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CLARION

Point-of-Care Breath Diagnostics

Breath Analysis at the Point of Care for Non-Small Cell Lung Cancer Detection

In collaboration with
H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida

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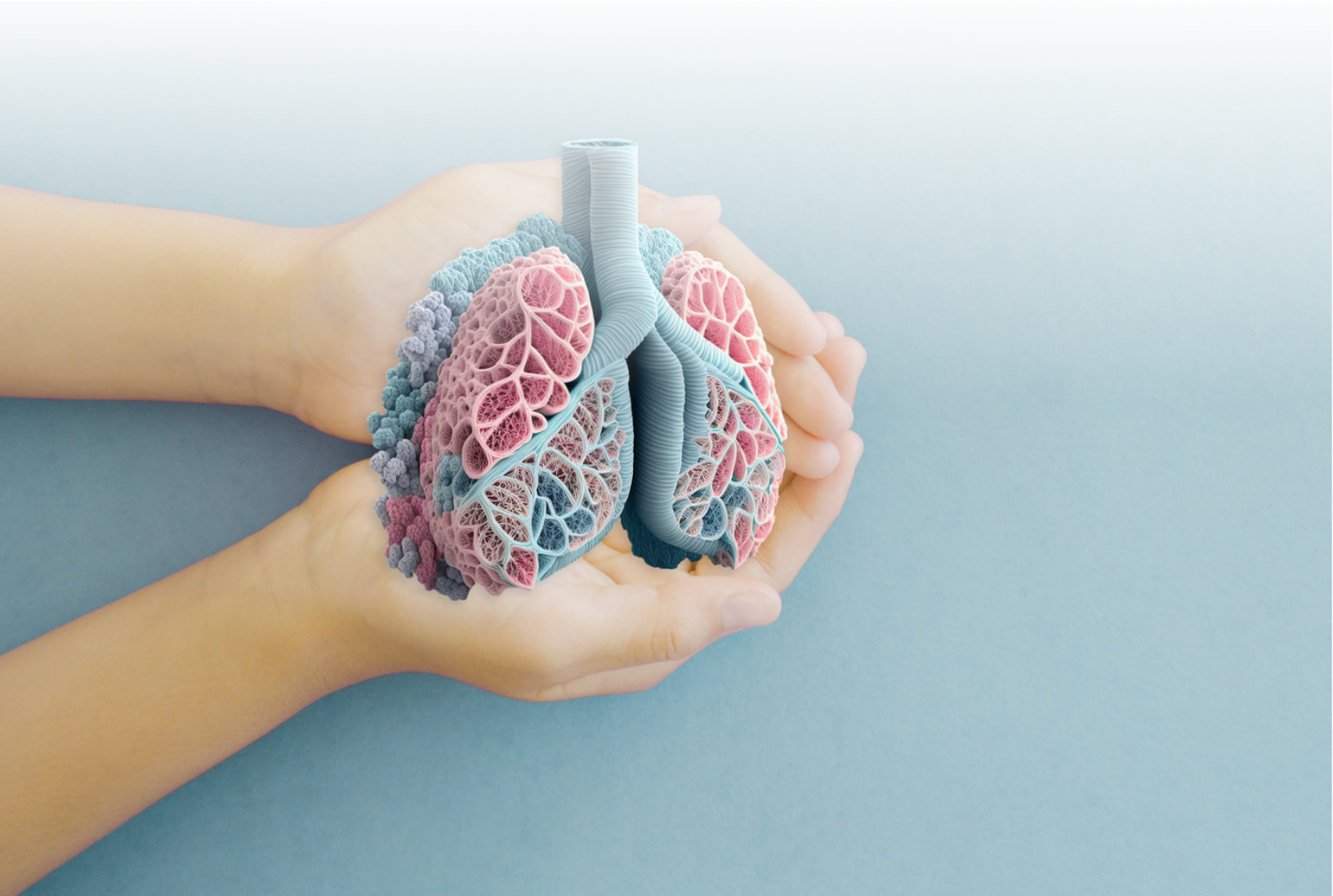


Executive Summary

CLARION, a point-of-care breath diagnostics platform, matched a laboratory high-resolution mass spectrometer analysis and detected early-stage non-small cell lung cancer.

Detect-ION deployed the CLARION breath diagnostics platform at the H. Lee Moffitt Cancer Center & Research Institute in Tampa, Florida, in an internally funded clinical pilot: to our knowledge, the first head-to-head clinical evaluation of a point-of-care gas chromatography mass spectrometry (GC-MS) platform against a laboratory high-resolution mass spectrometry (HRMS) reference for the detection of non-small cell lung cancer (NSCLC) from 2 minutes of exhaled breath collection and spontaneous analysis.

Between December 2025 and June 2026, paired breath specimens were collected from 40 treatment-naive patients with pathologically confirmed NSCLC and 25 lung-cancer-screening-eligible controls. Every participant provided two samples from the same visit: one captured directly onto CLARION at the point of care, and one collected on a sorbent tube for benchtop HRMS analysis. Diagnostic classifiers were built independently for each platform, so the two measurement systems could be compared on the same patients, on the same day, against the same histopathologic ground truth.

