

# Optimizing MSI Testing with AI Using H&E Histology Slides of Colorectal Cancer Biopsies

ESCP | Sept 7-9, 2024 | Abstracts

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## Background

- Microsatellite Instability (MSI) is a key biomarker for the management of colorectal cancer (CRC) patients.
- Reflex testing is now recommended by most of the medical organizations in the US<sup>1</sup> and EU<sup>2,3</sup>. Just recent real world evidence reports a MSI testing rate of 37% in 2019<sup>4</sup>.
- NCCN<sup>5</sup> is still demonstrating unsatisfactory results by using non-adjacent immune checkpoint inhibitors (ICI) in patients with non-metastatic MSI colon cancer<sup>6</sup>, paving the way for MSI reflex testing on biopsies.
- In 2021, Owkin developed MSHistAI (CCE-VD) for the pre-screening of MSI patients with colorectal cancer with a deep learning model directly on H&E resection slides<sup>7</sup>.

## Objectives

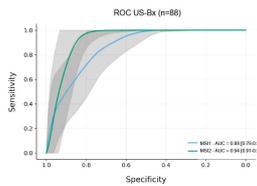
- Evaluate performance of two model candidates on biopsy samples: MS1 and MS2
- Explore the clinical impact of a MSI pre-screening tool on CRC biopsies

## Method

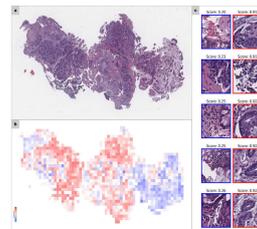
- MS1 was trained on TCGA-COAD dataset and MS2 has an enhanced model architecture and is trained on additional MPMATH and TCGA-READ dataset
- MS1 and MS2 were then validated on US-Bx and FR-Bx, using AUROC, sensitivity and specificity metrics to assess the model's performance

	Cohort name	Number of cases	Number of slides	MSI patients n (%)
Training cohorts	TCGA-COAD	434	859	78 (18%)
	TCGA-READ	172	184	25 (15%)
	MPMATH	600	1200	123 (21%)
Validation cohorts	US-Bx	68	68	35 (40%)
	FR-Bx	643	643	238 (37%)

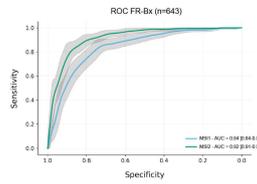
## Results



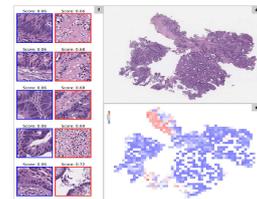
	Sensitivity	Specificity	PPV	NPV
MS1	0.94 [0.80-1.00]	0.62 [0.42-0.82]	0.19 [0.17-0.20]	0.99 [0.97-1.00]
MS2	0.99 [0.80-1.00]	0.85 [0.65-0.97]	0.38 [0.36-0.39]	1.00 [0.98-1.00]



Above, true positive case from US-Bx cohort with  
 → threshold of the MS1 (a)  
 → heatmap of the model prediction (b)  
 → Slides with minimum and maximum scores (c)



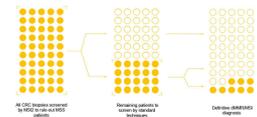
	Sensitivity	Specificity	PPV	NPV
MS1	0.94 [0.85-1.00]	0.44 [0.14-0.68]	0.47 [0.38-0.56]	0.84 [0.80-0.88]
MS2	0.95 [0.89-0.99]	0.81 [0.55-0.79]	0.57 [0.44-0.69]	0.87 [0.83-0.90]



Above, true negative case from US-Bx cohort with  
 → threshold of the MS1 (a)  
 → heatmap of the model prediction (b)  
 → Slides with minimum and maximum scores (c)

## Discussion

- MS2 initially developed to predict MSI on surgical resection shows great performance on biopsy samples
- MS2 with an improved architecture and increased size of training dataset outperforms MS1 with an improved specificity at equivalent sensitivity level
- MS2 model could act as a pre-screening tool to identify MSI patients can have a strong clinical impact for digital pathology labs willing to improve their MSI testing capabilities



## Conclusions

- Promising results of neoadjuvant (N) in colon cancer underlines the importance in the future of reflex MSI testing on biopsies
- Despite a growing agreement across medical organizations to perform reflex MSI testing for all new CRC cases, the testing rate remains low, highlighting potential underdiagnosis
- MS2 model paves the way for an innovative approach to screen CRC patients directly from H&E biopsy slides in few minutes enabling pathology labs to streamline their testing capabilities
- The robust performances of the algorithm enable an efficient rule-out of 62% of the patients while maintaining a critical-gate sensitivity

## References & acknowledgements

1. Arch Pathol Lab Med (2023) 144 (10): 1164-1170.
2. Avast of Owkin (2023) 144 (10): 1164-1170.
3. NCCN - Evaluation du cancer M&M (version - septembre - 2021)
4. NCCN - Diagnostic pathway (ESOP) (22 février 2017)
5. McQuaid et al., European Journal of Human Genetics, 2018
6. Chakrabarti et al., Annals of Oncol. (2022) 33 (10): 1669-1679
7. Salbut et al., Nature Comm. vol 14, Article number: 6895, 2023

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