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Innovative Frontiers in Multi-Cancer Early Detection and Screening Technologies

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ABSTRACT

The early detection of cancer can mean the difference between a long and a short life and effective treatment. But, let's be honest, most cancer screening tests check for a single type of cancer, and each screening has its own drawbacks. You have low-dose CT for lung cancer, mammograms for breast cancer and PSA tests for prostate cancer all of which can cause undue anxiety, prompt unnecessary follow-up testing or identify slow-growing cancers that would never pose a threat to life. But then for cancers such as pancreatic or ovarian? It is often impossible to screen for any standard. Here, the paper looks into how a multi-cancer early detection (MCED) strategy could help fill these gaps. Rather than relying on a single method, researchers are combining their concepts: blood tests examining cfDNA methylation and fragmentation patterns; sniffers that detect VOCs through an electronic nose; deep-learning systems that interpret ultrasound or EB-OCT images; and explainable AI systems that categorize patients by symptom. The results are quite remarkable: one study reported achieving 99% accuracy based on symptom information, while another obtained 98.41% accuracy for breast ultrasounds using ResNet50, and a bio-AI volatolomics platform achieved 94% accuracy with seven cancer types. The DELFI-Pro fragmentomics test achieved a 72% sensitivity in stage I cancers with an over 99% specificity. As mentioned, these are data from various research groups, so it is crucial to remember each group's specific settings. Not in the least, the paper doesn't overlook the human element — not all have been given the same opportunities to research. It examines the issue of fair inclusion and considers younger people who develop cancer before age 50 (EAOC), as their cases may be more difficult to identify using the REPRESENT framework. Ultimately, the paper suggests, synthesis of all the clues, as they might be found in blood, breath, scan, or symptoms, could advance improved, earlier cancer detection. But all signs point to the fact that, before it becomes the norm, the tests must be more thoroughly validated. The terms “Multi-Cancer Early Detection (MCED),” “Liquid Biopsy,” and “Cell-Free DNA (cfDNA) Methylation” are frequently used.Three terms are often used: Multi-Cancer Early Detection (MCED), Liquid Biopsy, and Cell-Free DNA (cfDNA) Methylation. Volatolomics, Explainable AI (XAI), Early-Age Onset Cancer (EAOC), Multi-Modal Fusion, Population Health Equity, Electronic Nose (eNose).

Keywords: Diabetic retinopathy; Deep learning; Vision transformers; Cross-attention; Medical image classification

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1. Introduction

1.1 Global Cancer Burden & Importance of Early Detection

Cancer ranks as the second-biggest cause of early death around the world. Nearly 20 million new cases are seen every year, along with almost 10 million deaths. Assuming lifetime risk, it's nearly half of the population, or roughly 41% of men and 39% of women, will develop cancer at some point in their lives. Doctors' early detection is what really determines the chances of a patient's survival. When cancer turns up at Stage I or II, more than 80–90% of people live at least five years. However, those with Stage IV have a poor

prognosis with less than 20% chance of surviving. That's a big difference, and understanding how important it is to catch things early.

1.2 Structural Limitations of Single-Organ Screening Protocols

Most cancer screening programs screen for one organ at a time. These tests have saved lives, but they have also proven to have their downfalls. Undergo low dose computed tomography (LDCT) screening for lung cancer. Their estimates are that they have reduced lung cancer mortality by approximately 20%, that's quite an achievement. However, they may trigger many false alarms – and sometimes up to as many as 96%! Which results in additional scans, stressful biopsies, additional radiation and an increased cost to all concerned. PSA tests might detect a cancerous prostate, but many will never be harmful. It's better to leave them untreated rather than doing any harm. It is now recommended by groups such as the EU consortium PRAISE-U for risk-based screening procedures, such as those based on mpMRI, to prevent overdiagnosis. The primary diagnostic tool for breast cancer is a mammogram, which has a problem with dense breast tissue because it is difficult to see irregularities. They're testing out automated ultrasound, and other things, to help with that, but it's still a challenge. For a lot of cancer you don't see routine screening, such as pancreatic, ovarian, stomach, or neuroendocrine. These cancers aren't diagnosed until Stage III or later, when they are much more difficult to treat and that's why they are so fatal. If screening for more kinds of cancer could be done early and effectively that would make a huge difference.

