Clinical Grade AI Model to Streamline MSI Testing An External and Multi-centre Validation Study

USCAP | March 22-27, 2025 | Abstract #2503

Rémy Dubois[1], Charlotte Saillard[2], Damien Jacobs[1], Lionel Guillou[2], Corentin Wilacer[1], Arnaud Fouillet[1], Estelle Macquet[1], Lysiviane Van Frael[1], Mehdi Mirsh[2], Paul Klein[1], Alexandra Leppagnol[1], Nathalie Rioux-Leclercq[3], Jean-François Pitéro[3], Gilrash Kate Uguela[4], Solène-Florence Kammerer-Jacquet[5], Brendan O'Sullivan[4], Katharina Von Loga[4]

[1]Owkin, Paris, France [2]Bioptimus, Paris, France [3]Certa Path, France [4]Department of Pathology, University of Groningen, University Medical Centre Groningen, Groningen, The Netherlands [5]Centre Hospitalier Universitaire de Rennes, Rennes, France [6]University Hospital Birmingham NHS Foundation Trust, Birmingham, United King

Background

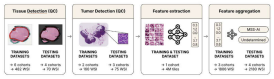
- Microsatellite Instability (MSI) is a key biomarker for the management of colorectal cancer (CRC) patient for which the reflex testing is recommended by most of the medical organizations in the US[1] and EU[2,3,4]
- NICHE-2 trial demonstrated unprecedented results by using neo-adjuvant immune checkpoint inhibitors (ICI) in patients with non-metastatic MSI colon cancer[5], paving the way for MSI reflex testing on biopsies
- In 2021, Owkin developed MSIntuit CRC (CE-IVD) for the pre-screening of MSI patient with colorectal cancer with a deep learning model directly on H&E resection slide[6]

Objectives

- Improve MSIntuit CRC algorithm to make it compatible with CRC biopsies
- Conduct state of the art clinical validation with multiple external centers cohorts
- Demonstrate improved accuracy of MSIntuit CRC as a rule-out solution for MSI testing

Method

- An updated model architecture and additional training cohorts have been leveraged to improve MSIntuit CRC performance



- 7 independent cohorts of archived specimen from clinical routine coming from 5 centers have been collected to validate MSIntuit CRC.
- MMR/MSI labels of each tumor were determined using validated gold standard techniques in 67% with MMR-IHC, in 10% with MSI-PCR and in 23% with both techniques
- The validation was carried out in a single run meaning that no experiments were carried out beforehand to prevent bias in the interpretation of the results

Results

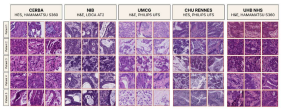
- When evaluated independently on +2000 biopsies and surgical resections specimens, MSIntuit CRC model shows high sensitivity and NPV, confirmed at center level with 7 independent cohorts from 5 centers

Specimen Type	Overall Performances				
	n_{TOTAL}	n_{MSI} (%)	Sensitivity [95%CI]	Specificity [95% CI]	NPV at 15% prevalence
Biopsies	1576	320 (20%)	**0.95 [0.89-0.99]**	**0.56 [0.43-0.71]**	**0.99 [0.97-1.00]**
Surgical Resections	622	209 (34%)	**0.96 [0.86-1.00]**	**0.78 [0.56-0.89]**	**0.99 [0.97-1.00]**

Performance breakdown per center

Center	n_{TOTAL}	n_{MSI} (%)	Sensitivity	Specificity	NPV at 15% prevalence
CERBA	223	18 (8%)	**0.95**	**0.58**	**0.99**
CHU de Rennes	302	53 (17%)	**0.95**	**0.56**	**0.99**
NI Biobank	108	17 (16%)	**0.97**	**0.73**	**0.99**
UHB NHS	512	46 (9%)	**0.95**	**0.52**	**0.99**
UMCG	281	36 (13%)	**0.95**	**0.56**	**0.99**
CHU de Rennes	349	135 (39%)	**0.96**	**0.74**	**0.99**
UHB NHS	213	14 (7%)	**0.95**	**0.82**	**0.99**

- MSIntuit CRC has been validated on heterogeneous data, highlighting its ability to take over the variability across pathology labs



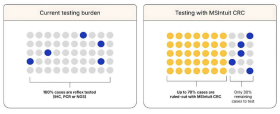
- Interpretable by design, MSIntuit CRC enables to identify most predictive regions at tiles level for a better understanding of the predictions features in the slide

Clinical workflow

- The result of MSIntuit CRC indicates whether or not a confirmatory test is needed, enabling MSS patients to be directly ruled-out with only one H&E slide

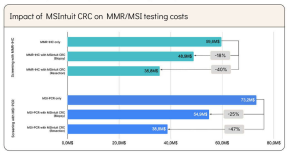
Discussion

- At laboratory level, MSIntuit CRC enables to decrease the workload associated with MMR/MSI testing up to 70%, this would enable centers to streamline their workflow, liberate auto-stainers and time for tasks with more added value and compensate for pathologist and technician shortage.



- At payer level, MSIntuit CRC could be an economic alternative to current MMR/MSI testing techniques enabling costs to decrease between 31% and 57% depending on the specimen analyzed and the testing technique used*

Impact of MSIntuit CRC on MMR/MSI testing costs



*All assumptions are based on US market CRC incidence of 151,000 patients, IHC cost = 395$[1], PCR cost = 485$[7]

Conclusions

Robustness
MSIntuit CRC demonstrates strong performance during clinical validation with independent multicentre cohorts

Efficiency
With shrunken ressources and increased testing complexity, MSI testing can benefit from an efficient rule-out solution

Cost-effectiveness
Combination of triage solution and confirmatory testing may enable a decrease of the cost associated with MSI testing

References & acknowledgements

1. Arch Pathol Lab Med (2022) 146 (10): 1194–1210.
2. Annals of Oncology 30: 1232–1243, 2019
3. INCa - Evaluation du statut MMR tumoral – synthèse - 2021
4. NICE - Diagnostics guidance (DG37) P22 February 2017
5. Chalabi et. al. Annals of Oncol. (2022) 33 (suppl_7): S808–S869
6. Saillard et. al. Nature Comm. vol 14, Article number: 6895, 2023
7. J. Hao et. al. *J. Pers. Med.* **2021**, *11*, 1284

The results published here are in part based upon data generated by the TCGA Research Network. This work was granted access to the HPC resources of IDRIS under the allocation AD011012519 made by GENCI. We thank Medpath, Cypath and Neogenomics teams for their help on the data collection for the development of MSIntuit CRC.
We thank our partners University Hospital Birmingham NHS, CHU de Rennes, University Medical Center Groningen, Certa Path and the Northern Ireland Biobank for their contribution on the data collection for the validation of MSIntuit CRC.

© 2025 OWKIN, INC.
Confidential information. Do not share without written permission from Owkin Inc.