

ctDNA Analyses in Early Detection

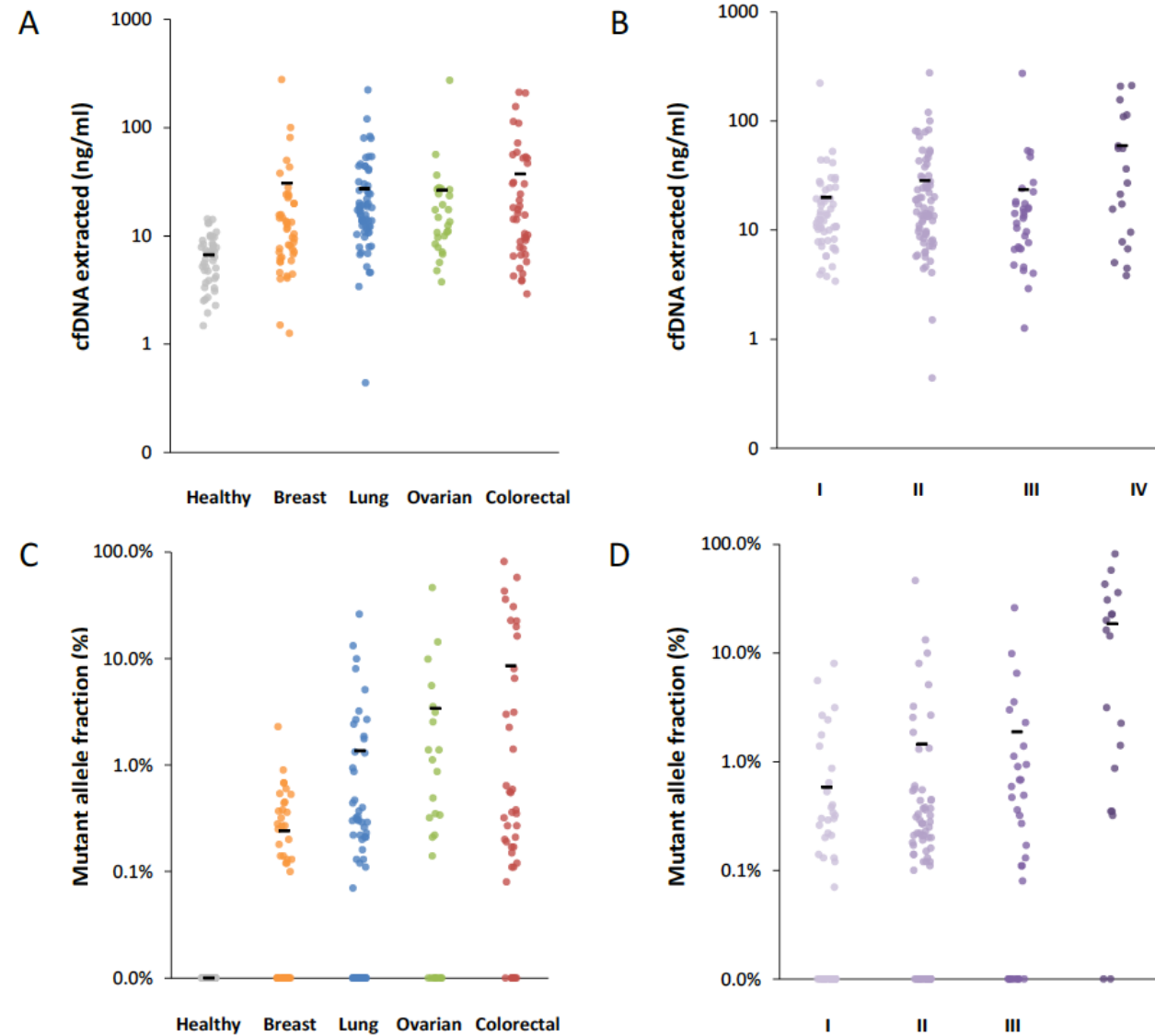
Methylation, Proteomics and Other Efforts for Early Lung Cancer Detection