CLARION resolved 103 volatile organic compounds (VOCs) across the breath specimens. HRMS resolved more than 900. Despite that difference of nearly an order of magnitude in VOCs detected, the two platforms performed the same: CLARION distinguished NSCLC cases from controls with an area under the receiver operating characteristic curve (ROC-AUC) of 0.864, against 0.863 for HRMS. The pattern held for early-stage disease, where detection matters most clinically (0.854 versus 0.841), and across histologic subtypes.
Three findings carry strategic weight and promising paths forward.

First, a point-of-care device delivered laboratory-equivalent diagnostic performance on a real clinical question. Analytical breadth is not the operative currency in breath diagnostics; resolving the right VOCs reproducibly is. **Second**, the early-stage NSCLC VOC signal was detectable by the point-of-care device. Breath tests are most valuable exactly where imaging is least decisive, and CLARION's early-stage performance was indistinguishable from the laboratory HRMS reference. **Third**, the discriminating signal is chemically identified rather than a device-specific pattern. Seven named, library-matched VOCs form the NSCLC "VOC panel", most of them with prior support in the peer-reviewed breath literature. A signature made of identified molecules can be validated once and deployed across sites and devices, which is the precondition for a regulatorily viable breath diagnostic.

Together, these results establish the evidentiary foundation for a non-invasive, point-of-care breath test that adds independent, biology-based discrimination to the lung cancer pathway: at the indeterminate pulmonary nodule first, and ultimately across screening, diagnosis, treatment response, and surveillance.

Problem Statement

Lung cancer remains the leading cause of cancer death in the United States, and non-small cell lung cancer accounts for roughly 85% of diagnoses[1]. Outcome is dominated by a single variable: stage at diagnosis. Five-year relative survival is approximately 67% for localized NSCLC and about 12% once disease has reached distant sites[2]. Because most lung cancers are still found late, overall five-year survival remains below 25%. The clinical objective is therefore simple to state and difficult to achieve: find the disease earlier, in more people, without harming the many who do not have it.

Lung cancer screening with low-dose computed tomography (LDCT) is the tool built for that job, and it works. Randomized evidence in the United States and Europe shows that LDCT screening reduces both all-cause and lung-cancer-specific mortality[3], and screening is now guideline-driven standard of care for high-risk adults. Yet its real-world impact is constrained by two persistent gaps.

Gap 1: Most eligible people are never screened.

As of 2024, an estimated one in five screening-eligible individuals in the United States had received lung cancer screening, with only 18.7% reporting being up to date[4]. LDCT requires a fixed imaging facility, a referral, a scheduled appointment, and a radiology workflow. Every one of those dependencies is a place where an eligible patient falls out of the funnel, and the losses fall hardest on rural, uninsured, and underserved populations. Eligibility criteria themselves exclude a meaningful share of people who go on to develop lung cancer.

Gap 2: The people who are screened generate an enormous benign workup burden.

In the National Lung Screening Trial, 39.1% of participants in the LDCT arm had at least one positive screen, and 96.4% of those positives were false positives[3,5]. Under the Lung-RADS classification system, false-positive rates run at 12.8% at baseline and 5.3% on subsequent screens, and positive predictive value across the broader screening literature ranges as low as 3.3%[6]. A positive screen is not a diagnosis; it is the discovery of a nodule whose nature is unknown.

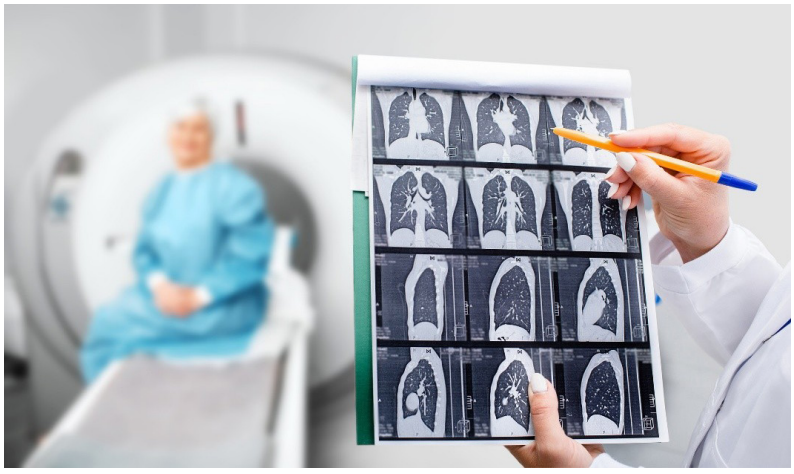


Figure 1. The two gaps in lung cancer screening. Most eligible individuals are never screened, and most of those who screen positive do not have cancer. A non-invasive point-of-care test addresses both losses: it extends reach where LDCT infrastructure does not, and it adds independent molecular evidence where imaging is indeterminate.

That is a real cost. Guidelines route an indeterminate pulmonary nodule into watchful waiting, repeat and diagnostic imaging, PET/CT, and for a fraction, transthoracic biopsy or surgical resection. Those invasive procedures carry genuine morbidity, cost, and anxiety, and a meaningful share of them are ultimately performed for benign disease[5,7]. Roughly 29% of nodules in the 8 to 30 mm indeterminate range turn out to be benign lesions.

