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Clinical scoring and validation of a comprehensive AI-powered tumour content and lung macrodissection algorithm

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INTRODUCTION

Growing demand for targeted therapies has significantly increased molecular testing on formalin-fixed, paraffin-embedded (FFPE) tissue samples, resulting in higher workloads for pathologists. Traditionally, pathologists manually review H&E-stained slides, identify tumour-dense regions for macrodissection, and estimate the percentage of tumour cells within these regions. This tumour content scoring, is crucial to ensure the viability of molecular testing. However, manual scoring is often labour-intensive and prone to observer variability, leading to inconsistencies and delays.

We present Lung Macrodissect AI, an automated AI-driven algorithm designed to standardise and streamline tumour content scoring and macrodissection workflows. By providing more accurate and consistent results, Lung Macrodissect AI not only reduces pathologists' workload, it decreases turnaround times and inaccurate results, ultimately improving patient care.

OBJECTIVE: To analytically and clinically validate Lung Macrodissect AI for tumour content scoring of non small cell lung adenocarcinoma.

Macrodissection Algorithm Workflow

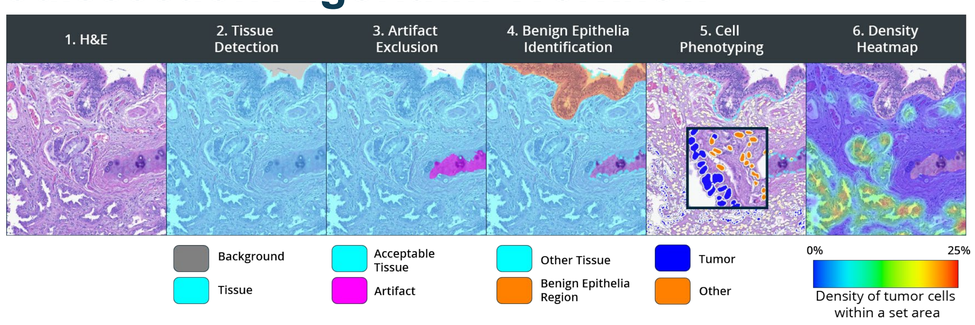
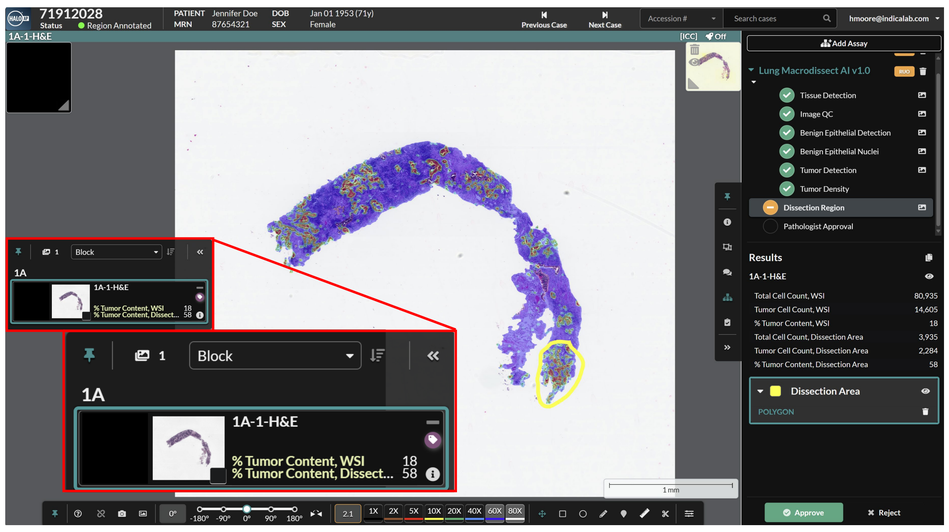


Figure 1: Lung Macrodissect AI detects all tissue present on the slide, removing background glass and artifacts from the analysis. Benign epithelial regions are classified separately and their cell count is added to the tumour content results. Cells are then phenotyped as either 'tumour' or 'other' cells. A detailed tumour density heatmap is generated, which assists pathologists in creating precise ROI annotations for downstream macrodissection.