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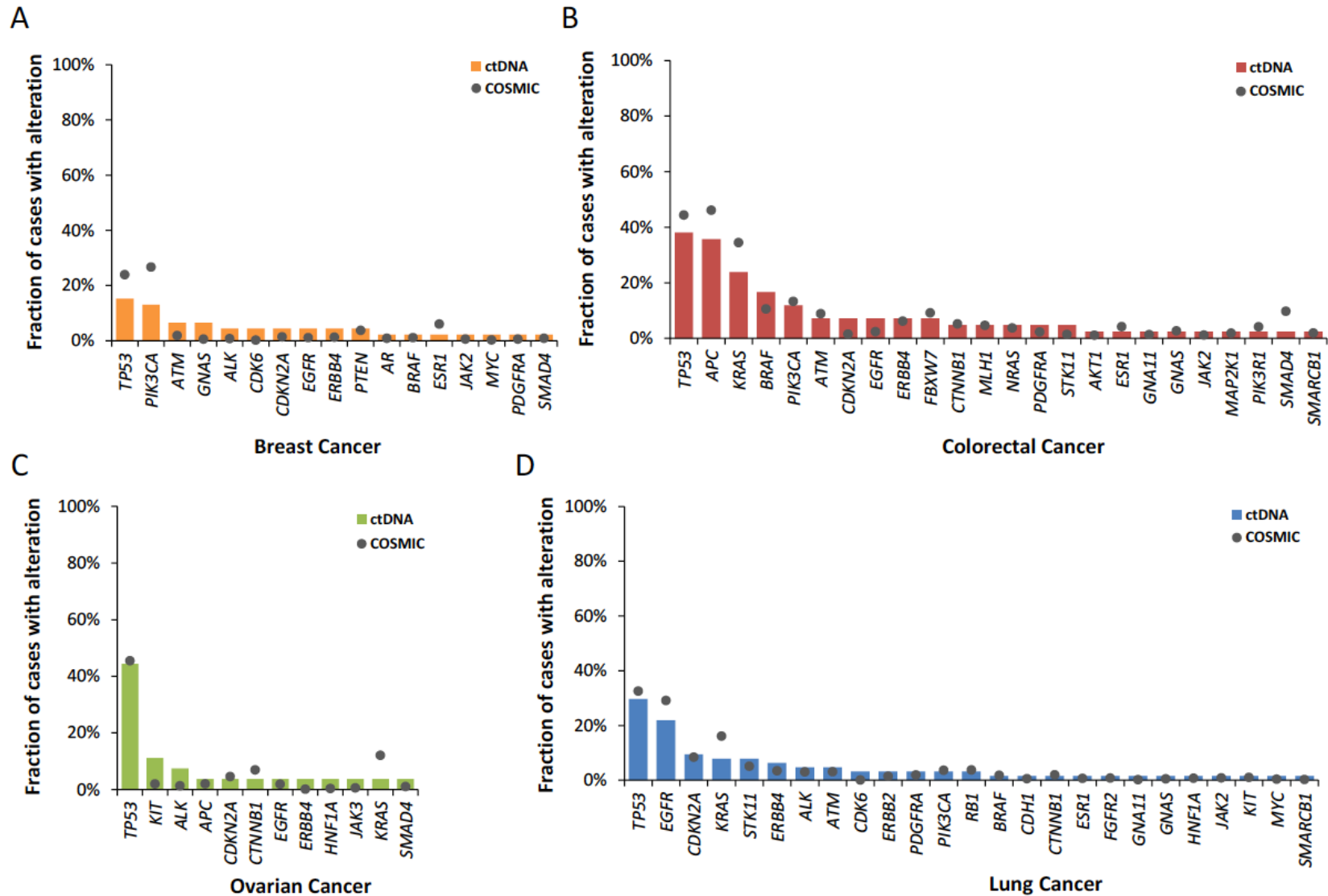
Cancer Patients Detected Using Tec-Seq

Cancer Type	Patients (n)	Patients with ctDNA Alterations (n)	Fraction of patients with ctDNA Alterations (%)
Colorectal			
I	8	4	50%
II	9	8	89%
III	10	9	90%
IV	15	14	93%
I-IV	42	35	83%
Lung			
I	29	13	45%
II	31	22	71%
III	4	3	75%
IV	0	NA	NA
I-IV	64	38	59%
Ovarian			
I	14	7	50%
II	4	3	75%
III	5	5	100%
IV	4	3	75%
I-IV	27	18	67%
Breast			
I	3	2	67%
II	30	17	57%
III	13	6	46%
IV	0	NA	NA
I-IV	46	25	54%
All			
I, II	128	76	59%
III, IV	51	40	78%
I-IV	179	116	65%