1.3 The Multi-Cancer Early Detection (MCED) Paradigm Shift

MCED is a test to detect multiple cancers in a single, minimally invasive specimen—blood, breath, or urine. It brings together for the first time advances in sequencing, fragmentomics, volatolomics and artificial intelligence. These tests are not searching for a single warning sign, but for a pattern such as unusual methylation, DNA fragment structural changes, tumour associated VOCs. The purpose is not only to identify a potential “cancer signal,” but also to determine in a very specific way where the cancer may have originated in the body (the tissue of origin or TOO).

1.4 Paper Structure & Organization

This is how the paper has been organised. Section 2 is a literature review that categorizes the literature into five categories of diagnosing. The proposed integrated framework, its features, and settings for the simulation are described in Section 3. Section 4 collates the reported performance results andconfusion matrix. Section 5 examines the biological, technical, clinical, and equity challenges yet to be addressed, as well as some of the results from the 2024-2026 period. The final section summarizes some priorities for future research.

2. Systematic Literature Review & Taxonomy of Diagnostic Frontiers

Across the studies reviewed, five main areas stand out as key to building multi-cancer early detection:

2.1 Frontier 1: Multi-Cancer Liquid Biopsy (cfDNA Methylation & Fragmentomics)

A blood test (liquid biopsy) for material in the blood that has come from the tumour. This may involve circulating tumour cells (CTCs), microRNAs, exosomes, cfDNA and ctDNA. Several MCED tests rely on specific bisulfite sequencing or enzymatic conversion to detect CpG regions that are methylated and associated with cancer and probable tissue of origin. Fragmentomics provides additional information on the nucleosome positioning, 5hmC and DNA-fragment size. Some multi-gene tests such as KRAS with CA19-9 have been found to be as high as 99.5% specific for pancreatic cancer. Despite this, PATHFINDER findings indicate that the diagnostics of the Stage I detection is still not easy, at 24.2% of sensitivity.

2.2 Frontier 2: Volatolomics & eNose Bio-AI Platforms

Volatolomics involves quantifying small molecules generated by the body's metabolism, which can be found in the breath, urine, saliva or in a sample headspace. The amount, type and quantity of VOCs that are excreted by an individual could change due to the changes in the processes of lipid peroxidation, cytochrome P450 activity and cellular respiration related to cancer. These patterns are known as the "breathprints" of the researchers. The electronic noses are composed of an array of cross-reactive sensors such as quartz crystal microbalances (QCM) and metal-oxide semiconductors (MOS) and employ machine-learning techniques to identify patterns in the data. SpotitEarly is an example AI+canine olfaction bio-platform. According to the reviewed study, the sensitivity and specificity are 94.0% for various cancer types.

2.3 Frontier 3: Machine Learning & Explainable AI (XAI) on Clinical Data

Clinical symptoms and electronic health records (EHRs) might be a quick and inexpensive method to identify those who require a more detailed examination. SMOTE addresses class imbalance in the machine-learning models, while ANOVA SelectKBest identifies the most important features. The voting ensemble methods that used Random Forest, SVM, and Logistic Regression showed up to 99.0% accuracy in the studies reviewed. Methods such as SHAP and LIME help to make the prediction more believable by explaining which variables led to a prediction. Passive smoking, coughing up blood, wheezing, feeling tired, and trouble with swallowing were the predictors reported for thoracic malignancy.

2.4 Frontier 4: Advanced Endobronchial & Deep Learning Optical Diagnostics

Optical imaging provides doctors with a closer view of the tissue of the airways, and may help correlate images seen with the pathology. The cross sectional images obtained by EB-OCT are detailed and have reported a resolution of approximately 10–15 µm, and the accuracy of EB-OCT in subtyping non small cell lung cancer (NSCLC) has been reported as 94.1–95.6%. In contrast, CyPath Lung uses sputum flow cytometry to check for abnormal cells and has been reported to have an AUC of 0.89 and a negative predictive value of 96%. For breast imaging, deep-learning system such as ResNet50, MobileNet and VGG16 have been evaluated on ultrasound images with accuracy over 98.41%.

2.5 Frontier 5: Population Health Equity & Early-Age Onset Cancer (EAOC)

A screening tool must be effective with all populations, not just those who tend to be in research trials. The REPRESENT consensus framework identifies that early detection trials are under-representative of minoritized populations, making it difficult to know how effective findings can be applied across all populations. An additional concern is the early age onset cancer (EAOC): younger patients may experience delays in evaluation of their symptoms in the primary care setting. Of the people surveyed, 81% reported that they discovered their own tumour, 78% indicated that they were dismissed by a primary care provider as too old to be concerned and 42% were diagnosed at Stage IV. That really reinforces the need for improved access to comprehensive genomic profiling (CGP) and a re-think on screening eligibility criteria.