The system concentrates procedural risk on people who never had cancer, while doing nothing to accelerate the minority who do. Neither radiographic risk models nor imaging alone resolves this. They narrow the probability; they do not settle it. Today, only biopsy settles it[7]. The gap in the pathway is a non-invasive test that adds independent, biology-based discrimination at the point of care, before a nodule is committed to invasive workup.

The Meaningful Clinical Intervention

Exhaled breath carries a continuously renewed record of systemic and pulmonary biochemistry. Tumor-associated metabolism, notably oxidative stress and the lipid peroxidation that produces aldehydes and specific hydrocarbons, alters the volatile organic compounds a patient exhales, and breath VOC profiling has repeatedly been shown to signal lung cancer[8-10]. The specimen requires no needle, no sputum, no cold chain, and no laboratory. It can be collected in a clinic hallway, repeated as often as clinically useful, and produced by a patient who would never consent to a biopsy.

The reason breath has not translated is not the absence of signal. It is the absence of a standardized measurement engine that can read the signal reliably outside a laboratory. Clinical value in this field is bounded by specificity: a signal that cannot be separated from a chemically similar background produces false positives, and false positives are precisely the problem breath is being asked to solve. This is why GC-MS is the right foundation. It separates VOCs chromatographically and then identifies each one by its mass spectrum, matched against standard reference libraries[11,12]. Because it yields chemical identification and quantitation rather than an instrument-specific pattern, a GC-MS signature validates once and deploys everywhere. That transferability is what makes a breath diagnostic regulatorily tractable.

The unmet need, then, is narrow and concrete: adapt the gold standard to the breath matrix at the point of need, without sacrificing its performance.

The Instrument Problem

The biology is real, but it is subtle. A lung tumor does not switch on a single marker; it shifts the relative abundance of dozens of endogenous VOCs, most of them present at parts per trillion, inside a matrix that also carries hundreds of exogenous ones. Individual studies have reported promising discrimination on exactly that signal for four decades. Almost none of it has reached clinical workflow, for three reasons.

First, the instrument that can read the signal does not leave the laboratory. Benchtop GC-MS, the gold standard for VOC analysis, is bulky, costly, and bound to vacuum systems, carrier gas, and a trained operator. The specimen has to travel to the instrument, so the measurement happens days after the breath and somewhere other than the clinic.

Second, the instruments that do leave the laboratory cannot read the signal. Sensor arrays, electronic noses, GCs, and ion-mobility spectrometers (IMS) buy logistical simplicity but give up analytical performance.

They report a composite response pattern rather than identified, quantified VOCs, and lack the sensitivity and specificity to separate a subtle endogenous shift from a chemically similar background. A pattern that cannot be assigned a structure also cannot be transferred to the next instrument or the next site.

Third, the laboratory result itself, the one generating the promising literature, rests on protocols that were never standardized: not specimen collection, not analytical method, not data analytics. The tolerances here are unforgiving. A VOC present (e.g., *toluene*) at 10 parts per trillion in a one-liter breath sample amounts to roughly 40 picograms, and the case-control differences that carry diagnostic weight are often a fraction of that, on the order of 10 to 15 picograms. Breath-hold and exhalation maneuver, mouthpiece material, sorbent tube batch, storage interval before desorption, room-air background, and column condition can each move a measurement by more than the effect being measured. When collection and analysis are not locked down, the variance of the protocol exceeds the variance of the biology, and a model trained under one set of conditions degrades when it meets a different site, a different ambient environment, a different patient population, or a different operator. Reproducibility across cohorts fails for that reason, not for lack of biomarkers. Genomics sat at the same impasse until next-generation sequencing made standardized, reproducible measurement possible at scale[13]. Breath has been waiting on its equivalent.

CLARION is engineered to be it. A patented miniature thermal-desorption GC-MS designed from first principles for the lowest achievable size, weight, power, and cost rather than adapted down from a benchtop instrument, it fits a low-thermal-mass gas chromatograph, a chip-scale ion-trap analyzer[14,15] running hundreds of microfabricated traps in parallel, and a miniature turbomolecular pump[16] into roughly 15 pounds and 10 liters. It reaches part-per-trillion sensitivity, produces full spectra searchable against the standard NIST, EPA, and NIH reference libraries, powers up in about 30 seconds, and returns a result in minutes rather than hours. Its subsystems were matured through IARPA (MAEGLIN, PICARD), DARPA (SIGMA+), and the integrated platform has been clinically deployed in Tampa under the DTRA and DIU's EXHALE program[17] and in Brazzaville, Republic of Congo, under the Gates-funded MATTHIAS study[18].

Three design choices carry the clinical weight. **Collection is instrument-controlled**: an invariant exhalation maneuver, volume, and desorption cycle across participants and devices, with separation and mass analysis minutes after the breath rather than days after shipping, so labile aldehydes and reactive hydrocarbons never degrade or partition into container walls and an entire class of pre-analytical variability never arises[19]. **Background is referenced**: an ambient-air mode pairs every breath with its own room profile, so the VOCs contributed by cleaning agents, plastics, and clinical materials are subtracted and only the endogenous fraction advances. **Identification is molecular, not pattern-based**: where sensor arrays, IMSs, and GCs report signatures that cannot be assigned a structure or transferred between instruments, CLARION reports named VOCs.