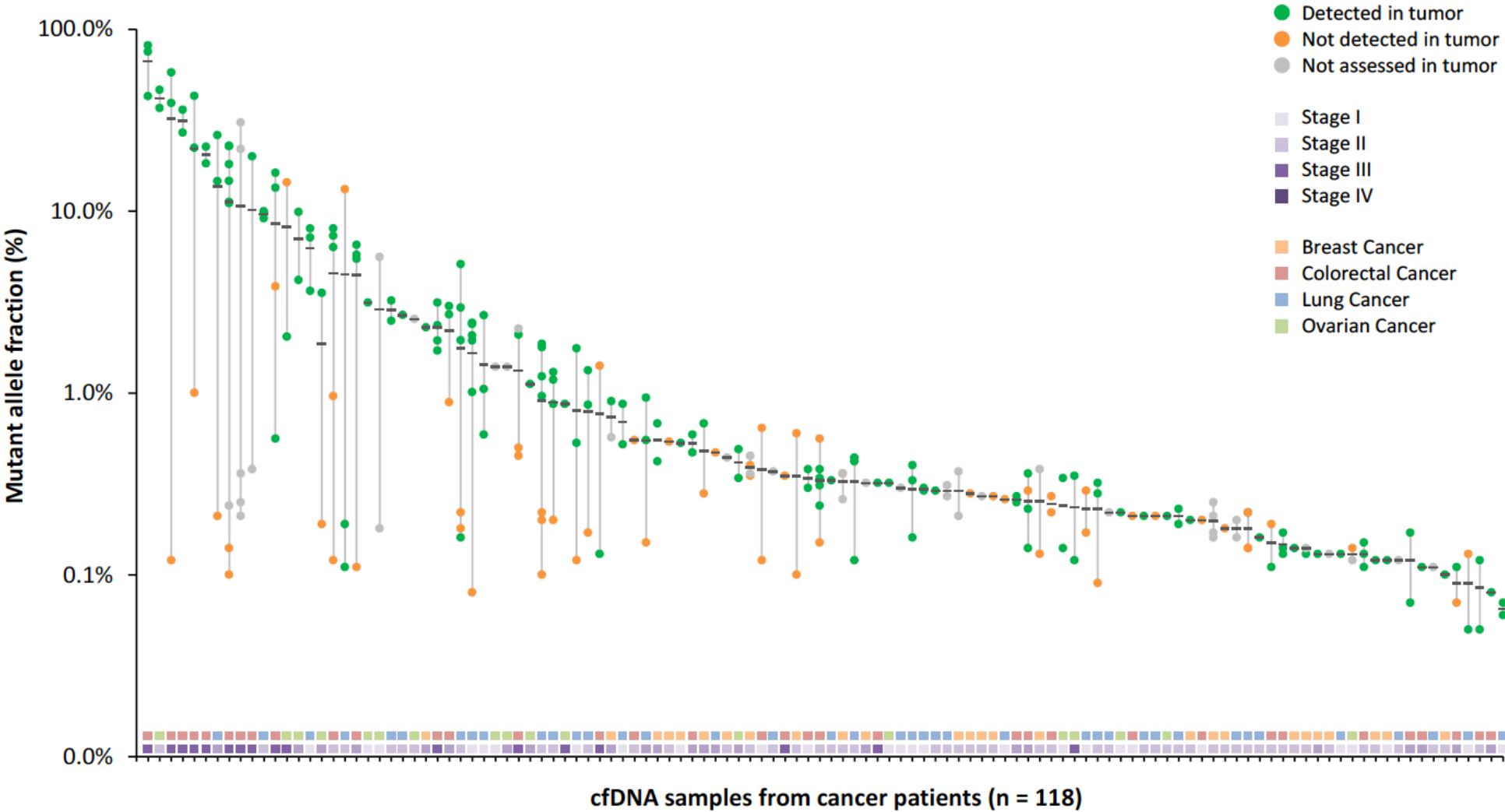
cfDNA in Healthy Patients and Patients with Cancer



Mutant Allele Frequencies in Cancer Genes

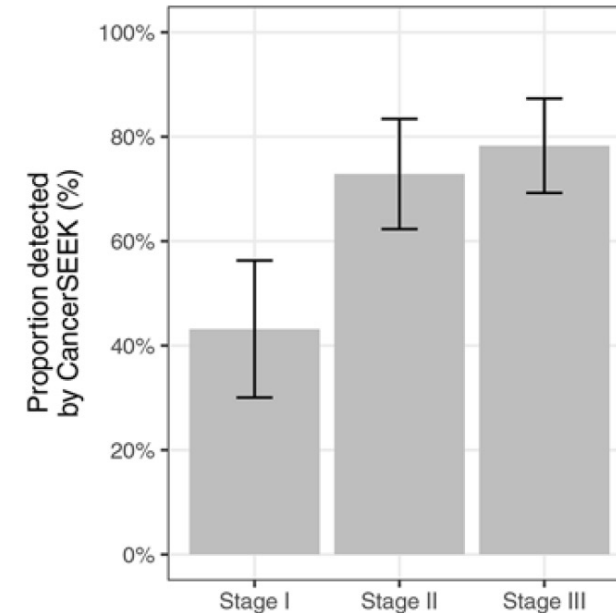
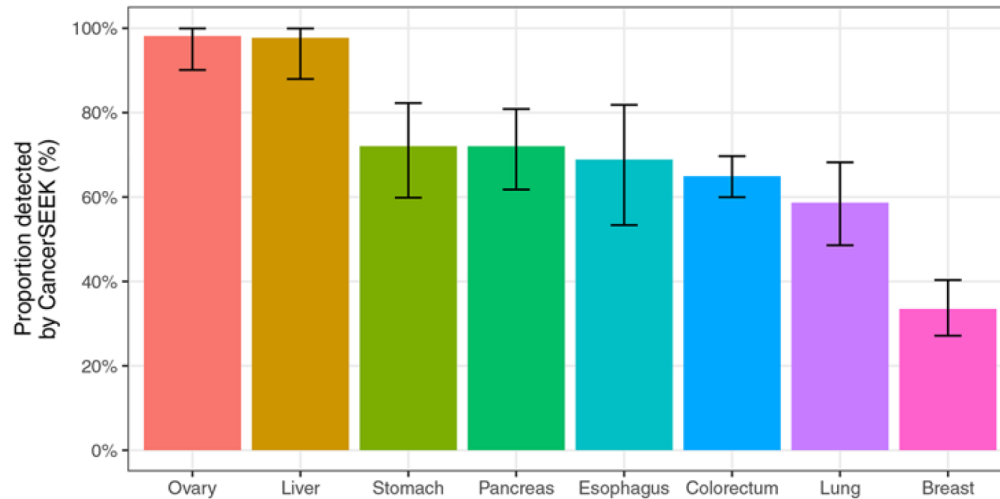


