


Automated PD-L1 Tumor Proportion Scoring Algorithm in Non-Small Cell Lung Cancer for Multiple Companion Diagnostic Assays

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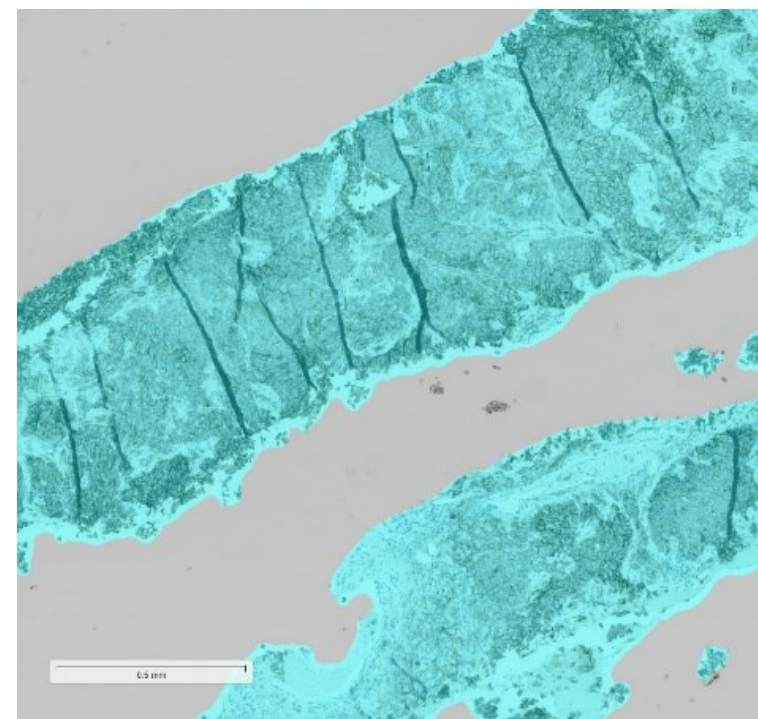
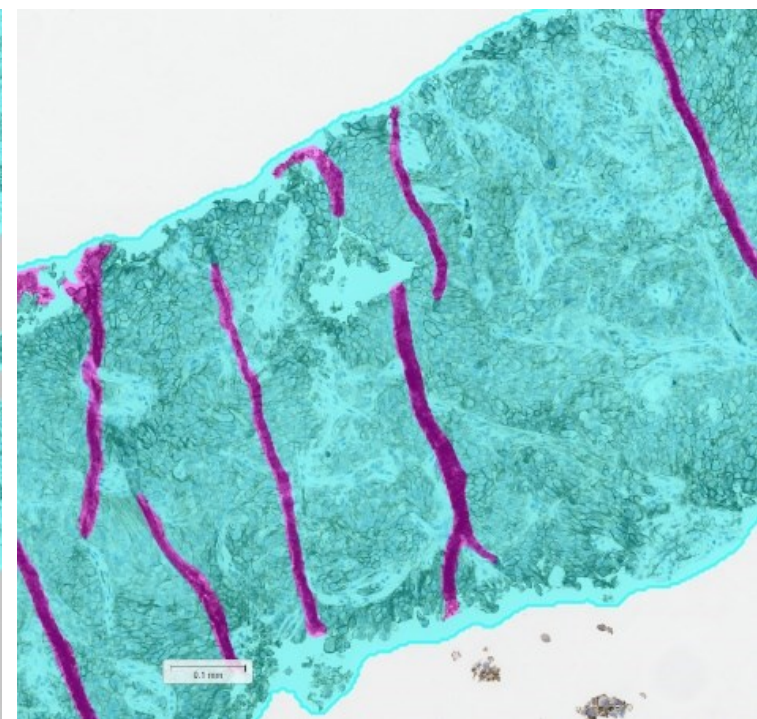
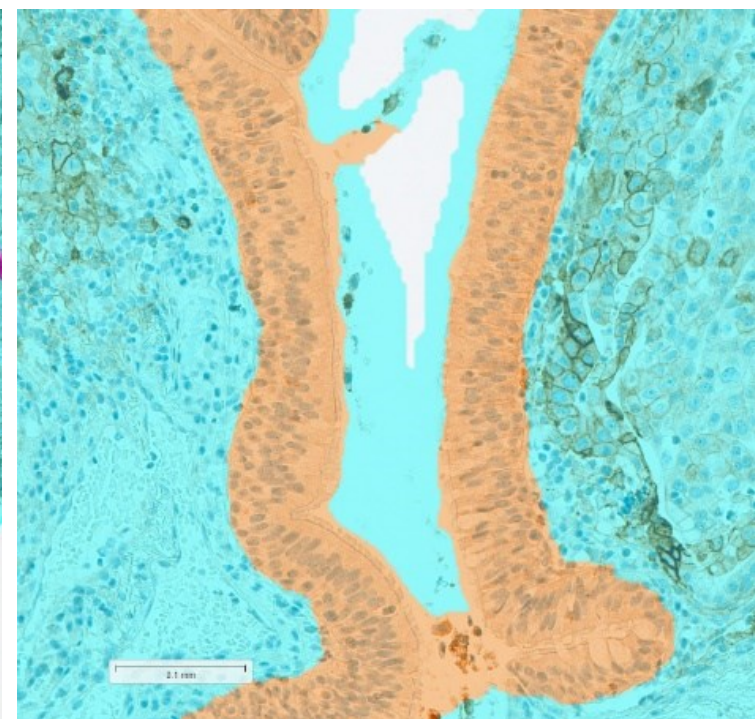
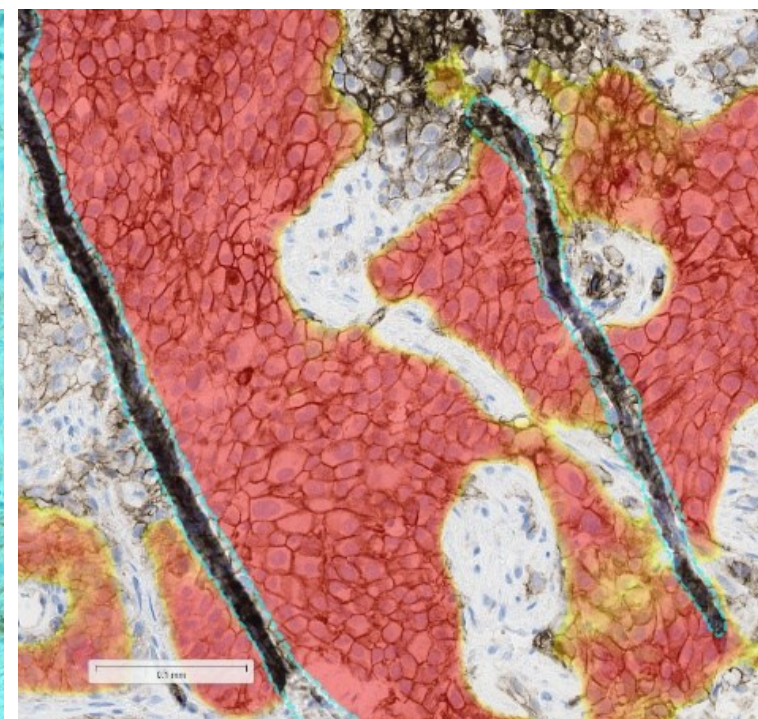
INTRODUCTION