The Moffitt Lung Cancer Pilot

Validating a breath diagnostic requires more than controlled laboratory conditions. It requires paired, ground-truth-referenced specimens from real patients, and a reference measurement rigorous enough that a favorable result cannot be attributed to a favorable comparison. Detect-ION designed this pilot around both requirements.

From December 2025 to June 2026, the Moffitt team enrolled 40 patients with lung cancer and 25 healthy control participants. Case patients were treatment-naive with pathologically confirmed NSCLC and no history of cancer other than non-melanoma skin cancer. Control participants were recruited from Moffitt's lung cancer screening program: all were screening-eligible, all had a Lung-RADS 1 or 2 result on their most recent LDCT, and all had no prior cancer history other than non-melanoma skin cancer. Choosing controls from an actively screened, screening-eligible population rather than from healthy volunteers is deliberate. It places the comparison in the population where a breath test would actually be used, and it holds the smoking-exposure background of cases and controls in the same clinical range. All breath collections were conducted in Moffitt's Population Engagement and Research Laboratory. Two breath samples were collected per participant at a single visit: one captured directly onto CLARION and one collected on a sorbent tube and analyzed on a commercial benchtop reference chain (Markes TD-100xr thermal desorber, Agilent 8890 gas chromatograph, Agilent 7250 Q-TOF HRMS). On every collection day, paired room-air samples were also acquired on both CLARION and sorbent tubes, so environmental contributions could be subtracted from the VOC data at the level of the day on which each specimen was taken. A small number of samples were excluded from analysis on one or both platforms for insufficient breath volume. All participants provided written informed consent, and the research was approved by an independent institutional review board (Advarra, Inc., Columbia, Maryland).

Table 1. Pilot study design. NSCLC: non-small cell lung cancer; LDCT: low-dose computed tomography; LCS: lung cancer screening; HRMS: high-resolution mass spectrometry; Q-TOF: quadrupole time-of-flight; IRB: institutional review board.

Parameter	Pilot Study
Study Period	December 2025 to June 2026
Site	H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida
Design	Cross-sectional, case-control, paired-platform comparison
Cases	40 treatment-naive, pathologically confirmed NSCLC (29 adenocarcinoma, 9 squamous cell carcinoma, 2 other or not specified)
Controls	25 LCS-eligible participants with Lung-RADS 1 or 2 on most recent LDCT
Reference standard	Biopsy or surgical histopathology (diagnostic ground truth)
Point-of-care instrument	CLARION chip-scale thermal-desorption GC-MS
Analytical comparator	Sorbent-tube HRMS (Markes TD-100xr / Agilent 8890 GC / Agilent 7250 Q-TOF)
Environmental control	Paired room-air samples collected daily on both platforms
Ethics oversight	Advarra, Inc. IRB; written informed consent from all participants

The two groups differed in ways that a breath study must holistically consider. Cases and controls were closely matched on age (mean 66.3 years overall) and cumulative smoking exposure (mean 36.1 pack-years). They differed on sex distribution and, importantly, on active smoking: 36.0% of controls were current smokers against 7.5% of cases, and 25.0% of cases were never-smokers against none of the controls. Controls also reported more current secondhand smoke exposure. Because tobacco smoke is the single largest exogenous contributor to the breath VOC background, this imbalance runs against the naive expectation and could obscure a true cancer signal rather than manufacture one. It was handled explicitly in the analysis through covariate adjustment, described below. Figure 2 lays out the cohort details in full.

Cohort at a glance

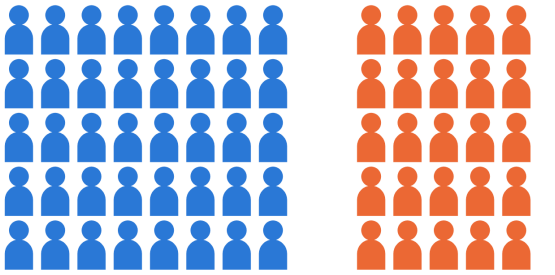
65 participants enrolled at Moffitt Cancer Center, December 2025 to June 2026

A. Who was enrolled

Each figure represents one participant

CASES n = 40
Treatment-naive, pathologically confirmed NSCLC

CONTROLS n = 25
Screening-eligible, Lung-RADS 1 or 2 on LDCT



CASE HISTOLOGY

Adenocarcinoma	29
Squamous cell	9
Other / not specified	2

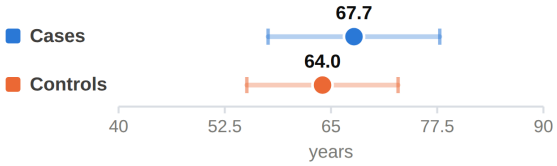
STAGE AT DIAGNOSIS

Early stage (I–II)	23
Late stage (III–IV)	12
Not analyzed / not staged	5

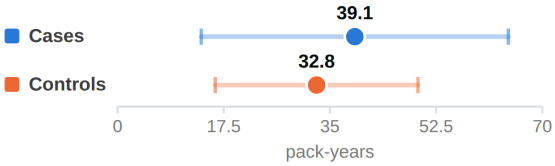
B. Matched on

Mean with ±1 SD · no significant difference

Age p = 0.143



Cumulative smoking exposure p = 0.292



Cases and controls are drawn from the same age band and the same lifetime tobacco-exposure range, so neither variable can account for the diagnostic signal.