Concordance Between Alterations in Plasma and Tissue

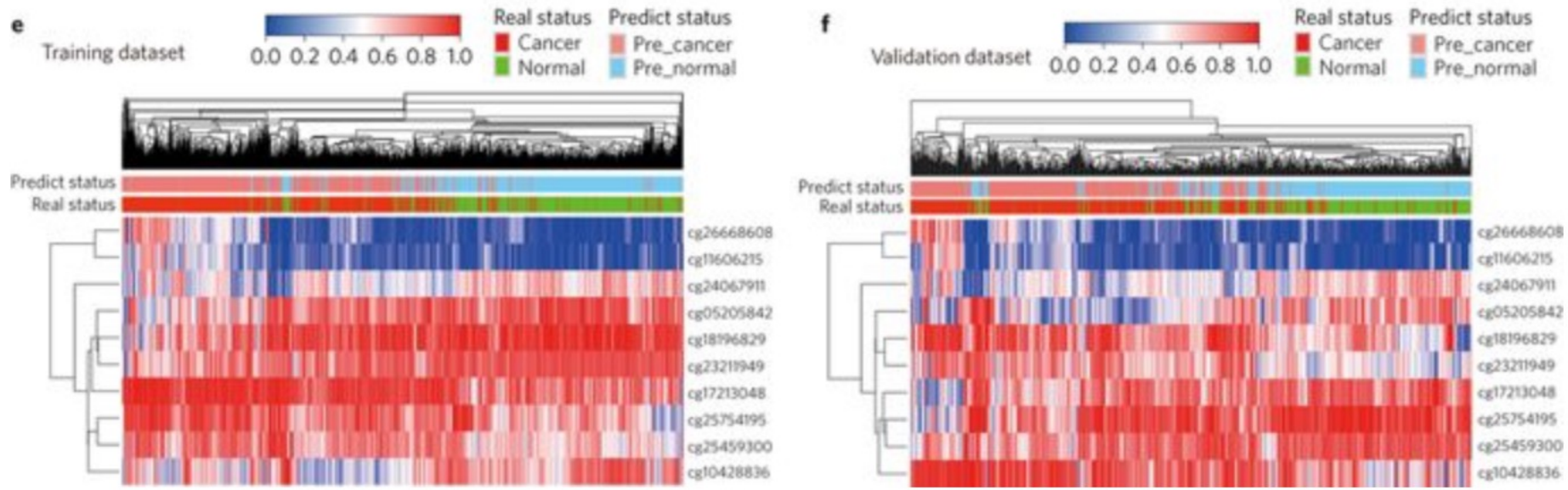


CancerSeek

- Protein markers and ctDNA evaluated to increase sensitivity and specificity
- Ovary, liver, stomach, pancreas, esophagus, colorectum, lung, or breast



Methylation Signatures Can Identify Tissue of Origin

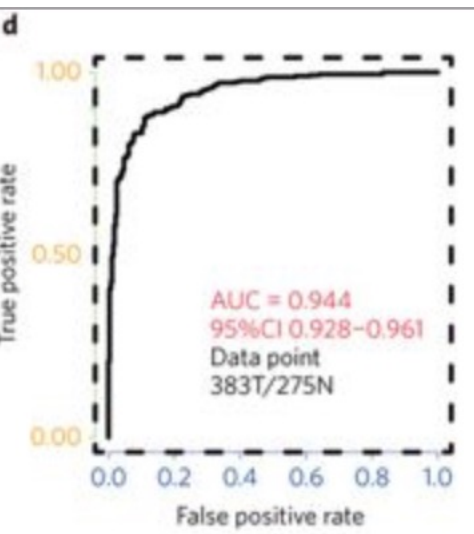
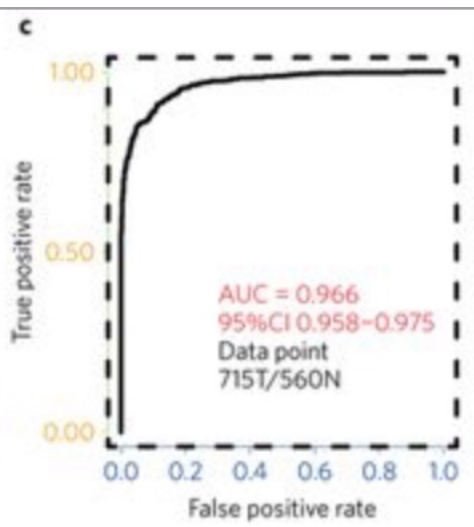