High interobserver disagreement when reporting programmed cell death ligand 1 (PD-L1) expression may result in suboptimal treatment decisions.

HALO PD-L1 Lung AI aims to support pathologists in quantifying SP263 and 22c3 PD-L1 companion diagnostic assays in non-small cell lung cancer (NSCLC).

HALO PD-L1 Lung AI – Algorithm setup

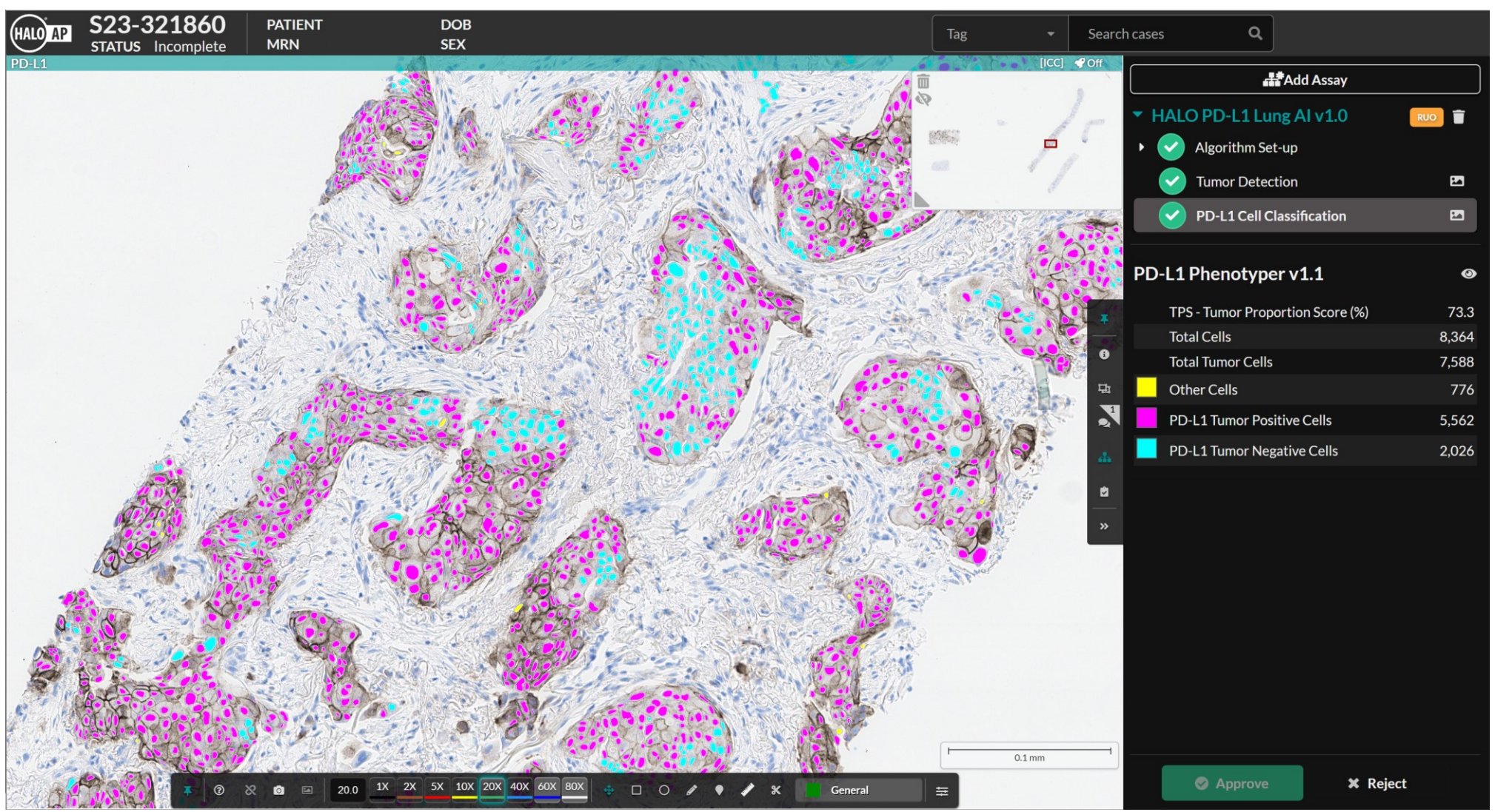
Pre-processing

Tissue Detection	Artifact exclusion	Benign Regions Exclusion	Tumor detection
			
Tissue Background	Acceptable Tissue Artifact	Tissue Benign regions exclusion	Tumor Probability

PD-L1 Cell Classification


Res-18 Based network

146 984 Training annotations



HALO PD-L1 Lung AI user interface within Indica Labs' HALO AP® software

VALIDATION SP263



The algorithm was validated by comparing the TPS score from three pathologists with the TPS score obtained from HALO PD-L1 Lung AI on 203 whole slide images.

Interobserver pathologist agreement – Clinically relevant cut-offs

Pathologist B TPS Score	<1%	1-49%	>50%
Pathologist A TPS Score <1%	57	6	0
Pathologist A TPS Score 1-49%	26	47	17
Pathologist A TPS Score >50%	0	2	48

Pathologist C TPS Score	<1%	1-49%	>50%
Pathologist B TPS Score <1%	59	4	0
Pathologist B TPS Score 1-49%	27	60	3
Pathologist B TPS Score >50%	0	12	38

Pathologist C TPS Score	<1%	1-49%	>50%
Pathologist A TPS Score <1%	73	10	0
Pathologist A TPS Score 1-49%	13	41	1
Pathologist A TPS Score >50%	0	25	40

Percent Agreement	
All Pathologists	64.0
Pathologist A vs Pathologist B	74.9
Pathologist A vs Pathologist C	77.3
Pathologist B vs Pathologist C	75.9

Figure 1. Interobserver pathologist agreement and confusion matrix plots for the pairwise pathologist agreement.