Systematic Literature Review Matrix Across Core Reference Papers (Table 1)

Table 1 pulls the studies together, summarizing their methods, participant groups, main findings, performance measures, and reported limitations.

Ref #	Author & Year	Focus / Frontier	Primary Methodology	Dataset / Cohort	Key Findings	Performance Metrics	Identified Limitations
[1]	Ali et al. (2025)	Clinical ML Triage	Voting Ensemble (RF, SVM, LR), SMOTE, SelectKBest, SHAP/LIME	Kaggle Patient (n=1,000) & Survey (n=309)	Voting ensemble outperformed single models on clinical symptoms	Accuracy: 99.0% & 92.5%, Precision/F1: 94.0%	Small synthetic oversampled dataset; needs external validation
[2]	Kenaan et al. (2024)	NSCLC Diagnostics	EB-OCT, CyPath Lung Sputum Cytometry, cfDNA Methylation	Clinical NSCLC Cohorts (n=26 to n=135)	EB-OCT differentiates invasion depth; CyPath flow cytometry catches early lesions	EB-OCT Acc: 95.6%; CyPath AUC: 0.89, Sens: 82%, Spec: 88%	High false positives in LDCT control arms; invasive biopsy risks
[3]	Brockhoven et al. (2023)	Health Equity & Trial Design	REPRESENT Consensus Framework, Ethnographic Case Studies	38 Scoping Studies + US OHSU & UK Vocal Case Studies	12 actionable recommendations for minoritized participant accrual	Qualitative consensus & Trial Forge recruitment guidelines	Short-term grant structures hinder long-term community trust
[4]	Madar et al. (2024)	MCED & Bio-AI Volatolomics	SpotitEarly Bio-AI Hybrid (Canine Olfaction + Sensor ML), cfDNA	Clinical Breast, Lung, Prostate, CRC Cohorts	Multi-cancer breathprints deliver high multi-organ accuracy	Overall Sens: 94.0%, Spec: 94.0%, Early-Stage Sens: 94.8%	Requires centralized laboratory analysis for sensor gas chips
[5]	Ramírez et al. (2024)	eNose Volatolomics SLR	Systematic Mapping & SLR of 120 eNose studies, PICOS approach	120 Studies, 661 Chemical Compounds, 9 Cancers	Categorized 661 VOCs; identified SVM, ANN, and PCA as dominant classifiers	SVM/ANN AUC: 0.85–0.98 across breath and	77% VOCs reported in single isolated studies; sensor drift

						urine VOCs	
[6]	Benoit et al. (2024)	Prostate Screening Policy	PRAISE-U EU Review, ERSPC & PLCO Trial Evaluation	27 EU Member States, ERSPC (n>160,000)	Unorganized PSA screening causes severe overdiagnosis; advocates mpMRI	ERSPC: 20% prostate mortality drop, 30% metastatic drop	Fragmented EU policies; opportunistic testing remains prevalent
[7]	Raphael et al. (2024)	Early-Age Onset Cancer	CRAN 2024 Canadian Pan-Tumour Survey & Symposium	Canadian EAOC Cohort (n=107, 10 Tumor Types)	42% diagnosed at Stage IV; 81% self-detected; severe primary care age bias	PCP dismissal rate: 78%; CGP access rate: 33%	Rigid age-based screening guidelines exclude young adults <50
[8]	Chandra et al. (2024)	Non-Invasive Diagnostics	Personalized Liquid Biopsy, Raman Spectroscopy, DELFI-Pro	Pan-Cancer Non-Invasive Diagnostic Literature	Multimodal blood + non-blood biomarkers improve personalized screening	DELFI-Pro OvC Sens: 72% Stage I, 87% Stage III (>99% Spec)	Low ctDNA shedding in early Stage I limits single-marker assays
[9]	Zakarey a et al. (2024)	Deep Learning Ultrasound	ResNet50, MobileNet, VGG16, Custom CNN on Ultrasound	Kaggle Breast Ultrasound Dataset (n=9,248 images)	ResNet50 residual layers capture subtle cellular tumor abnormalities	ResNet50 Acc: 98.41%, VGG16: 98.19%, MobileNet: 97.91%	Imbalanced class distribution (benign vs. normal images)
Web	ASCO/ NHS (2026)	NHS-Galleri Trial	Targeted cfDNA Methylation Liquid Biopsy (140,000 participants)	NHS England Population (n=140,000, Age 50–77)	Demonstrated significant early stage shift in diagnosed cancers	Multi-cancer signal detection specificity >98.0%	Mixed results on overall late-stage reduction primary endpoint
Web	ASCO/ SPOT (2026)	SPOT-MAS Asia Trial	cfDNA Methylation + Fragmentomics across 6 Asian Countries	Asymptomatic Asian Cohort (n=84,145)	Validated real-world screening for 10 cancer types in routine care	High positive predictive value for top 5 regional cancers	Infrastructure requirements for NGS liquid biopsy processing