a

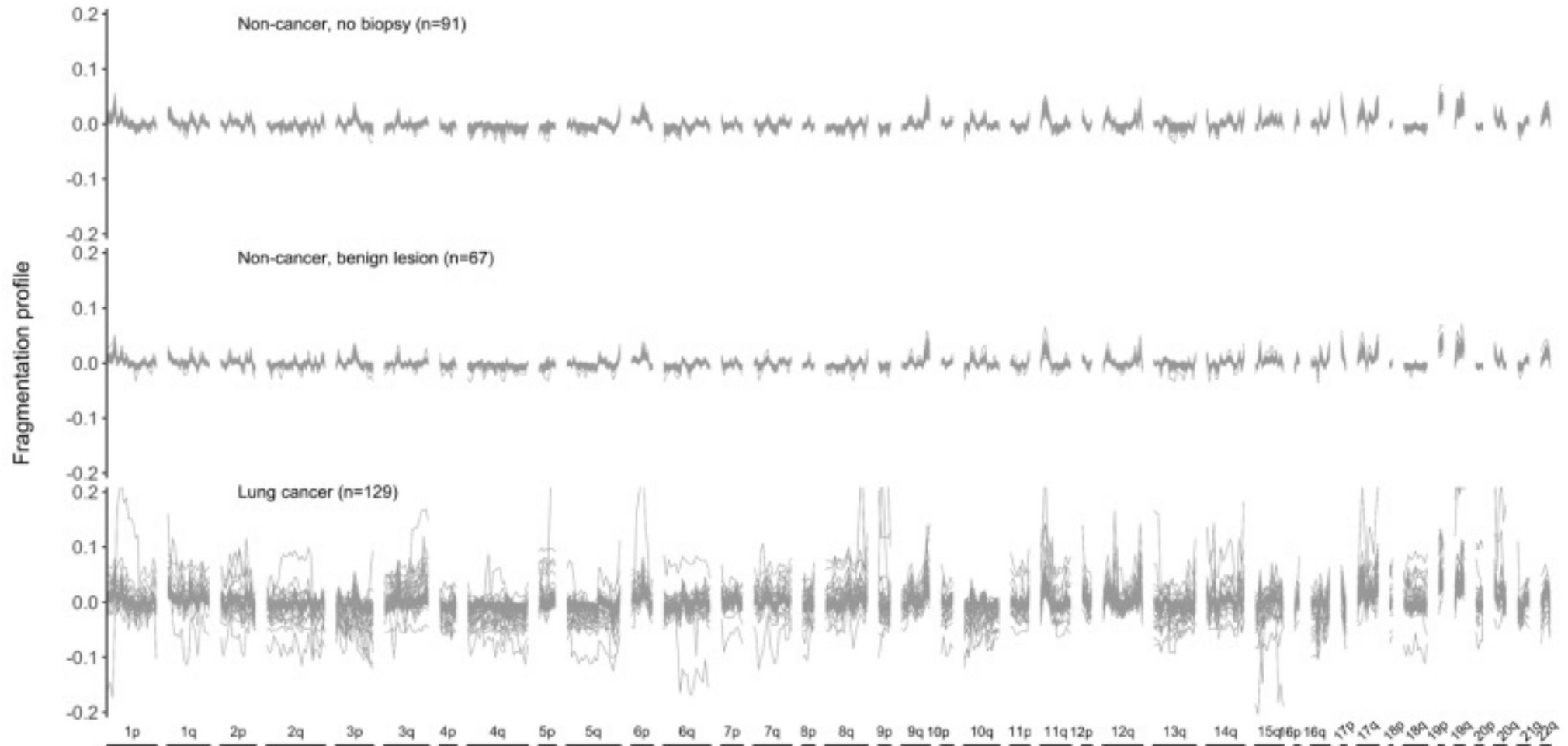
Training dataset	Real HCC	Real normal	
Predict HCC	613	32	
Predict normal	102	528	Totals
Totals	715	560	1,275
Correct	613	528	1,162
Sensitivity (%)	85.7		
Specificity (%)		94.3	