Clinical Deployment



HALO AP®

Figure 2: Lung Macrodissect AI launched in HALO AP®, a browser-based case management system where researchers and clinicians can collaborate on slide QC, case review, and deployment of AI-based analysis pipelines like HALO Macrodissection Solutions. Tumour content across the WSI and within the macrodissection ROI (yellow annotation) are displayed in the slide tray and within the assay results window.

METHODS: Clinical Validation

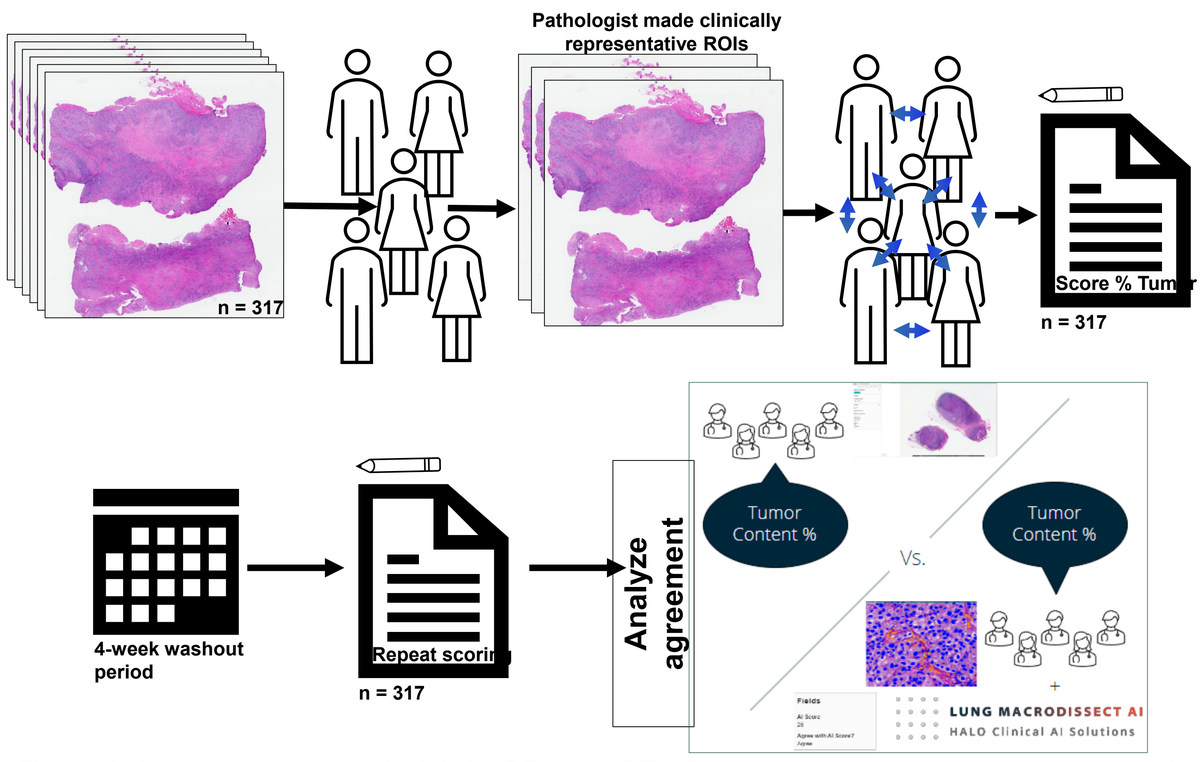
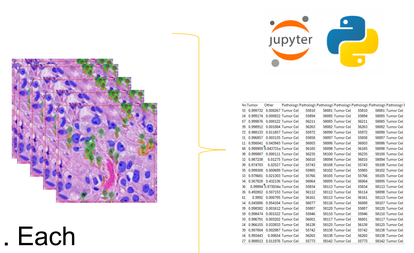


Figure 3. 317 (primary and metastatic) H&E Leica GT450 scanned images previously unseen by the algorithm and from an external site were used for clinical validation. Each pathologist generated clinically representative ROIs on 1/5th of the images prior to scoring the % tumour content on all 317 images. Repeat scoring was performed with the assistance of Lung Macrodissect AI after a 4-week washout period. ICC and Fleiss' Kappa were calculated to measure agreement between pathologists with and without AI assistance.