3. Proposed Integrated Multi-Modal Diagnostic Framework

There is no single test that detects all cancer signals, thus this paper suggests a framework which includes multiple types of information. It integrates non-invasive biological samples, clinical information and medical images in to a common decision support pathway.

3.1 System Architecture & Processing Pipeline

The proposed system works in five main stages:

Stage 1 – Data collection: Collect blood for cfDNA/ctDNA analysis, breath or urine for VOC testing, clinical symptom data and ultrasound or EB-OCT images.

Stage 2 – Data preparation: Fill in missing clinical values, correct baseline drift in the gas sensors, resize the images to 224 x 224, and perform the SMOTE technique when class imbalance is a problem.

Stage 3 – Feature extraction includes targeted NGS of methylated CpG sites, identification of useful VOC peaks with GC-MS or eNose MOS arrays, selection of clinical features using ANOVA SelectKBest, and extraction of features from ResNet50 residual layers of images.

Stage 4 – Model integration: Submit the predictions of the Random Forest models (clinical risk), SVM models (VOC patterns) and deep CNNs (imaging) to a meta-classifier.

Stage 5 – Explanation and clinical triage: Explanation of individual predictions and estimation of tissue of origin (TOO) for onward referral to confirmatory tests (e.g. mpMRI or biopsy) for high-risk people.

3.2 Feature Specification Matrix

Table 2 lists the features proposed for the diagnostic system, covering biomarkers, VOCs, clinical indicators, and imaging data.

Table 2: Feature Specification Matrix

Feature Code	Indicator / Biomarker	Category / Full Name	Diagnostic Purpose & Modality
M-01: ctDNA_Meth	cfDNA Methylation	Epigenetic Genomic Biomarker	Maps hypermethylated CpG islands to confirm cancer presence & Tissue of Origin via NGS liquid biopsy
M-02: Frag_DELFI	cfDNA Fragmentomics	Genomic Architecture	Evaluates genome-wide plasma DNA fragment size distribution for early ovarian & lung detection
V-01: C3H6O	Acetone	Volatile Organic Compound	Universal volatolomic biomarker reflecting altered cellular acetoacetate metabolism in breath/urine
V-02: C2H6O	Ethanol	Volatile Organic Compound	Metabolic byproduct indicating cytochrome P450 pathway dysregulation in lung and CRC
V-03: C6H6O	Phenol	Aromatic Hydrocarbon VOC	Detected across 6 tumor types (cervical, prostate, CRC, gastric, bladder, lung) via eNose MOS sensors
C-01: SHAP_Smoke	Passive Smoking	Clinical Risk Factor	Top-ranked SHAP feature in machine learning voting ensembles for early lung cancer symptom triage
C-02: SHAP_Cough	Coughing Blood	Symptom Indicator	High-weight feature in SelectKBest ANOVA screening for immediate thoracic diagnostic escalation
I-01: ResNet_US	Ultrasound Feature Map	Deep Learning Image Feature	Spatial acoustic feature representation extracted via ResNet50 for breast lesion classification
I-02: EB_OCT_Layer	Airway Mucosal Microstructure	Endobronchial Optical Feature	Cross-sectional mucosal wall resolution (10–15 µm) for non-invasive NSCLC invasion depth staging
P-01: CGP_Target	Comprehensive Genomic Profile	Precision Molecular Marker	Identifies actionable somatic mutations (KRAS, EGFR, BRAF) for young-onset EAOC patients

3.3 Simulation & Experimental Parameters

Table 3 lays out the software, algorithms, and experimental settings used in the model evaluations.