b

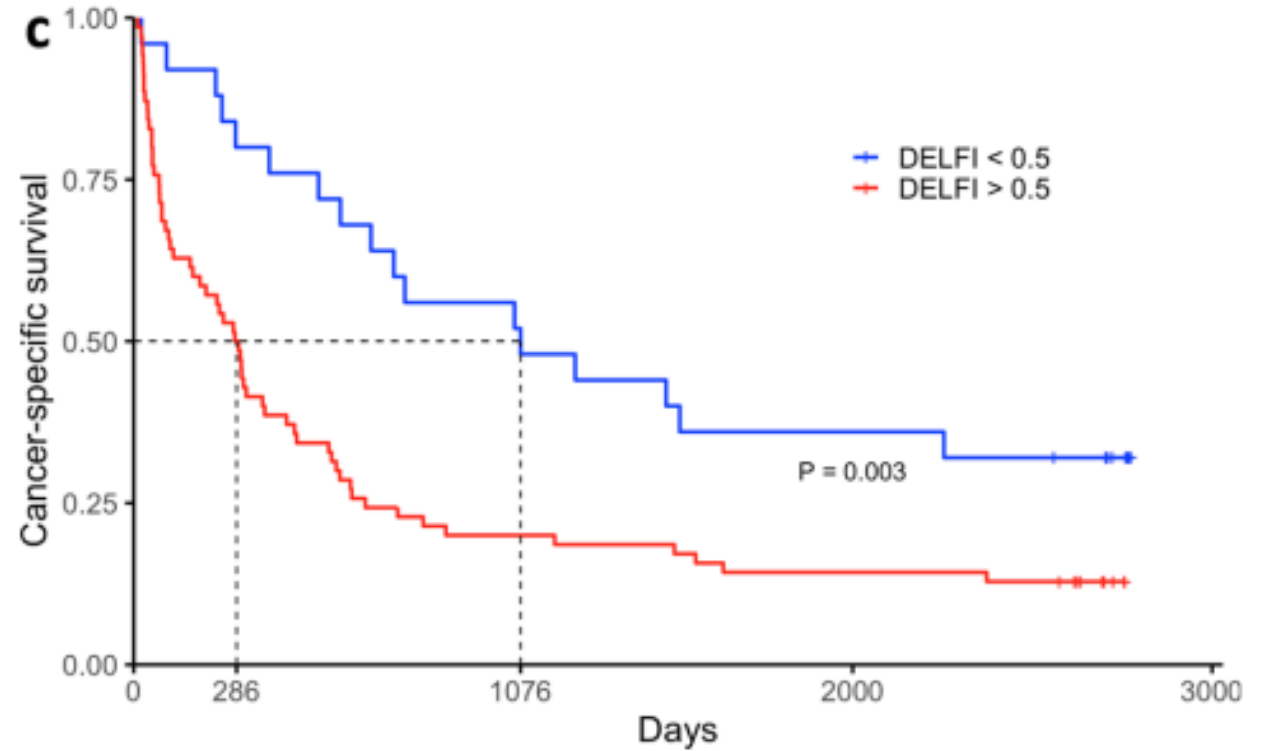
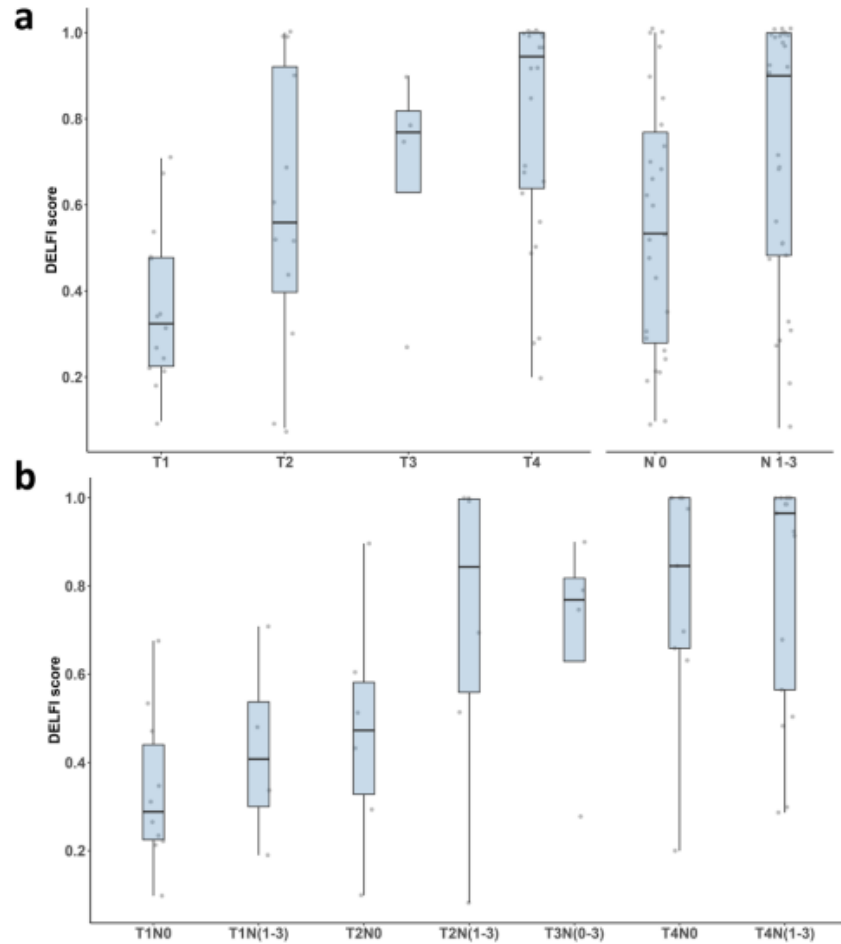
Validation dataset	Real HCC	Real normal	
Predict HCC	319	26	
Predict normal	64	249	
Totals	383	275	658
Correct	319	249	568
Sensitivity (%)	83.3		
Specificity (%)		90.5	



