

# Lung Macrodissect AI: a tumor cell estimation algorithm for use in a pulmonary adenocarcinoma molecular pathology workflow

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## INTRODUCTION

The development of targeted therapies has led to an increasing volume of molecular testing on FFPE tissue samples. This has increased the workload for pathologists, who review H&E-stained slides, mark a tumor dense region suitable for macrodissection, and estimate the percentage of tumor cells within the area. These estimates suffer from subjectivity and inter-observer variability. Computational assessment of cell counts can standardize tumor fraction measurements, bringing efficiency and quality gains to the molecular pathology workflow. More accurate results and faster turnaround times will reduce workloads and benefit patients.

**Objective:** To develop an AI-based algorithm for the clinical scoring of pulmonary oncology samples to support pathologists and increase consistency.

## METHODS: Algorithm Setup

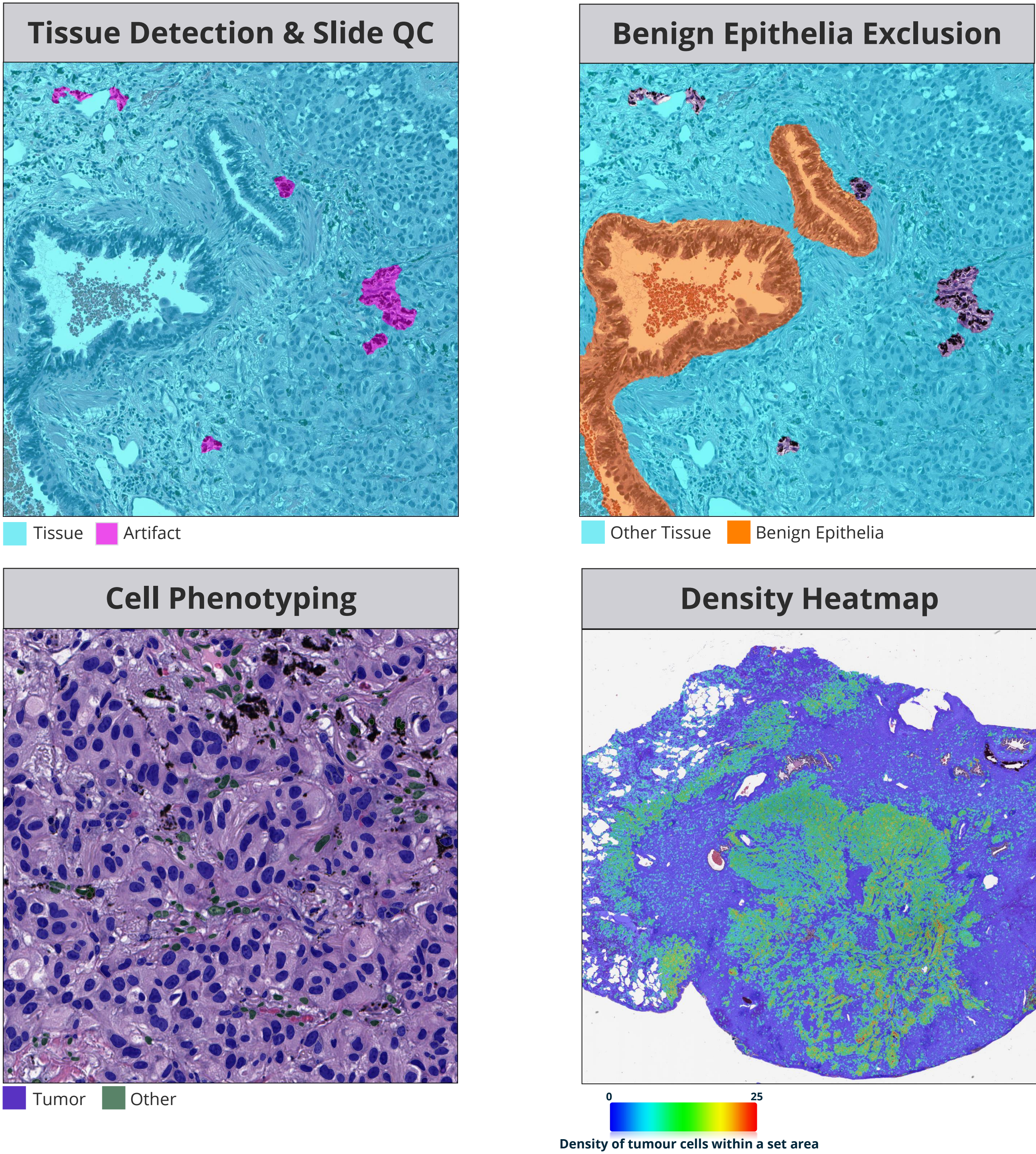