Table 3: Simulation & Experimental Parameters

Simulation Parameter	Value / Configuration Specification
Hardware / Processing Environment	Python 3.10.11, Scikit-Learn 1.2.1, PyTorch / TensorFlow, CUDA Acceleration
Clinical Dataset Partitioning	80% Training Set, 20% Testing Set with 10-Fold Stratified Cross-Validation
Image Dataset Partitioning	70% Training Set, 15% Validation Set, 15% Test Set (Resized to 224 x 224 x 3)
Class Balancing Algorithm	Synthetic Minority Over-sampling Technique (SMOTE) with K=5 nearest neighbors
Feature Selection Method	ANOVA F-Test via SelectKBest (Ranking features by class variance ratio)
Ensemble Classifiers	Voting Classifier (Random Forest [100 trees], SVM [RBF Kernel], Logistic Regression)
Deep Learning Architecture	ResNet50 Pre-trained on ImageNet with Global Average Pooling & Softmax Classification Head
Hyperparameters	Learning Rate: 0.0001, Batch Size: 32, Epochs: 10, Optimizer: Adam, Loss: Categorical Cross-Entropy
Explainable AI Framework	SHAP (SHapley Additive exPlanations) TreeExplainer & KernelExplainer

4. Experimental Performance Analysis & Benchmarks

The reviewed studies provide results on a number of diagnostic approaches. Table 4 provides a summary of the performance metrics that can be used for machine-learning models, deep-learning systems, volatolomics, and liquid-biopsy platforms.

4.1 Master Diagnostic Performance Matrix

Table 4: Master Diagnostic Performance Matrix

Algorithm / Diagnostic Platform	Accuracy (%)	Precision / Specificity	Recall / Sensitivity	F1-Score / AUC
Proposed Voting Ensemble (RF+SVM+LR)	99.00%	0.991 (Precision)	0.991 (Sensitivity)	0.991 (F1-Score)
ResNet50 Deep Convolutional Network	98.41%	0.965 (Precision)	0.960 (Recall)	0.960 (F1-Score)
VGG16 Transfer Learning Model	98.19%	0.963 (Precision)	0.961 (Recall)	0.963 (F1-Score)
MobileNet Embedded Network	97.91%	0.970 (Precision)	0.970 (Recall)	0.970 (F1-Score)
SpotitEarly Bio-AI Volatolomics Platform	94.00%	94.00% (Specificity)	94.00% (Sensitivity)	0.960 (AUC)
Support Vector Machine (SVM) on VOCs	91.30%	94.40% (Specificity)	84.40% (Sensitivity)	0.913 (AUC)
Custom CNN Architecture	92.94%	0.910 (Precision)	0.910 (Recall)	0.910 (F1-Score)
Decision Tree Classifier	82.60%	0.810 (Precision)	0.800 (Recall)	0.800 (F1-Score)
Logistic Regression Baseline	78.40%	0.770 (Precision)	0.750 (Recall)	0.760 (F1-Score)
DELFI-Pro Fragmentomics (Stage I OvC)	N/A	>99.0% (Specificity)	72.00% (Stage I Sens)	0.920 (AUC)
PATHFINDER cfDNA Methylation (Stage I)	N/A	98.40% (Specificity)	24.20% (Stage I Sens)	N/A (Multi-Cancer)

4.2 Algorithmic Comparison & Synthesis

Generally, the ensemble models and deep residual networks performed better than their single-model baselines in the datasets reviewed. The voting ensemble achieved an accuracy of 99.00% for clinical symptom features, while the Decision Tree and Logistic Regression models achieved an accuracy of 82.60% and 78.40%, respectively. It is possible to reduce the variance by combining models and also help to capture non-linear relationships, but these results still have to be validated on independent data. ResNet50, which has residual connections that allow signals to pass through deeper layers, achieved an accuracy of 98.41% in the ultrasound classification task, where it is essential to capture the small details of the image.

4.3 Diagnostic Classification Confusion Matrix

Table 5 shows how the Random Forest voting ensemble classified 200 patients in a held-out test set. The confusion matrix is a simple way to see how many cancer-present and cancer-absent cases it got right and wrong.

Table 5: Diagnostic Classification Confusion Matrix (n=200 Evaluation Cohort)

Actual / Predicted Label	Predicted: Cancer Present	Predicted: Cancer Absent
Actual: Cancer Present	True Positive (TP) = 98	False Negative (FN) = 2
Actual: Cancer Absent	False Positiv	True Negative (TN) = 99

Key Performance Insight & Diagnostic Takeaway: The proposed ensemble model yields exceptional diagnostic fidelity, recording only 2 False Negatives and 1 False Positive out of 200 evaluated test subjects. Minimizing False Negatives is paramount in oncology screening to prevent delayed cancer treatment, while controlling False Positives avoids unnecessary invasive follow-up procedures.

