

# Assessing Risk of Oral Cancer Progression Using an S100A7 Immunohistochemical Signature-Based Assay

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## BACKGROUND & PURPOSE

Oral squamous cell carcinomas (OSCCs) are thought to usually arise from potentially pre-malignant oral epithelial lesions (PPOELs) demonstrating oral epithelial dysplasia (OED) [1]. Traditionally, the degree of OED seen in these oral lesions is used as a predictor of the risk for malignant transformation. Because of a lack of sensitivity, and high inter- and intra-observer variability among pathologists, a more accurate predictor for progression to OSCC is needed [2]. Emphasizing the need to improve existing standard of care, one approach to identifying lesions at risk for progression to cancer is to assess protein biomarkers quantitatively in suspicious lesions. **In this study, an S100A7 immunohistochemical (IHC) signature-based grading platform [3] was compared to the three-tiered WHO OED grading system [4] to evaluate its ability to predict the risk of progression of clinically suspicious oral lesions to OSCC.**

## MATERIALS & METHODS

Oral epithelial biopsies were obtained from patients in a prospective observational study evaluating the utility of S100A7 IHC signature-based risk assessment for clinically suspicious lesions (ClinicalTrials.gov #NCT04622462). Oral lesions were assessed by community-based surgeons and biopsies were performed when clinically indicated. Formalin-fixed paraffin-embedded biopsy specimens were stained with H&E and graded using three-tiered WHO OED grading assessment. Samples from the same biopsy specimen were also IHC stained with S100A7, digitally scanned, and risk-stratified using a proprietary, quantitative, IHC signature-based, AI-driven software platform (Proteocyte AI, Toronto, Canada; Figure 1) designed to deliver an individualized risk score for progression to OSCC.