Figure 1: Lung Macrodissect AI workflow

- A Resnet 18-based network (165,860 annotations) was developed to classify cells within the tissue as ‘tumor’ (blue) or ‘other’ (green). A density heatmap highlights regions containing cancer cells.
- Data was sourced from two independent institutions.

## RESULTS: Analytical Validation

**Lung Macrodissect AI** was validated on 30 images unseen during algorithm development, using 38,153 pathologist-reviewed annotations for the cell phenotyper.

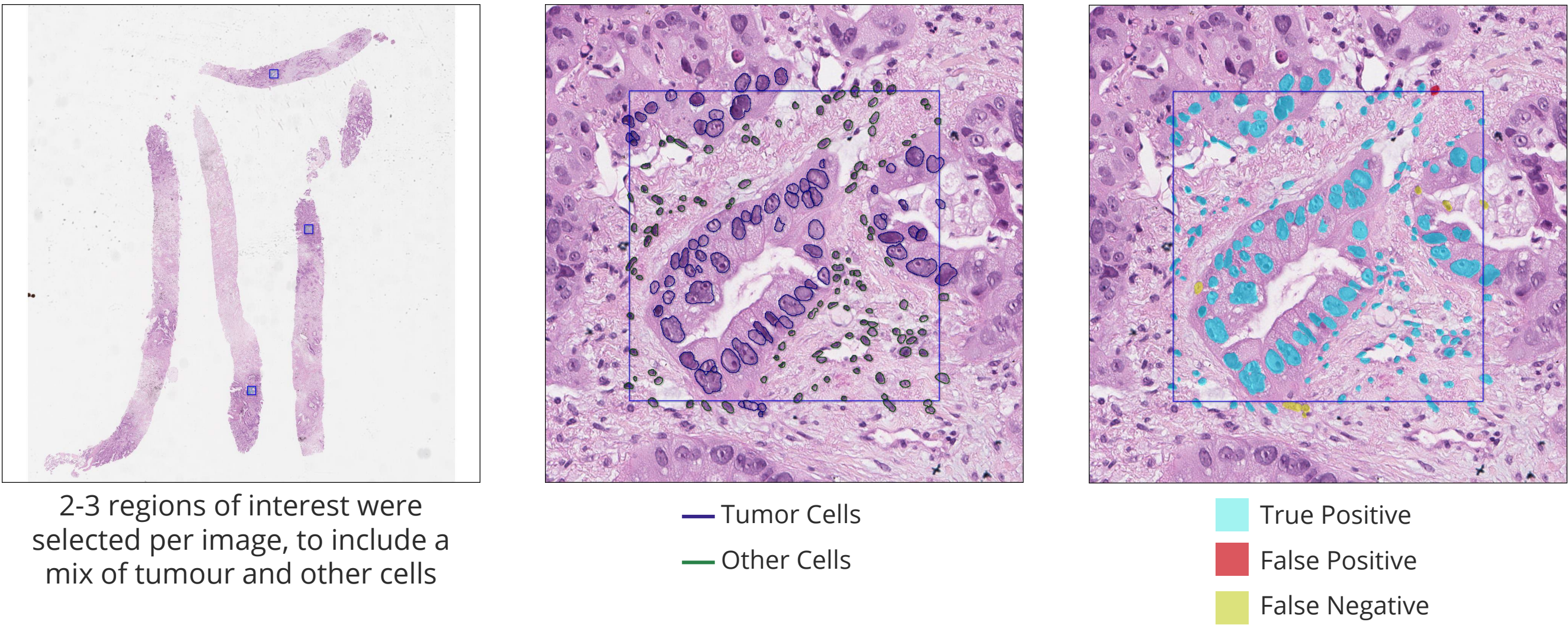


Figure 2: Lung Macrodissect AI analytical validation workflow

	Precision	Recall	F1-Score
‘Tumor’ Class	0.93	0.83	0.87
‘Other’ Class	0.80	0.93	0.84
Cell Phenotyper	0.87	0.88	0.85

## RESULTS: Internal Clinical Validation

**Lung Macrodissect AI** was validated on 68 cases (Institute 1 n=53, Institute 2 n=15) unseen during algorithm development.