C. Differed on

Distribution within each group

Sex at birth Male Female **p = 0.043**

Smoking status Never Former Current **p = 0.001**

Secondhand smoke exposure Never Former Current **p = 0.005**

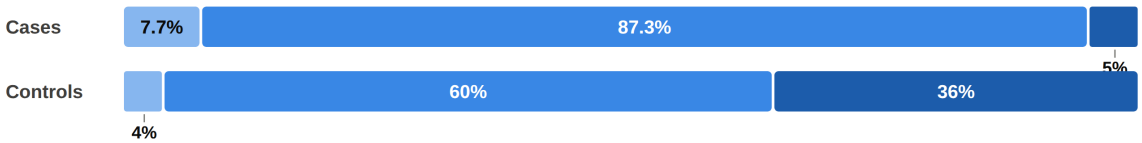


Figure 2. Cohort at a glance. Section A, enrollment: 40 treatment-naive, pathologically confirmed NSCLC cases and 25 screening-eligible controls with Lung-RADS 1 or 2 imaging, with case histology and stage at diagnosis below; the stage groups match those used in Table 3, and the 5 cases neither analyzed nor staged do not enter the stage-stratified models. Section B, variables on which the groups were matched: age (p = 0.143) and cumulative smoking exposure in pack-years (p = 0.292), shown as mean with ±1 SD. Section C, variables on which the groups differed: sex at birth (p = 0.043), smoking status (p = 0.001), and secondhand smoke exposure (p = 0.005), shown as the distribution within each group. P-values from Fisher's exact test for categorical variables and Student's t-test for continuous variables. All models were adjusted for sex, smoking status, pack-years, and secondhand smoke exposure.

Data Analysis

CLARION produced GC-MS analysis of the participant breath data on site, in near real time, while the paired sorbent tubes were processed on the benchtop HRMS chain to provide an independent, higher-resolution dataset against which CLARION's outputs could be compared. Custom software detected and quantified VOC intensities in both datasets under matched criteria: a minimum signal-to-noise ratio of 5, and presence in at least 10 samples for a VOC to enter the feature table. VOCs were identified by matching retention indices and mass spectra against NIST reference libraries, and CLARION VOCs were linked to their HRMS counterparts through the same retention-index and spectral matching, so that the two platforms could be discussed in a common chemical vocabulary rather than as two unrelated feature spaces.

Peak-area and peak-height feature tables were normalized using probabilistic quotient normalization to correct for differences in breath sample concentration between participants. Background drift and environmental contamination were removed by subtracting daily and multi-day room-air VOC intensities. The breath VOC signal was then adjusted for sex, current smoking status, pack-years of active smoking, and both current and cumulative secondhand smoke exposure, so that the imbalances shown in Figure 2 could not drive the classification result.

Diagnostic classification models were developed independently for each platform and each comparison of interest, using the covariate-adjusted, background-subtracted feature tables. Within each leave-one-out cross-validation training fold, features were pre-screened by univariate discriminatory performance, quantile-transformed, and used to fit an elastic-net regularized logistic regression classifier. Performing feature selection inside the fold rather than across the full dataset is the methodological point that keeps the resulting estimates honest at this sample size. Out-of-fold predicted probabilities were used to generate a receiver operating characteristic (ROC) curve for each comparison.

Key Results

VOC Biomarker Discovery & Validation

CLARION identified 103 VOCs across the breath specimens. HRMS, analyzing the same sample set, identified more than 900. The VOCs that varied between NSCLC patients and healthy controls were largely the same on both platforms, and they concentrated in a compact set: the aromatics p-cymene, phenol, and propylbenzene, alongside tetradecane, β-ocimene, 2,3-dihydroindole, and 1-(methylthio)-(Z)-1-propene.

Table 2. Predictive VOCs quantified via CLARION. Effect sizes are Hedges' g with 95% confidence intervals; positive values indicate elevation in NSCLC cases relative to controls. P-values derived via Mann-Whitney U-test on VOC intensities.

VOC	Effect size (Hedges' g)	P-value	Direction in NSCLC
Tetradecane	0.90 [0.36, 1.44]	0.0031	Elevated
β-Ocimene	-0.58 [-1.11, -0.049]	0.0032	Decreased
Propylbenzene	-0.84 [-1.38, -0.30]	0.0037	Decreased
p-Cymene	-0.57 [-1.10, -0.043]	0.0115	Decreased

VOC	Effect size (Hedges' g)	P-value	Direction in NSCLC
Indole, 2,3-dihydro-	-0.82 [-1.36, -0.28]	0.0241	Decreased
1-Propene, 1-(methylthio)-, (Z)-	-0.49 [-1.01, 0.004]	0.0340	Decreased
Phenol	0.50 [-0.021, 1.04]	0.0482	Elevated

The biological plausibility of this VOC panel is well grounded in the existing literature, and where it departs from prior reports it does so in an informative way. Phenol has been reported as elevated in a prior study of lung cancer breath biomarkers[20], consistent with what CLARION observed, and p-cymene has previously been found decreased in patients with NSCLC[21]. Tetradecane was elevated here, agreeing with earlier work[22], although alkanes of this class are generally elevated in conditions of heightened oxidative stress and are not specific to malignancy on their own. β-Ocimene has been reported as elevated in cases[20], where this cohort showed a marked decrease, a discrepancy that larger cohorts will need to adjudicate.