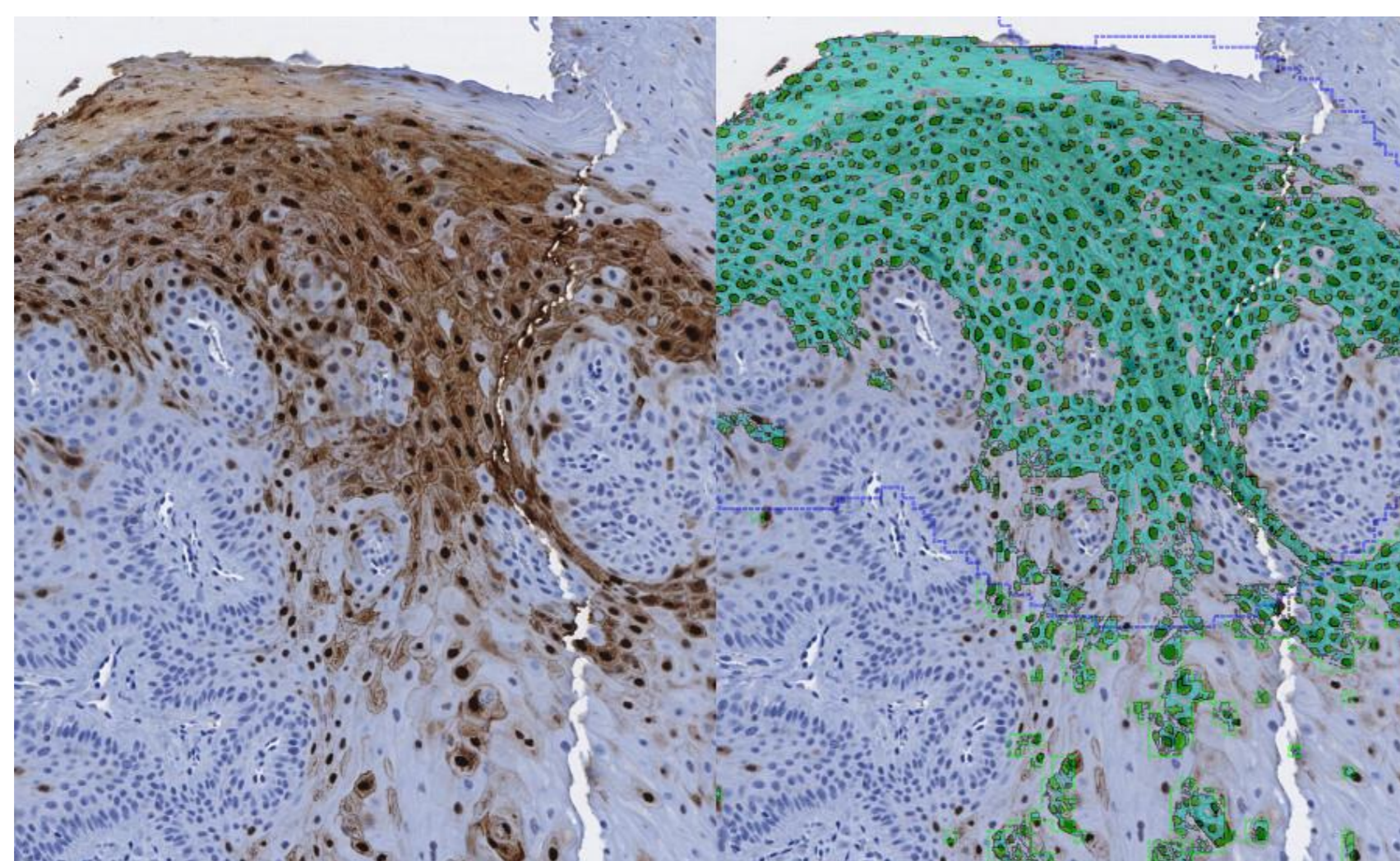


Figure 1. S100A7 IHC signature-based assessment.

## SELECTED REFERENCES

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## RESULTS

- Sixty-six (of 446) lesions from two community-based oral and maxillofacial surgical practices with a mean follow-up of 24.5 months were included in this subset study cohort (Table 1).

**Table 1. Histopathological diagnoses with patient demographics and characteristics of study cohort.**

	n	OED Grade				
		Total	No OED	Mild	Moderate	Severe
Malignant transformation	66	25	27	8	6	
Sex						
Male	35	15	14	3	3	
Female	31	10	13	5	3	
Smoking						
Yes	25	6	12	4	3	
No	32	17	12	2	1	
Unknown	9	2	3	2	2	
Alcohol						
Yes	20	4	10	3	3	
No	6	3	3	0	0	
Unknown	40	18	14	5	3	
Biopsy						
Incisional	24	8	10	3	3	
Excisional	39	17	14	5	3	
Not Indicated	3	0	3	0	0	
Lesion						
Persist	3	0	2	1	0	
Recur	12	3	7	1	1	
Tongue	26	5	15	4	2	
FOM	13	1	7	2	3	
Lip	8	5	0	2	1	
Other	17	14	3	0	0	
Not Indicated	2	0	2	0	0	
Age (years)						
Mean	61	59	61	61	65	
Median	62	57	63	63	64	
Min	19	19	30	44	56	
Max	94	84	94	81	72	
Follow-up (months)						
Mean	25	29	21	29	19	
Median	22	30	19	24	12	
Min	1	1	1	15	7	
Max	94	94	58	58	58	

- Eight (8) lesions progressed to OSCC with an overall malignant transformation rate of 12%
  - 2/25 non-OED (8%)
  - 2/27 mild OED (7%)
  - 2/8 moderate OED (25%)
  - 2/6 severe OED (33%)
- In contrast, in the “Low-Risk” S100A7 IHC signature-based assessment group, no patients progressed (0%).
  - One-hundred percent (100%) of those progressing to OSCC were identified as “Elevated-Risk (>20% Probability)” by the assay.
  - S100A7 IHC signature-based assay demonstrated 100% sensitivity and 100% negative predictive value in this subset cohort of the prospective observational study.

**Table 2. Patient characteristics of those that progressed to OSCC**

Progression to OSCC Patient No.	Sex	Location of Lesion	Biopsy Type	Final Histologic Diagnosis Prior to OSCC	S100A7 IHC signature-based Probability (%) of Transformation	Months to OSCC Transformation
1	Male	Lip	Incision	Actinic cheilitis	28	59.2
2	Male	Lip	Incision	Actinic cheilitis	30	94.2
3	Female	Tongue	Excision	Mild OED	61	25.2
4	Female	Soft Palate	Incision	Mild OED	47	20.5
5	Male	Tongue	Excision	Moderate OED	56	58.3
6	Female	Tongue	Incision	Moderate OED	53	14.9
7	Female	Floor of Mouth	Excision	Severe OED	70	7.03
8	Female	Floor of Mouth	Incision	Severe OED	62	16.8

- Average time to OSCC transformation decreased with an increase in S100A7 IHC signature-based probability:
  - 20 – 40%: 76.6 months
  - 40 – 60%: 31.2 months
  - 61%+: 16.3 months

## DISCUSSION & CONCLUSIONS

- The quantitative S100A7 IHC signature-based assessment offered better prognostic data than OED grade.
- Using an objective, quantitative, image-based, and reproducible platform, the S100A7 IHC signature-based risk assessment better identifies those patients at low risk for transformation of a clinically evident oral lesion to OSCC.
- The S100A7 IHC signature-based assay can be used to provide information on likely outcomes of PPOELs and OED lesions, regardless of the treatment or intervention rendered.