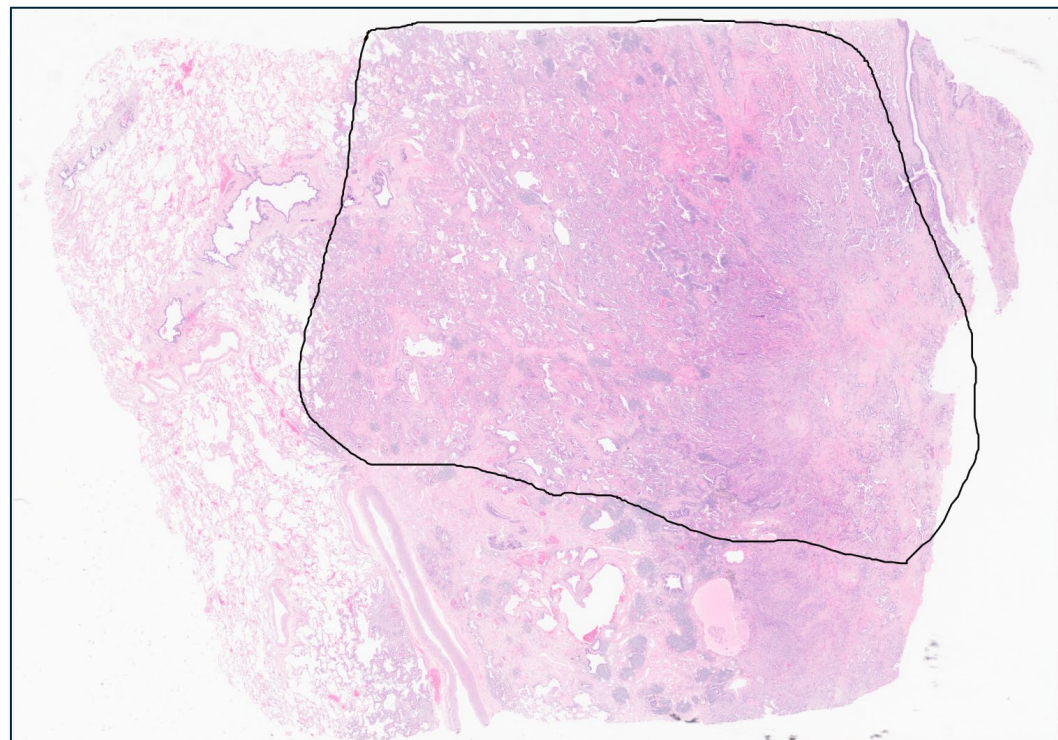


Figure 3: Representative image of primary lung specimen

- Regions of interest were marked for macrodissection by an experienced molecular pathologist.
- The percentage of tumor cells identified by the classifier was compared with a single pathologist’s estimate (Institute 1) or 3 pathologist scores (Institute 2).