Three VOCs extend the published picture rather than confirm it. Propylbenzene, an aromatic diminished in the breath of lung cancer patients here, is not reported in the prior breath studies cited above. Indoles are not typically described as lung cancer breath biomarkers, yet 2,3-dihydroindole was among the strongest discriminators, by effect size, in this cohort. 1-(Methylthio)-(Z)-1-propene has not been identified as a breath biomarker by other lung cancer studies, though a close isomer, allyl methyl sulfide, has been found altered across multiple lung cancer histologic subtypes[23]. These are candidate contributions to the field, not settled findings, and they are exactly the kind of result that only emerges when a platform reports identified molecules rather than an abstract pattern.

Diagnostic Model Performance

Using elastic-net logistic regression classifiers built independently on each platform's features, CLARION distinguished NSCLC cases from screening-eligible controls with an ROC-AUC of 0.864, against 0.863 for the laboratory HRMS reference on the same patients. The two platforms were, for this clinical question, diagnostically indistinguishable.

The pattern held where it matters most. For early-stage NSCLC versus controls, the population in which detection changes prognosis, CLARION achieved an AUC of 0.854 against 0.841 for HRMS. Histology-specific analyses were also comparable across platforms, for adenocarcinoma (0.770 versus 0.787) and squamous cell carcinoma (0.754 versus 0.774), indicating that CLARION's smaller VOC panel captures discriminatory signal broadly across NSCLC subtypes rather than being confined to a single histology. CLARION outperformed HRMS for late-stage disease (0.807 versus 0.677), but the subgroups involved are small and that particular comparison should be read as descriptive. Discrimination between early- and late-stage disease was modest on both platforms (0.661 and 0.696), reflecting both smaller subgroup sizes and a more subtle underlying biological contrast than the case-versus-control comparison.

103 VOCs versus more than 900. Equivalent diagnostic performance.
What determines clinical value is not how many VOCs a platform can see,
but whether it resolves the right ones, reproducibly, at the point of care.

Table 3. Diagnostic model performance. We report areas under the receiver operating curve (AUC), true predictive rate for the first set of samples (sensitivity), the true predictive rate of the second set of samples (specificity), along with the overall accuracy.

Comparison (N)	CLARION AUC (Sens/Spec/Acc %)	HRMS AUC (Sens/Spec/Acc %)
NSCLC (36) vs. controls (23)	0.864 (82.6 / 75.7 / 78.3)	0.863 (83.3 / 83.3 / 83.3)
Early NSCLC (23) vs. controls (23)	0.854 (87.0 / 73.9 / 85.4)	0.841 (73.9 / 87.5 / 80.9)
Late NSCLC (12) vs. controls (23)	0.807 (82.6 / 71.4 / 78.4)	0.677 (66.7 / 75.0 / 72.2)
Early (23) vs. late NSCLC (12)	0.661 (52.2 / 85.7 / 64.9)	0.696 (60.9 / 83.3 / 68.6)
Adenocarcinoma (27) vs. controls (23)	0.770 (73.9 / 70.4 / 72.0)	0.787 (70.4 / 87.5 / 78.4)
Squamous cell carcinoma (7) vs. controls (24)	0.754 (60.9 / 100.0 / 71.9)	0.774 (57.1 / 91.7 / 77.4)

What the pilot does and does not establish

This was a pilot, and its claims should be read at pilot scale. Enrollment was at a single institution, and performance was estimated by leave-one-out cross-validation rather than on an independent held-out cohort, so the AUC values are internally validated estimates carrying wide confidence intervals: at this sample size, the 95% interval around 0.86 spans roughly 0.77 to 0.95. Stage-specific and histology-specific subgroups are small, and the late-stage and squamous cell comparisons in particular rest on very few cases. Controls were drawn from a screening population with Lung-RADS 1 or 2 imaging, which is the right comparison for a screening-adjacent question but is not yet the indeterminate-nodule population in which the first clinical indication will be pursued. Current breath test performance does not replace LDCT, and this study was never designed to argue that it should.

What the pilot does establish is the thing that had to be established first. A 15-pound instrument, operated in a clinic by clinical research staff rather than by mass spectrometrists in a laboratory, extracted the same diagnostic information from exhaled breath as a benchtop HRMS, on the same patients, on the same day. The signal is real, it is chemically identified, and it is measurable where the patient is.

Vision

These results are our first look with an immediate clinical objective in managing indeterminate pulmonary nodules and identifies potential lung cancers earlier: an independent, biology-based discriminator deployable as a complement to, or eventually alongside, existing screening and diagnostic pathways.

The beachhead: adjudicating the indeterminate nodule

Detect-ION is targeting the indeterminate pulmonary nodule first, because that is where the comparator and the endpoints are most tractable and where the clinical need is most acute. A nodule in the 8 to 30 mm range sits at a genuine decision point: watch, image again, or intervene. The metric that matters there is negative predictive value.

