Clinical and Analytical Validation of a Comprehensive AI-powered Colorectal Tumor Content and Macrodissection Algorithm

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BACKGROUND

As targeted cancer therapies continue to be developed the demand for molecular testing on tissue samples has also increased. Accurate tumor content scoring is crucial for reliable molecular testing. However, manual scoring is time-consuming and suffers from inter- and intra-observer variability, affecting sample preparation and the molecular test.

We present the external validation of an AI-based algorithm designed to standardize tumor content assessment, aid macrodissection region selection and enhance scoring reliability to maximize efficiency in colorectal (CRC) molecular pathology.

CRC MACRODISSECT AI WORKFLOW

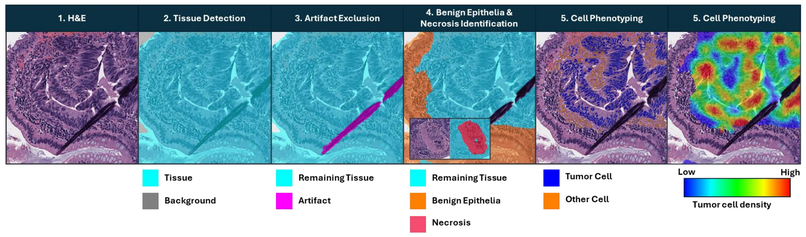
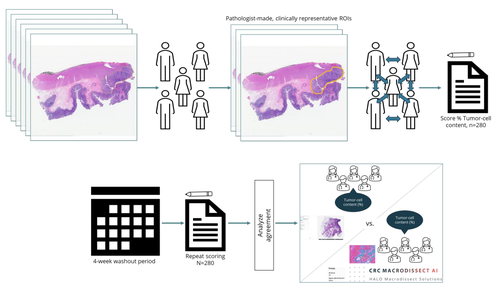


Figure 1: H&E slides are scanned and input into HALO AP®, where CRC Macrodissect AI detects all tissue present on the slide, removing background glass and artifacts from the analysis. Benign epithelial and regions of necrosis are classified separately. The benign epithelial cell count is added to the tumor content results. Remaining cells are then phenotyped as either 'tumor' or 'other' cells. A detailed tumor density heatmap is generated, which assists pathologists in creating precise ROI annotations for downstream macrodissection. The software displays the whole slide and macrodissection region tumor content results in the user interface.

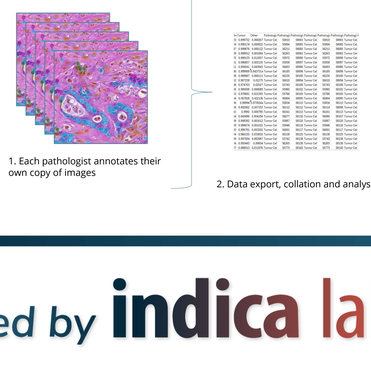
METHODS: Clinical Validation

Figure 2. 280 (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 % tumor content on all 280 images. Repeat scoring was performed with the assistance of CRC 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

Figure 3.
- 20,765 cells across 20 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

CLINICAL DEPLOYMENT

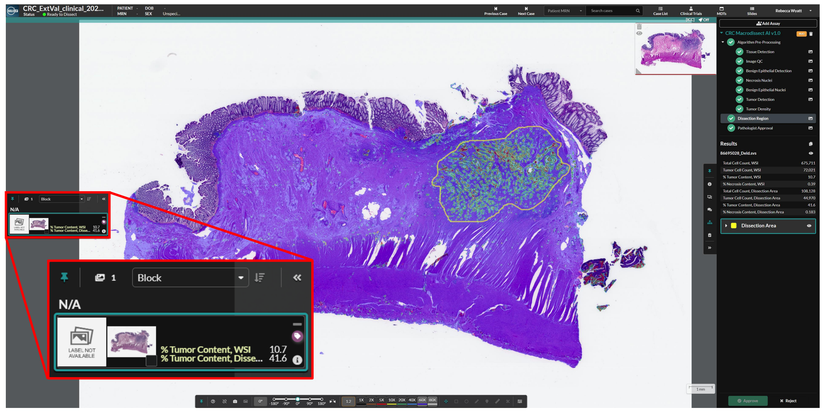


Figure 4: CRC Macrodissect AI launched in HALO AP®, a browser-based case management system where researchers and clinicians can collaborate on slide QC, case review, and deployment of AI-based analysis pipelines like HALO Macrodissection Solutions. Tumor content across the WSI and within the macrodissection ROI (yellow annotation) are displayed in the slide tray and within the assay results window.