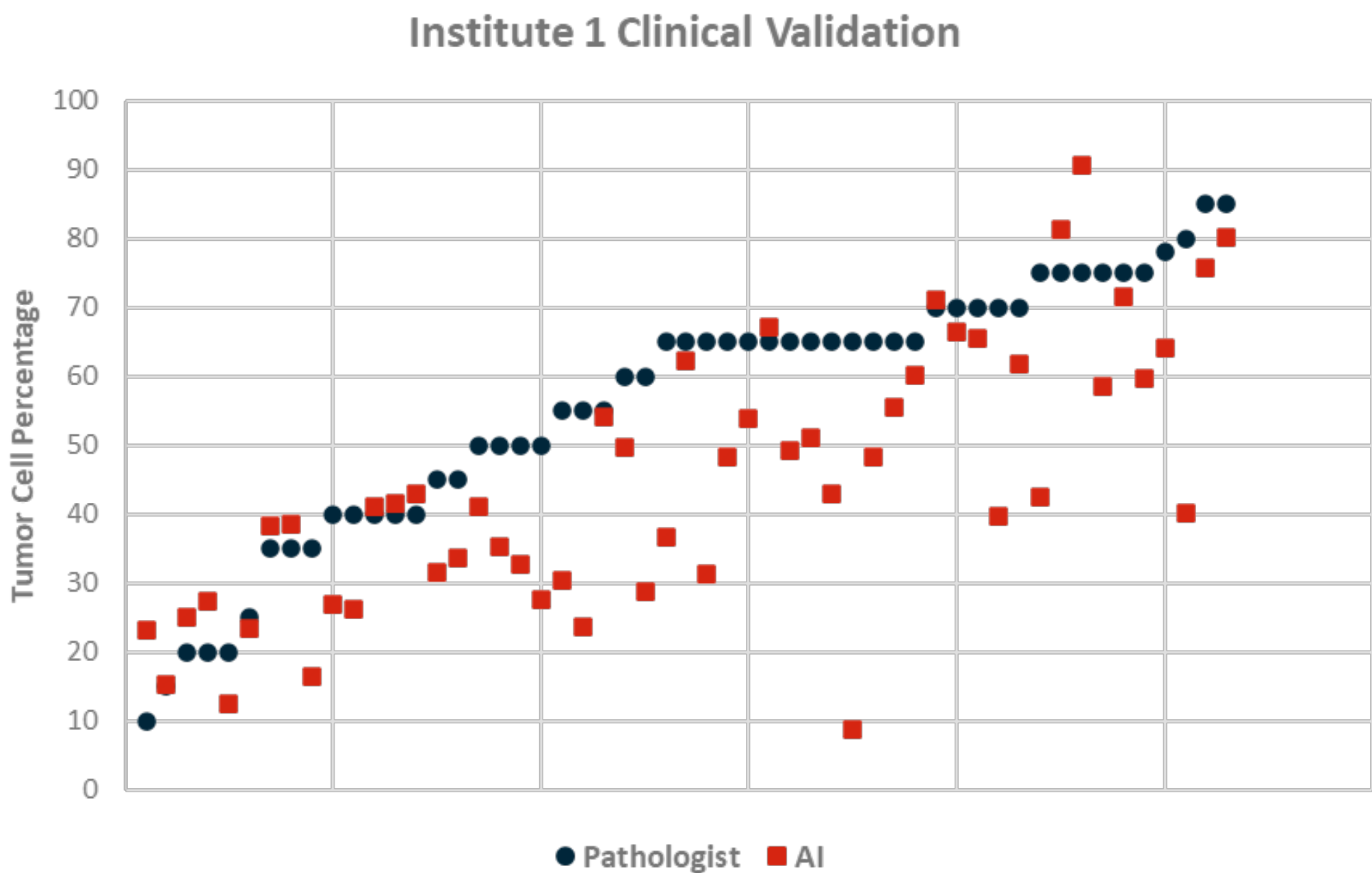


Figure 4: Tumor cell percentage scores of the pathologist (blue) and AI (red)

	Median Tumor Cell Percentage [IQR]	Median Difference to AI [IQR]	ICC Score [CI]
Pathologist	65% [40-70%]	13% [5-15%]	0.63 [0.19-0.82]
Algorithm	42% [31-60%]	-	-

