An Automated Clinical Workflow Integrating an AI-driven PD-L1 22C3 Scoring Algorithm into a Browser-Based Digital Pathology Solution

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CONTEXT

Quantitative image analysis of histopathologic tissue sections provides a promising approach for advancing precision medicine in clinical practice. However, there is limited literature on integrating digital pathology-based artificial intelligence algorithms and workflows in clinical practice. Here, we demonstrate a real-world integration for Lunit SCOPE PD-L1 (Lunit, Inc., Seoul, South Korea) currently deployed for clinical use at Guardant Health (Redwood City, California) via integration with the HALO AP® (Indica Labs, Inc., Albuquerque, New Mexico) digital pathology platform and with Guardant's laboratory information management system (LIMS). Lunit SCOPE PD-L1 was initially introduced at Guardant for PD-L1 analysis in non-small cell lung carcinoma (NSCLC), but was rapidly scaled to support all solid tumor types, including breast, colorectal, gastric, pancreatic, prostate and urothelial cancers.

DESIGN

Lunit SCOPE PD-L1 algorithm development and validation

Lunit SCOPE PD-L1 22C3 was developed from whole slide images (WSIs) of NSCLC, breast, biliary tract, colorectal, gastric, hepatic, pancreatic, prostate and urothelial cancers. The WSIs were too large to be used to train an AI model at once, so they were extracted into a grid of a certain size and then annotated by board-certified pathologists.

The AI model consists of a cell detection model and a tissue segmentation model. The cell detection model detects PD-L1 positive/negative tumor cells, lymphocytes, and macrophages that are included in the TPS or CPS calculation. A tissue segmentation model is used to detect invasive cancer area and then filter out tumor cells that are falsely detected in non-cancerous areas or to establish the tumor-adjacent region of lymphocytes/macrophages that are included in the CPS score.

The final TPS/CPS evaluation is calculated according to the guidelines as shown in Figure 1.[1,2]

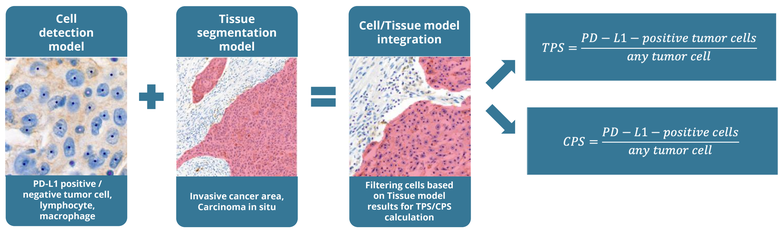

Figure 1. *Algorithmic flow of TPS/CPS score calculation for Lunit SCOPE PD-L1*

For analytic validation for use in the clinical setting, 221 unique NSCLC cases subjected to PD-L1 22C3 immunohistochemistry (IHC) were analyzed for overall percent agreement to mean score from two board-certified pathologists, reproducibility, repeatability, and interfering substances.

Three-way Integration of AI, IMS, and LIMS

Lunit ⟷ HALO AP ⟷ LabVantage®

A three-way integration was built by implementing Lunit SCOPE PD-L1, an AI-powered PD-L1 scoring algorithm, in HALO AP, a browser-based image management system (IMS), which was integrated with the LabVantage LIMS at Guardant Health. Each integration was designed to be bidirectional, allowing for seamless collaboration between the pathologist, diagnostic tools, and laboratory information repositories.

Integration of HALO AP with Guardant LIMS

The digital pathology IMS HALO AP was integrated with the LabVantage LIMS at Guardant Health utilizing each software's HTTP-based REST API (Figure 2).

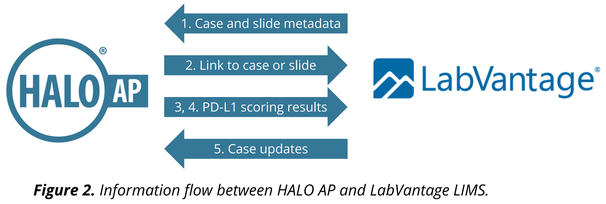

Figure 2. *Information flow between HALO AP and LabVantage LIMS.*

The integration was designed to include the following events:

1. LIMS sends HALO AP messages via the API containing case and slide metadata. Upon message receipt, HALO AP creates the case and generates slide placeholders. HALO AP also uses case and slide metadata from the LIMS to automatically add the Lunit SCOPE PD-L1 workflow to all cases with PD-L1 staining.
2. After the slide is scanned, HALO AP receives the WSI location from the scanner and sends LIMS a link to the case and/or slide which can be launched from the LIMS. All WSIs are stored on-premise at Guardant and displayed in HALO AP's browser-based interface.
3. HALO AP's integration with Lunit PD-L1 SCOPE is automatically triggered when PD-L1 stained slides are available.
4. After PD-L1 analysis is completed and the pathologist reviews the case, AI scoring results and the pathologist's report are returned to the LIMS by HALO AP.
5. Any case updates, such as additional slide orders, are sent from the LIMS to HALO AP.

