and developing countries