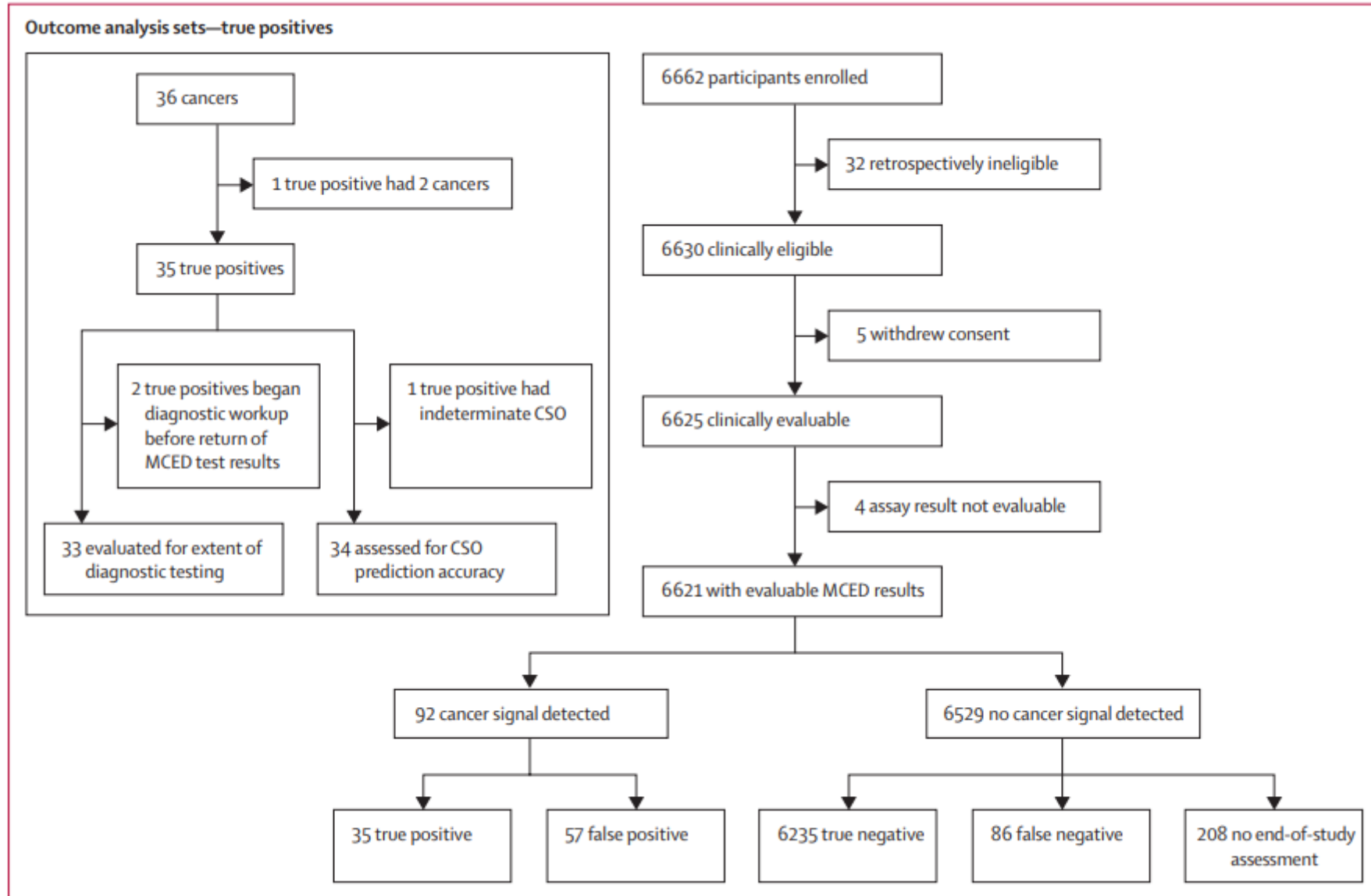
Fragmentomics can discern cancer vs non-cancer