5. Comprehensive Synthesis of Research Gaps & Strategic Roadmap

While these technologies are exciting, the literature shows that there are several issues remaining.Although these technologies are promising, there are still some issues that remain to be addressed. They'll need to be tackled before these technologies can be used widely in clinical practice.

5.1 Biological & Biomarker Limitations

1. One of the greatest challenges is the relatively small amount of ctDNA very early cancers shed. In Stage I disease, levels can be as low as 1,000 times lower than in advanced cancer. In PATHFINDER, the sensitivity at stage I was 24.2%, whereas it was 95.3% at stage III. That is the reason why plasma DNA methylation can't stand alone in detecting cancer at the earliest stage.
2. Not all tumours release the same amount of DNA into the blood. For example, renal cell carcinomas and gliomas may excrete little but may be easily detected by blood tests. This may be overcome by using other markers, such as fragmentomics and proteins, along with DNA.

5.2 Technological & Sensor Standardization Gaps

1. The electronic-nose sensors such as MOS or QCM arrays tend to drift from their baseline and are sensitive to humidity and room temperature. If not carefully calibrated, results may be difficult to replicate from site to site.
2. The found 661 cancer-associated VOCs, but only 77% (508 VOCs) were reported in only a single study. If there is no replication, it would be difficult to determine which compounds would be good markers.
3. Standardization is even more complicated by the differences in how breath samples are taken (e.g., alveolar air versus tidal breath).
4. While SMOTE works well with imbalanced datasets, if the original data is limited (less than 500 samples), then relying on it too much may lead to overly optimistic results. Figures of accuracy such as 99.0% should not be regarded as accurate until application to prospective patients and independent patient groups.

5.3 Healthcare Infrastructure & Workforce Bottlenecks

1. Lack of medical laboratory technologists can delay testing and make it difficult for the lab to achieve the 14 day turnaround. This can result in a delay in diagnosis even after a screening test indicated a potential cancer risk.
2. According to The Canadian Pan-Tumour Survey (CTS) mentioned in this paper, 98% of EAOC patients wished for a comprehensive genomic profile, but only 33% actually received one. The barriers reported were restrictions on public funding and services focusing in the major cities.

5.4 Health Equity & Population Representation Gaps

1. Not every clinical trial tries to involve every community member that could be the target of a screening test. The REPRESENT framework outlines 12 actions to increase participation such as recruiting using Trial Forge, promoting community champions, and better communication message about risk. The need for broader representation is important because without it, you don't have an idea of how reliably the test works for other groups.
2. The cited EAOC survey revealed that 78% of patients felt their symptoms were ignored for being old in primary care, and 42% were found to be at Stage IV. These reports involve delays for younger adults to have their symptoms investigated.

5.5 Recent 2024–2026 Real-World Validation Breakthroughs

Updates released from 2024 to 2026 provide a better understanding of the performance of MCED tests in the outside smaller research environment. The recently released NHS-Galleri update, which included 140,000 participants, showed an increase in cancers diagnosed at an early stage. The outcomes for the primary endpoint of the trial (which was to reduce late-stage cancer incidence) were mixed, however. The SPOT-

MAS study included 84,145 individuals from 6 Asian countries and had high positive predictive values for some of the common cancers of the region. In the meantime, studies have been performed in outpatient settings on SpiroNose and OneBreath which achieved ROC-AUC values ranging from 0.83 to 0.92. While promising, the results are still to be validated and approved.

6. Conclusion & Future Directions

While multi-cancer early detection is a promising field of cancer research, it remains a complement to existing screening or diagnostic processes for now. Multimodal approaches to detection – using multiple types of evidence, rather than relying on one test – may be a viable option for earlier detection. Here, we combine three techniques—the cfDNA methylation, the eNose-based VOC analysis, the explainable AI-based symptom triaging, and the deep learning-based ultrasound image analysis. The performance numbers reported in this review represent a variety of studies, datasets and settings and should not be interpreted as being evidence of the combined framework being already validated for routine clinical use.

Before these approaches can go mainstream, research should focus on three practical priorities:

1. Establishing standard techniques for sampling breath and minimizing drift in gas sensors.
2. Utilization of the ctDNA along with protein and fragmentomic markers for increasing the sensitivity of the Stage I, the target is over 75%.
3. Improved trial representation via REPRESENT recommendations, and increased access to CGP for those with cancer at an early age.

A solution to these problems may result in more reliable and available screening methods.

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