A breath result that reliably says “this is very unlikely to be malignant” can spare a patient a biopsy, and a result that says the opposite can accelerate a patient toward definitive care. The same test also has a role after that first decision: nodules judged unlikely to be malignant still require surveillance, and breath analysis is cheaper and more accessible than serial CT, making it practical to monitor these patients routinely, at the point of care and at intervals imaging economics do not support. A second question follows immediately: whether breath used adjunctively with LDCT can reduce the false-positive rates that dominated positive screens in the National Lung Screening Trial.

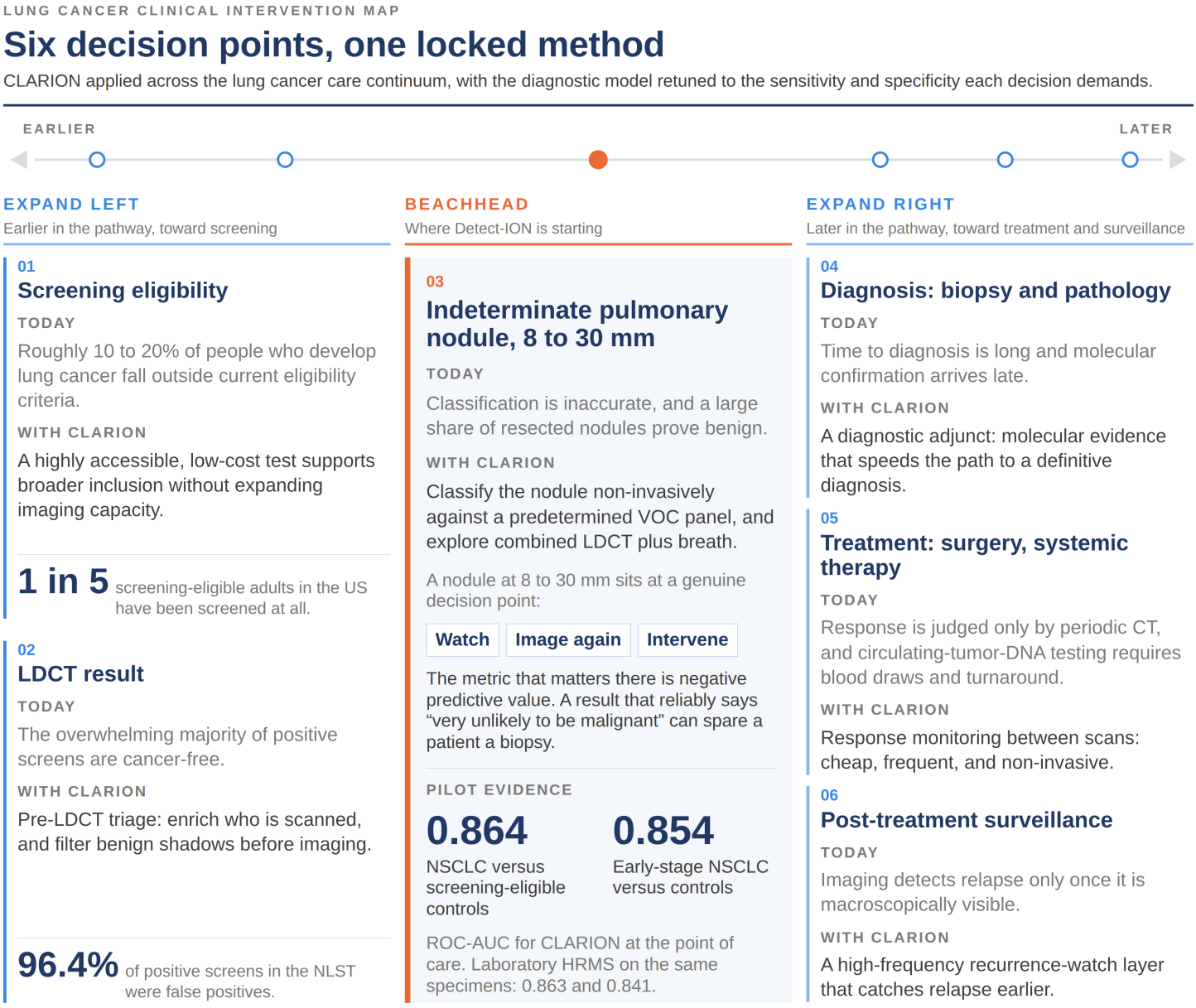


Figure 3. Lung cancer clinical intervention map. CLARION could be applied across six decision-points, each with a diagnostic model optimized for that use. “Expand left” denotes movement earlier in the pathway, toward screening; “expand right” denotes movement later, toward treatment and surveillance. The screening uptake and false-positive figures shown are those cited in the Problem Statement; the ROC-AUC values are from Table 3.

The expansion: one VOC panel, many decision-points

The longer-term objective is more expansive. The same measurement architecture, retuned for the sensitivity and specificity profile each use demands, could provide clinical decision support across the lung cancer care continuum. Each indication inherits the analytically locked method validated at the beachhead, which is what makes staged expansion credible rather than speculative.

The pilot's ROC-AUC of 0.86 is a strong preliminary signal and warrants a more thorough validation. It was achieved in a single-center cohort small enough that the confidence interval around the estimate remains wide. A substantially larger cohort, enrolled prospectively and ideally across multiple sites, would tighten that interval materially. It would also test the signal against the population heterogeneity, instrument handling, and collection variability that no single center can supply. Scale would also power detection of the individual VOCs driving the signal, admitting moderate-effect VOCs under the stringent multiplicity correction that a VOC panel of this size requires, and where this pilot is underpowered.