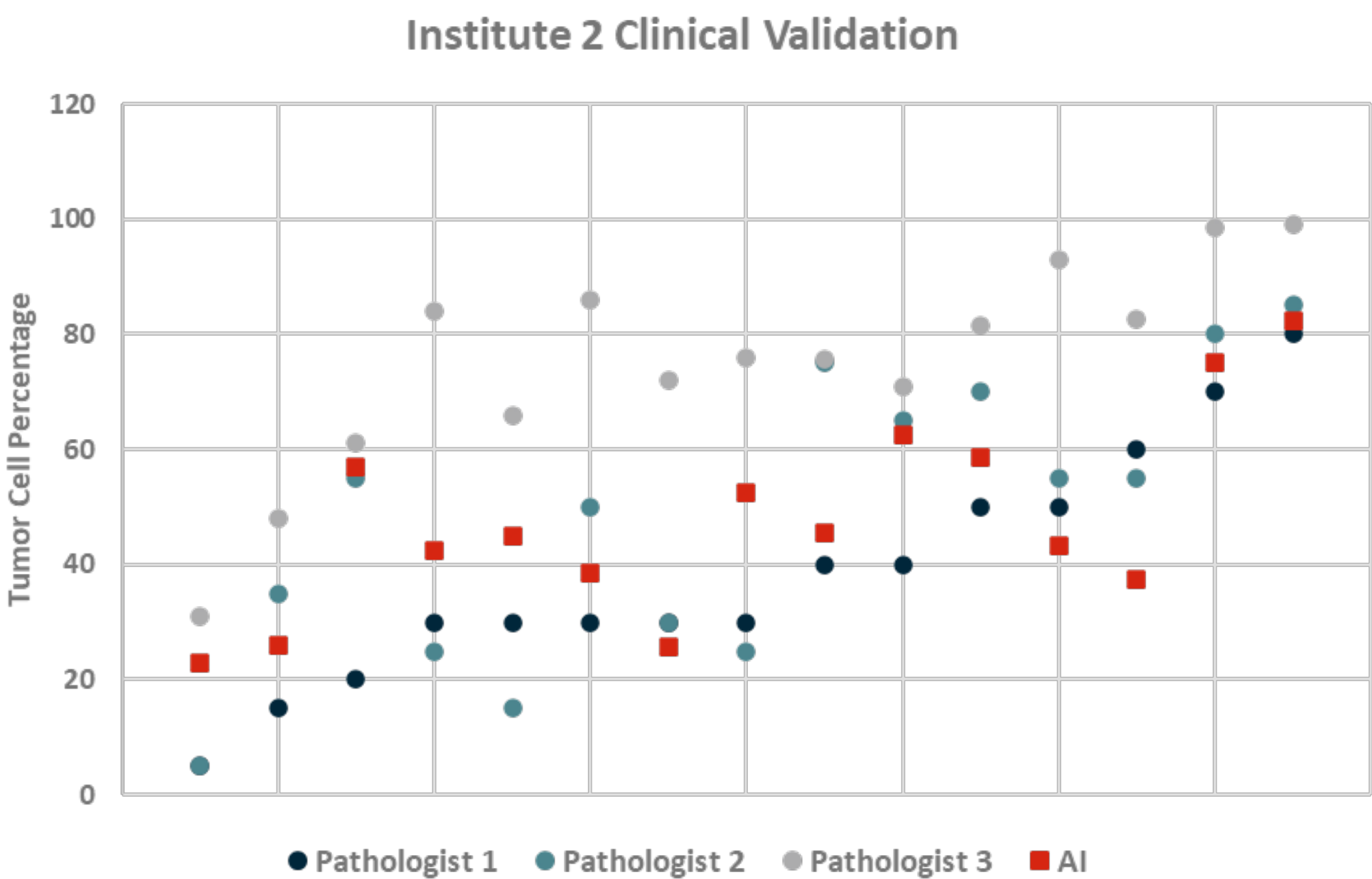


Figure 5: Tumor cell percentage scores of pathologist 1 (dark blue), pathologist 2 (light blue), pathologist 3 (grey) and AI (red)

	Median Tumor Cell Percentage [IQR]	Median Difference (vs AI) [IQR]	ICC Score (vs AI) [CI]
Pathologist 1	30% [30-50%]	11% [6-20%]	0.66 [0.21-0.88]
Pathologist 2	55% [28-68%]	12% [5-18%]	0.70 [0.30-0.89]
Pathologist 3	76% [69-85%]	23% [19-44%]	0.29 [0.10-0.69]
Pathologist Average	55% [44-66%]	9% [7-18%]	0.73 [0.34-0.90]
Algorithm	45% [38-58%]	-	-

## DISCUSSION & CONCLUSIONS

- Tumor cell percentage scores vary greatly between pathologists and this subjectivity makes generating a ground truth problematic. Using multiple scorers allows for the generation of a consensus-based ground truth to compare the AI against
- Scores from **Lung Macrodissect AI** have reasonable agreement with individual pathologist estimates in routine lung ADC cases annotated for macrodissection. Agreement with AI is improved when taking an average score from 3 pathologists.
- Cell level validation shows that the algorithm detects tumor cells with a high level of accuracy.
- Use of this classifier can support pathologists by saving time, standardizing results, and improving the quality of molecular readouts.