Cell-free DNA fragmentomic prescreening to re-engage patients declining low-dose CT

A multi-site, real-world implementation study

Jun Zhang, MD, PhD
On behalf of the study investigators
OSF HealthCare Cancer Institute | University of Illinois College of Medicine, Peoria, IL, USA

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Declaration of Interests

I have served as a scientific advisor/consultant for: AstraZeneca, BridgeBio, Daiichi Sankyo, DAVA Oncology, Fosun, Hengrui, IDEOlogy, Novocure, Regeneron and Johnson & Johnson.

I am on the speakers' bureau for AstraZeneca, MJH Life Sciences, Regeneron, Sanofi Genzyme, Daiichi Sankyo and Johnson & Johnson.

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Background: a screening gap imaging alone cannot close

- Lung cancer is the leading cause of cancer death worldwide.
- Low-dose CT (LDCT) screening lowers lung-cancer mortality, yet **uptake among eligible individuals remains critically low (~20% in the US).**
- Many eligible patients **actively decline** LDCT — citing inconvenience, radiation concerns, or absence of symptoms — and fall outside the screening safety net entirely.
- These patients remain at high risk but are unreached by imaging-based programs.

~20%

of eligible individuals in the US are screened with LDCT

↓

The remainder — including those who decline — are the target of this study

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A blood-based on-ramp for hard-to-reach patients

Cell-free DNA (cfDNA) fragmentomic analysis is a minimally invasive, blood-based alternative to imaging that may lower the threshold for participation in patients who refuse LDCT.

1

Simple blood draw

A single venous sample — no imaging appointment, no radiation, no bowel or breath prep.

2

Genome-wide fragmentomics

FirstLook Lung (DELFI Diagnostics) profiles genome-wide cfDNA fragmentation patterns.

3

Machine-learning readout

ML classifies fragmentation profiles; elevated results trigger referral to LDCT.

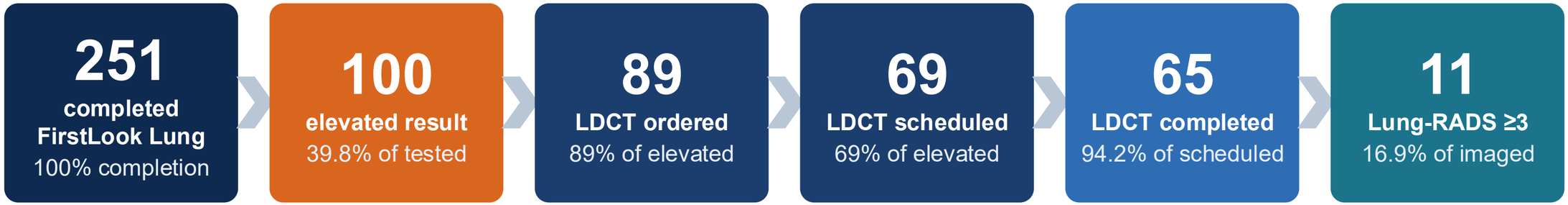
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Methods: prospective, multi-site implementation study

Design	Prospective real-world implementation study
Setting	OSF HealthCare — a multi-site system spanning urban and rural Illinois communities
Period	October 2024 – April 2026
Population	LDCT-eligible adults (USPSTF criteria) who had declined imaging-based screening
Intervention	Offered FirstLook Lung (DELFI Diagnostics) cfDNA fragmentomics; elevated results referred for LDCT
Endpoints	Test completion · LDCT follow-through · diagnostic yield by Lung-RADS

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Screening cascade & Results



20 of 89 did not proceed to CT scheduling:

unreachable (n=8), undocumented (n=7), refused (n=3), no longer needed (n=1), awaiting surgery (n=1).

Among the 11 Lung-RADS ≥3:

4 required immediate intervention; 2 referred to oncology.

Mean assay turnaround: 6.87 days — fast enough to act within a single outreach window

Every patient offered the blood test completed it, and roughly two-thirds of those with elevated results converted back into the imaging pathway they had previously refused. This is about a quarter of initial patient pool.

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Conclusions

- **cfDNA fragmentomic prescreening effectively re-engaged high-risk patients who initially refused LDCT,** converting a substantial proportion into the screening pathway.
- The high completion rate and clinically actionable findings support **blood-based prescreening as a complementary strategy** for lung-cancer screening programs targeting populations resistant to imaging-based approaches.
- **Considerations and next steps**: 1) Single health system → additional sites and larger, more diverse populations; 2) Link elevated results to biopsy-confirmed diagnoses and stage at detection; 3) Evaluate cost-effectiveness versus imaging-only outreach.

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Thank You!