Detect-ION hopes to build the next initiative accordingly. It will finalize and lock the CLARION collection-to-analysis standard operating procedure and acquisition method, and verify analytical performance (limits of detection, dynamic range, precision, and inter-device reproducibility) in a humidified breath matrix on CLARION-β prototypes, an advanced variant that adds parallel sorbent-tube collection so confirmatory HRMS and point-of-care results derive from a single exhalation. It will then apply that locked method unchanged to a prospectively enrolled, stage-specific case-control cohort spanning early-stage NSCLC, late-stage NSCLC, and matched cancer-free controls, sized to power the primary endpoints and distributed across more than one enrolling site, with acquisition blinded to case-control status and histopathology as ground truth. Because CLARION records a full spectrum for every breath, a pre-specified untargeted search will run alongside the fixed panel, so new candidate biomarkers can be surfaced from the same data that validates the existing ones. Finally, it will build a fixed classifier using penalized modeling with nested cross-validation, estimate negative predictive value, sensitivity, and specificity with confidence intervals at clinically relevant thresholds.

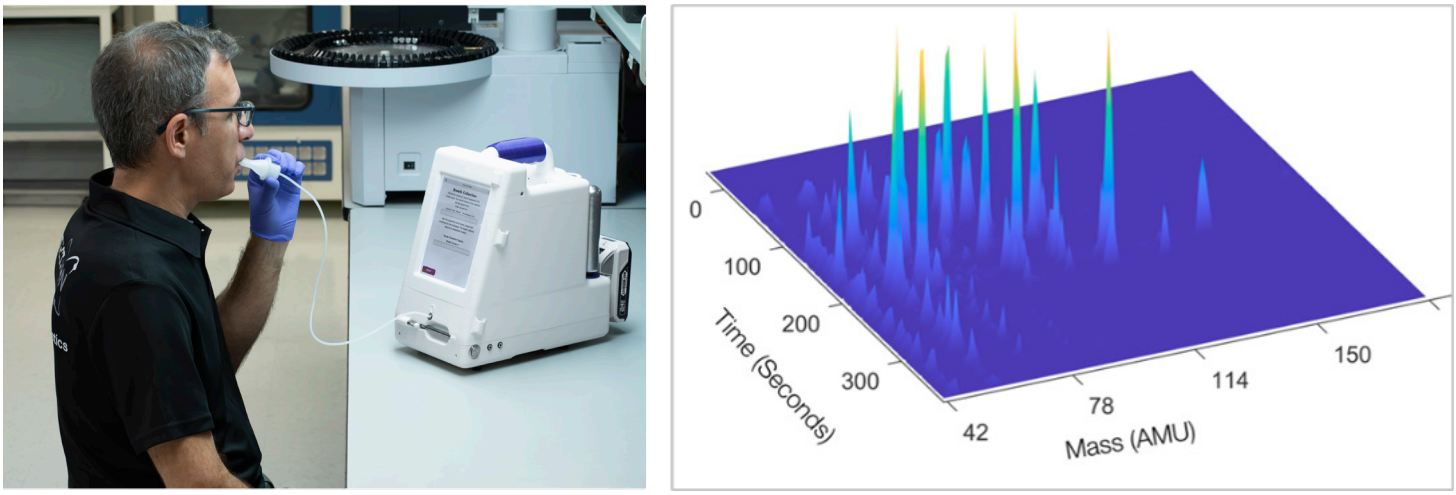


Figure 4. Left: A subject providing breath to CLARION-β via a single-use mouthpiece. Breath method requires subject to exhale for 2 min to collect 4 L of breath followed by 7 min of GC-MS analysis. Right: A 3D plot example of the individual VOCs detected showing the breath VOCs that are profiled by CLARION-β.

A pre-specified exploratory analysis will test whether the breath call adds discrimination on top of LDCT findings rather than restating them, since that combination, not breath in isolation, is how the test would enter the screening pathway. Multi-parametric MRI followed the same route in prostate cancer, where placing a non-invasive triage test ahead of biopsy improved detection of clinically significant disease while sparing a substantial share of men an invasive procedure[24].

Why this scales

Breath is attractive as a diagnostic specimen for reasons that compound: it is non-invasive, collected at the point of care, molecularly quantitative, and inexpensive. Detect-ION is targeting a per-test cost of roughly $25 against a device production cost target of approximately $10,000, economics that make the test repeatable at the individual level and deployable at population scale. That combination is what converts a diagnostic from a specialist referral into a routine measurement, and it aligns directly with the national priority of moving validated molecular technologies to the point of care[25].

The regulatory path follows the science. The test will be advanced as an FDA in vitro diagnostic, with a pre-submission meeting requested early to align on intended use, classification, and the analytical and clinical validation requirements that precede pivotal testing. CLARION's decisive advantage in that process is the same property that produced these results: because every feature is a library-identified VOC rather than a device-specific pattern, the signature can be validated once and transferred across sites and instruments.

One breath. Minutes, not weeks. A molecular answer delivered at the moment the clinical decision is made, for a disease whose entire prognosis turns on how early that answer arrives.

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