METHODS: Analytical Validation

- 9,374 cells across 22 WSI from an external institute (unseen during algorithm development)
- Images were from primary and metastatic tissue
- Validation performed for cell segmentation and classification (cancer vs. other)
- Ground truth provided by the mode of five independent pathologists' annotations



1. Each pathologist annotates their own copy of images

2. Data export, collation and analysis

RESULTS: Analytical Validation

Correct Cell Segmentation:
Precision (PPV) = 1.0
F1 score = 0.997

Correct Cell Classification (cancer vs. other):
Precision (PPV) = 0.942
F1 score = 0.944

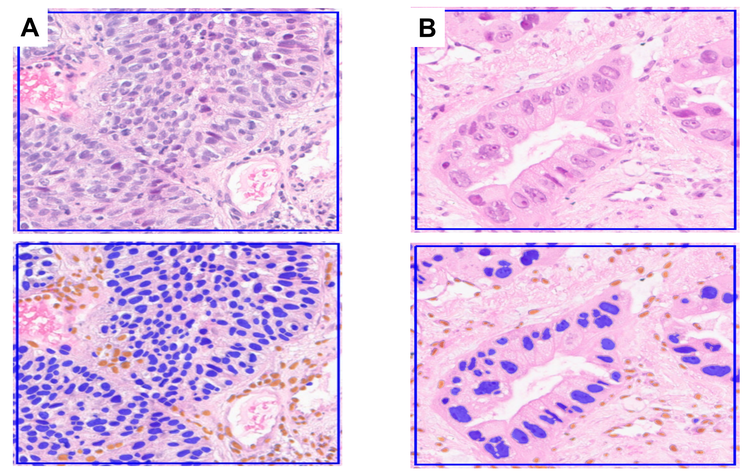


Figure 4: Example results of the tumour cell classification. A) primary lung, B) metastatic lung adenocarcinoma in the liver. Image mask: Blue = cancer cell class; Orange = other cell class.