The three pathologists were in complete agreement in 64.0% of the cases. In pairwise comparisons, percent agreement ranged from 74.9% to 77.3%.

HALO PD-L1 Lung AI – Categorical

Agreement with the mode of the pathologists' scores was 75.4%, with agreement at the clinically relevant cut-offs ranging from 0.70 to 0.78.

HALO PD-L1 Lung AI TPS Score	<1%	1-49%	>50%
Pathologist Mode TPS Score <1%	61	18	0
Pathologist Mode TPS Score 1-49%	9	65	0
Pathologist Mode TPS Score >50%	0	23	27

Figure 2. Percent agreement confusion matrix and confidence interval plots between the mode of the pathologists' and HALO PD-L1 Lung AI TPS scores.

HALO PD-L1 Lung AI – Continuous

ICC between the pathologists was 0.96 (95% CI 0.93-0.97).

ICC between the pathologists and HALO PD-L1 Lung AI was 0.95 (95% CI 0.93-0.97).

Comparison	ICC	95% CI
All Pathologists	0.96	0.93-0.97
Pathologists A & B + HALO PD-L1 Lung AI	0.93	0.91-0.95
Pathologists A & C + HALO PD-L1 Lung AI	0.94	0.92-0.96
Pathologists B & C + HALO PD-L1 Lung AI	0.93	0.91-0.95
All Pathologists + HALO PD-L1 Lung AI	0.95	0.93-0.97

Figure 3. Confidence interval plot for the intraclass correlation coefficient.

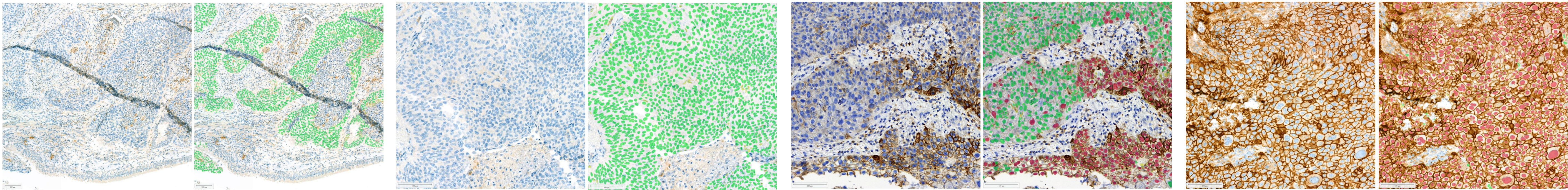



Figure 4. Representative markups of HALO PD-L1 Lung AI on SP263 stained slides.

VALIDATION 22C3 – Preliminary Results



The algorithm was validated by comparing the clinical report TPS with the TPS score obtained from HALO PD-L1 Lung AI on 238 whole slide images from a second independent institute.

Agreement of HALO PD-L1 lung AI with the pathologist TPS clinical report was 73.5% overall (95% CI 0.67 – 0.79).

ICC between the algorithm and the pathologist reported TPS scores was 0.95 (95% CI 0.93 – 0.96).

HALO PD-L1 Lung AI TPS Score	<1%	1-49%	>50%
Pathologist TPS Score <1%	41	28	1
Pathologist TPS Score 1-49%	10	76	6
Pathologist TPS Score >50%	0	18	58

Figure 5. Percent agreement confusion matrix and confidence interval plots between the pathologist report and HALO PD-L1 Lung AI TPS scores.

Figure 5. Representative markups of HALO PD-L1 Lung AI on 22c3 stained slides.

CONCLUSIONS

Immunotherapy has revolutionized advanced NSCLC treatment and several companion diagnostic assays are available to determine eligibility for this therapy. However, reporting of PD-L1 expression suffers from high interobserver disagreement. We developed HALO PD-L1 Lung AI to support pathologist PD-L1 scoring with the aim of saving pathologists time and ensuring consistency in the reported results. The algorithm is highly concordant with the pathologist TPS scores for SP263 and 22c3 companion diagnostic assays.

HALO PD-L1 Lung AI is for Research Use Only and not intended for clinical diagnostic use.