Relationship of size and invasiveness of lung cancer with DELFI score



Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study

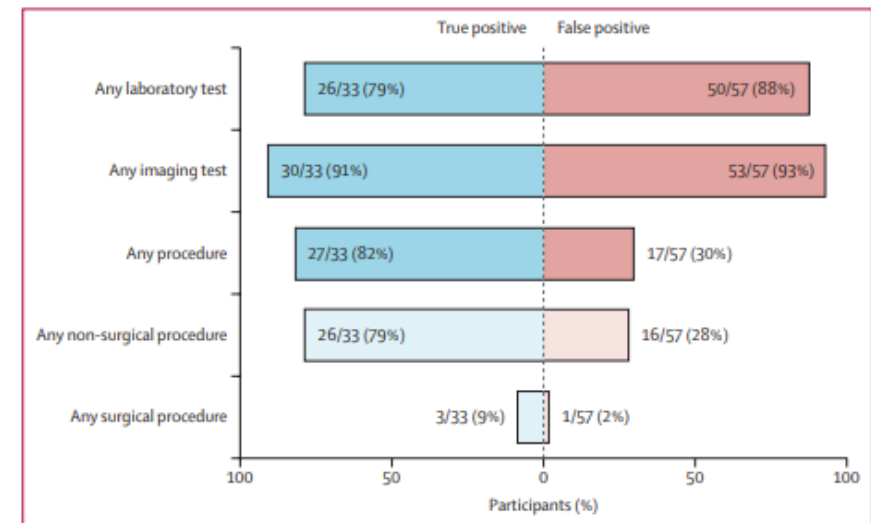
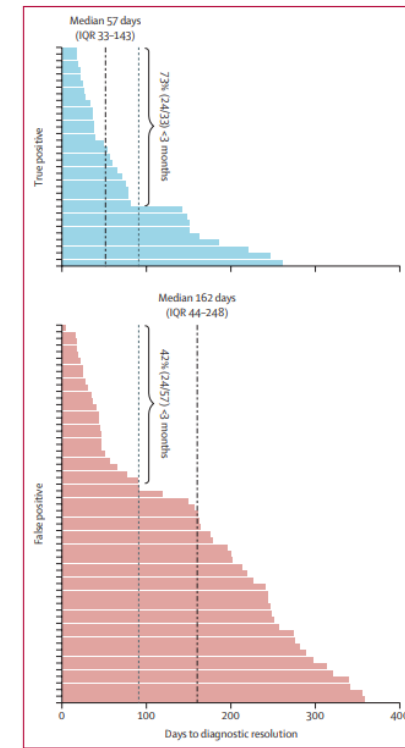
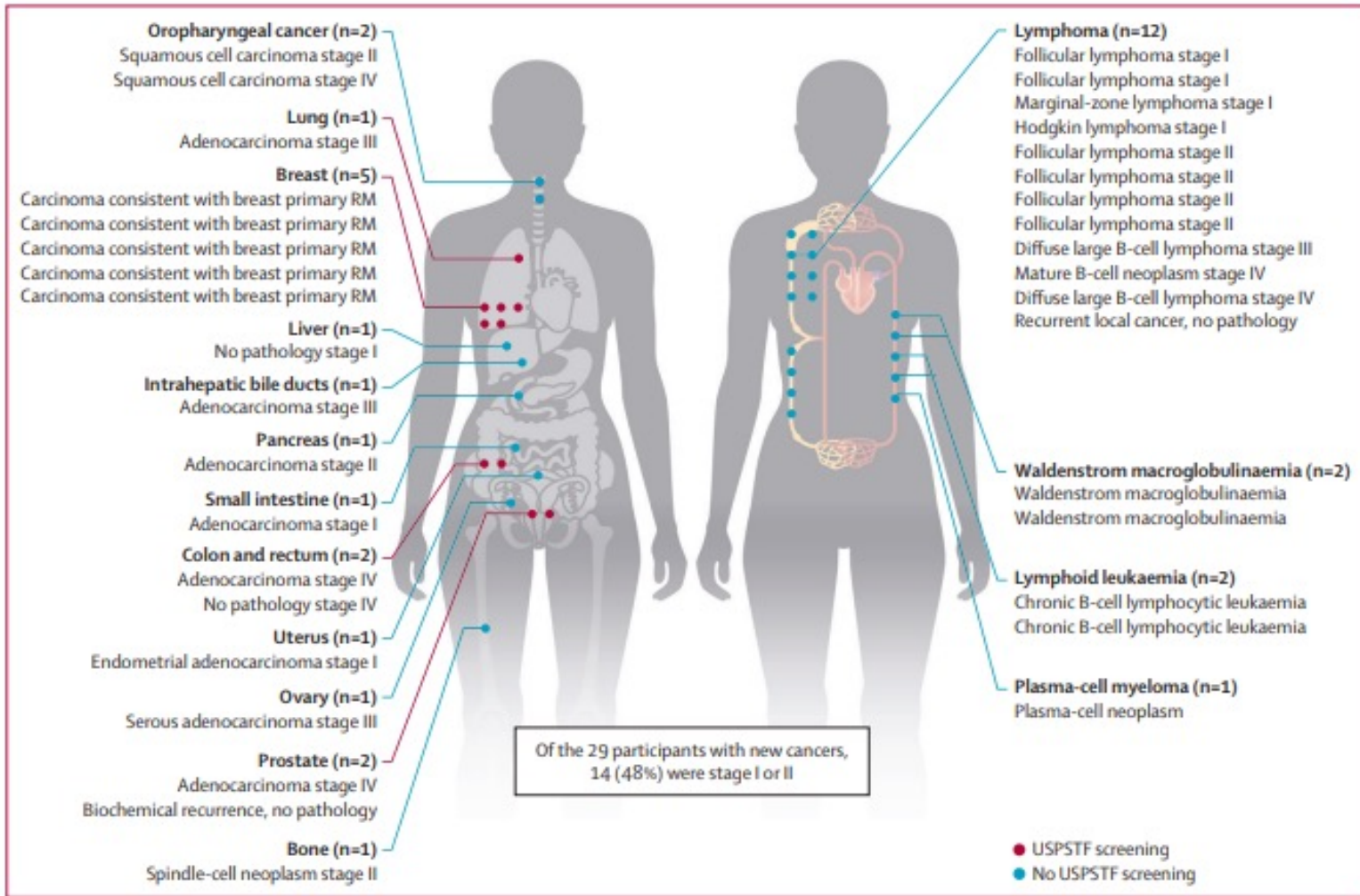


Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study

	Age ≥50 years with additional cancer risk (n=3681)	Age ≥50 years without additional cancer risk (n=2940)	Total (n=6621)
Resolution			
All	56 (1.5%)	36 (1.2%)	92 (1.4%)
True positive	24 (0.7%)	11 (0.4%)	35 (0.5%)
False positive	32 (0.9%)	25 (0.9%)	57 (0.9%)
Positive predictive value	24/56; 43% (30.8–55.9)	11/36; 31% (18.0–46.9)	35/92; 38% (28.8–48.3)
Negative predictive value	3449/3502; 98.5% (98.0–98.8)	2786/2819; 98.8% (98.4–99.2)	6235/6321; 98.6% (98.3–98.9)
Specificity	3449/3480; 99.1% (98.7–99.4)	2786/2810; 99.1% (98.7–99.4)	6235/6290; 99.1% (98.9–99.3)
Yield rate	24/3681; 0.65% (0.41–0.92)	11/2940; 0.37% (0.17–0.61)	35/6621; 0.53% (0.36–0.71)
Number needed to screen	3681/24; 153 (108–245)	2940/11; 267 (163–588)	6621/35; 189 (141–276)
Predicted origin accuracy*			
First CSO correct	20/23; 87% (67.9–95.5)	9/11; 82% (52.3–94.9)	29/34; 85% (69.9–93.6)
First or second CSO correct	23/23; 100% (85.7–100)	10/11; 91% (62.3–99.5)	33/34; 97% (85.1–99.8)

Data are n (%), n/N, or % (95% CI). CSO=cancer signal origin. *Excludes one participant with indeterminate CSO from the true-positive set.

Table 2: Multicancer early detection test performance



Schrag et al Lancet 2023

Conclusions

- Early detection assays are utilizing methylation, proteomics, and fragmentomics to help discern cancer vs non-cancer DNA
- Further studies are needed to align on LD-CT scan screening techniques
- Further work is moving into minimal residual disease post surgery and monitoring after initial tumor cytoreduction