RESULTS: External Clinical Validation

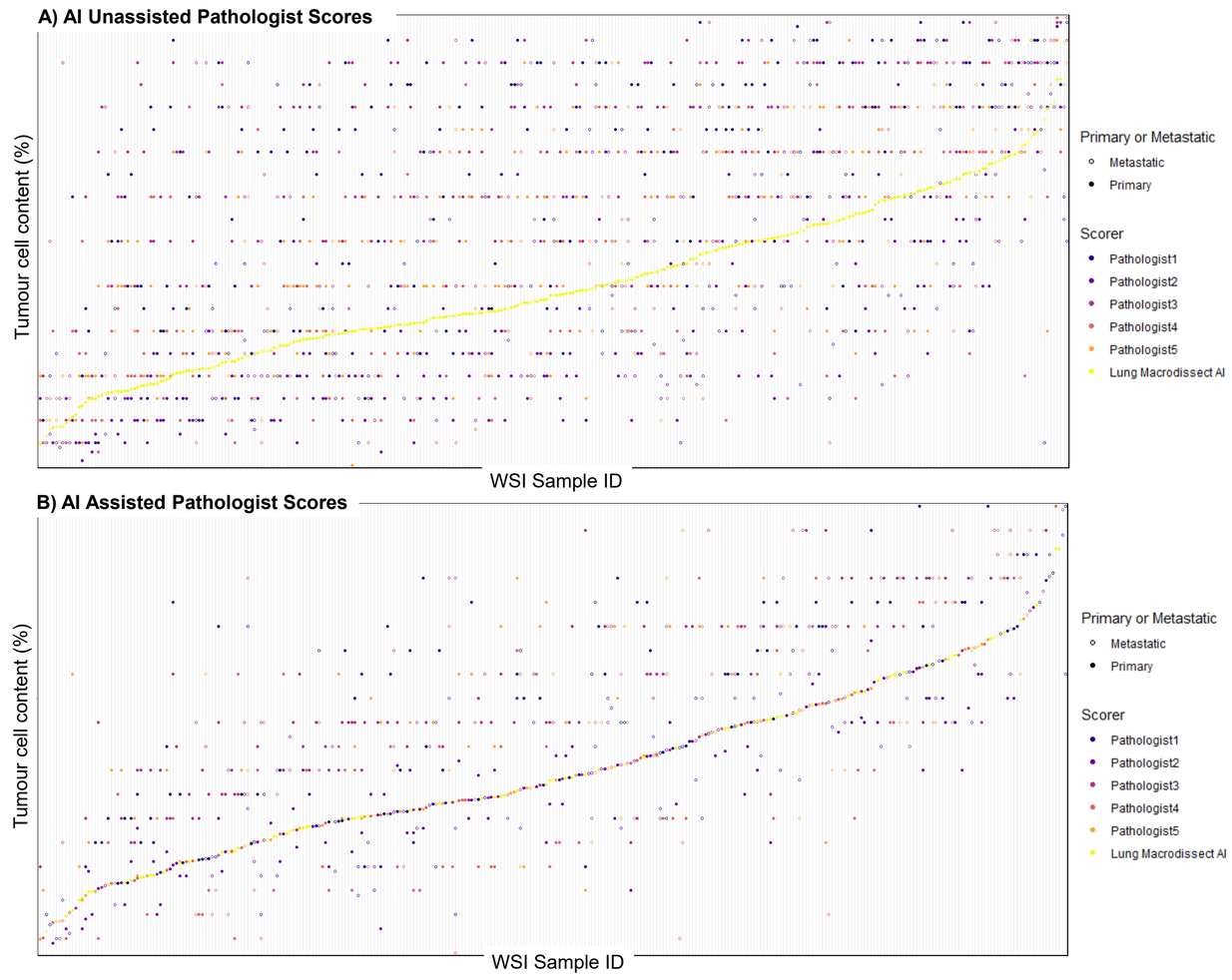


Figure 5. 317 samples (primary and metastatic) ordered by the algorithm's % Tumor cell score. **(A)** Pathologist unassisted scoring **(B)** Pathologist algorithm-assisted scoring. Pathologist tumour content scoring is more standardised when scoring with Lung Macrodissect AI.

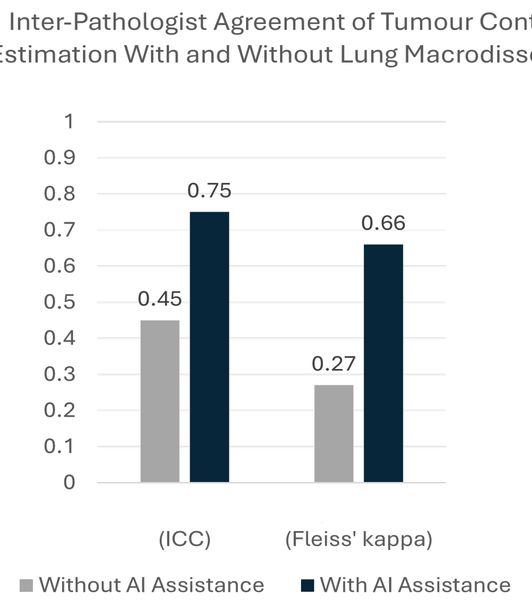


Figure 6. ICC statistic is calculated using continuous % tumour cell content. Fleiss' kappa statistic is calculated after binarising the % tumour cell content based on a 20% cut-off. Both measurements demonstrate higher agreement of tumour content by pathologists when assisted by Lung Macrodissect AI.

Discussion and Conclusions

- Lung Macrodissect AI is an AI-powered tool that quantifies tumour content and guides ROI selection to enhance macrodissection workflows and downstream molecular analysis.
- Cell-level analytical validation shows that the algorithm detects tumor cells with a high level of accuracy.
- Agreement between pathologist tumour content scoring without AI assistance is poor but increases significantly with AI assistance
- Use of this AI pipeline can support pathologists by saving time, standardising results, improving the quality, and reducing the failure rate of molecular readouts.

Lung Macrodissect AI is not a medical device in the EU/UK and is not intended to be used for diagnostic purposes. Lung Macrodissect AI is accessed via the HALO AP® enterprise digital pathology platform. Lung Macrodissect AI is For Research Use Only in the USA and is not FDA cleared for clinical diagnostic use. HALO AP® is CE-IVDR marked for in-vitro diagnostic use in Europe, the UK, and Switzerland. HALO AP® is For Research Use Only in the USA and is not FDA cleared for clinical diagnostic use. In addition, HALO AP® provides built-in compliance with FDA 21 CFR Part 11, HIPAA, and GDPR.