RESULTS: Clinical Validation

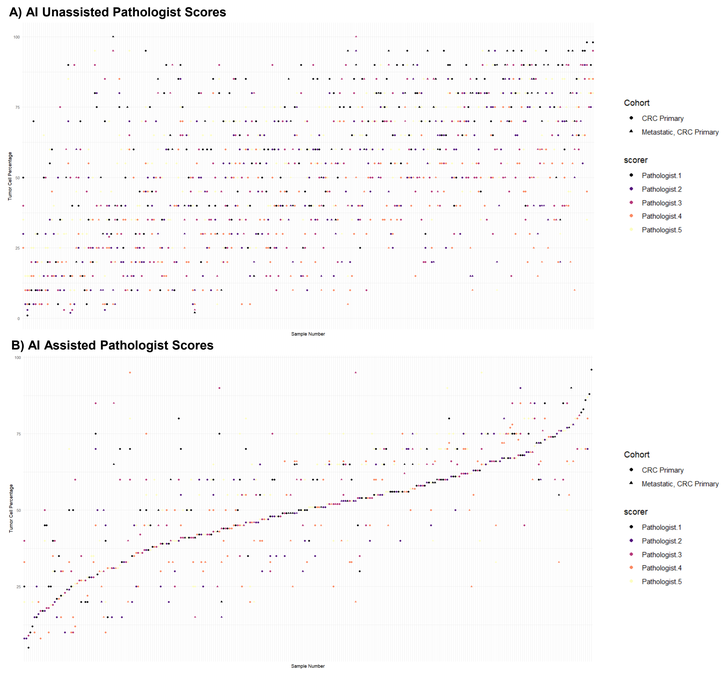


Figure 5. 280 samples (primary and metastatic) ordered by the algorithm's % Tumor cell score. **(A)** Pathologist unassisted scoring **(B)** Pathologist algorithm-assisted scoring. Pathologist tumor content scoring is more standardized when scoring with CRC Macrodissect AI.

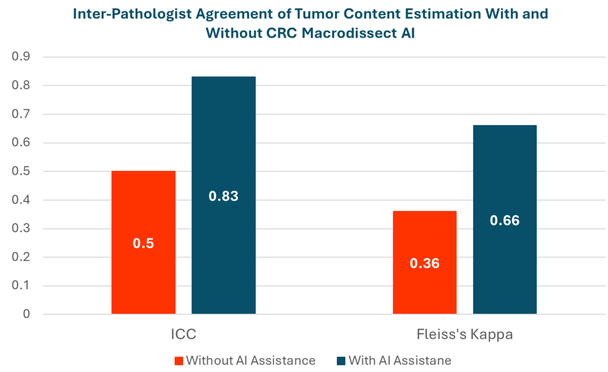
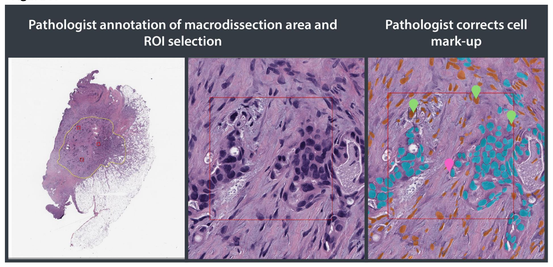


Figure 6. ICC statistic is calculated using continuous % tumor cell content. Fleiss' kappa statistic is calculated after binarizing the % tumor cell content based on a 20% cut-off. Both measurements demonstrate higher agreement of tumor content by pathologists when assisted by CRC Macrodissect AI.

RESULTS: Analytical Validation

Figure 7.



An area for macrodissection was drawn by pathologists and three ROIs were selected to include a mix of tumor and other cells. Pathologists corrected masks by dropping pins on false positives and false negative tumor cells.

Tumor
Other
Tumor False Positive
Tumor False Negative

Correct Cell Segmentation:
Precision (PPV) = 0.9997
F1 score = 0.9996

Correct Cell Classification (Tumor vs. Other):
Precision (PPV) = 0.961
F1 score = 0.970

CONCLUSIONS

- CRC Macrodissect AI is an AI-powered tool that quantifies tumor 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 tumor content scoring without AI assistance is poor but increases significantly with AI assistance.
- Use of this AI pipeline can support pathologists by saving time, standardizing results, improving the quality, and reducing the failure rate of molecular readouts.

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