Integration of Lunit SCOPE PD-L1 with HALO AP

Figure 3. *Information flow between Lunit SCOPE PD-L1 and HALO AP.*

Lunit SCOPE PD-L1 was integrated into HALO AP using HALO AP's flexible assay builder and each software's API. The integration was designed to include the following events:

1. Lunit is notified once PD-L1 stained slides are available matching the assay selection criteria. The WSI images are transferred to a cloud instance, the region of interest (ROI) to be analyzed is automatically chosen, and Lunit SCOPE PD-L1 analysis commences.
2. Results, including markup images, are returned to HALO AP via the API.
3. HALO AP automatically prefills a scoring report with the Lunit SCOPE PD-L1 results, including the TPS or CPS score, the number of PD-L1 positive- and negative cancer cells, and the number of PD-L1 positive and negative immune cells. The pathologist has the option to reject the automatically-chosen ROI and reflex to drawing the ROI manually before restarting analysis. The pathologist can also reject the Lunit SCOPE PD-L1 results and reflex to manual scoring.

RESULTS

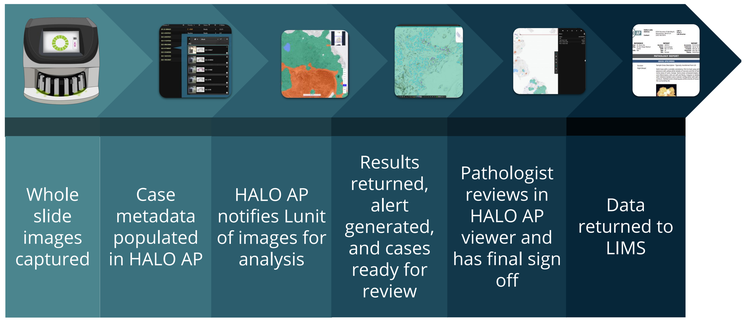

Figure 4. *Seamless three-way integration workflow between a LIMS, an IMS (HALO AP by Indica Labs) and an AI analysis tool (Lunit SCOPE PD-L1) implemented at Guardant Health.*

Integration workflow

PD-L1 22C3 IHC is performed on tissue sections and WSI files are generated using a Leica Aperio GT450 whole slide scanner (Leica Biosystems, Elk Grove, IL). After WSIs are received by the LIMS and made available in HALO AP, WSIs are automatically transferred to a cloud instance for AI analysis by Lunit SCOPE PD-L1. Within minutes, QC information, heatmaps, and tumor proportion (TPS) scores are returned to HALO AP, and a scoring report is prefilled. After the pathologist approves the results, TPS scores and heatmaps are automatically returned to the LIMS for clinical report generation and release.

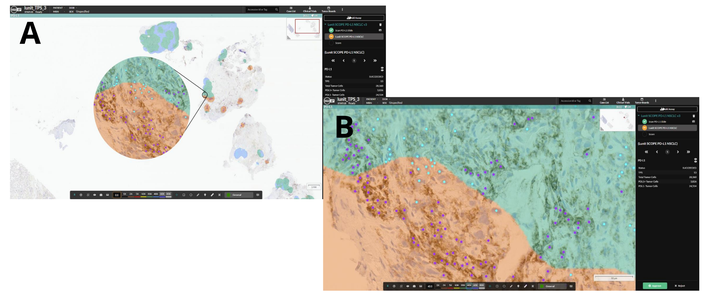

Figure 5. *Lunit SCOPE PD-L1 integrated into HALO AP. A) WSI of a 22C3-stained NSCLC sample analyzed by Lunit SCOPE PD-L1, with the heatmap integrated into the HALO AP IMS. Color coding (green, blue, orange) indicates areas with increased presence of PD-L1 positive tumor cells. The data tray on the right shows the TPS score and the cell counts that went into the TPS calculation. B) The same WSI, zoomed in to 40x magnification, with individual tumor cells indicated as PD-L1 positive (purple dot) or negative (green dot).*

Technical performance of integration in real-world setting

	Mean	SD
Throughput (WSIs/hour)	7.28	5.36
Turnaround time (minutes)	36.48	50.44
WSI file size (GB)	1.04	0.49

Table 1. *Means and Standard Deviations of WSI (≥ 400MB) analysis throughput, turnaround time, and file size under restricted analysis concurrency conditions. Throughput and turnaround time encompass WSI file download time, analysis waiting time, analysis execution time, and pyramidal annotation image file generation and upload time. Performance was evaluated using actual WSIs after product launch.*

The integrated Lunit SCOPE PD-L1 offers analysis performance tailored to lab requirements and workloads. For Guardant Health, it achieves a throughput of over 100 WSIs per day, processing WSI files averaging around 1GB in size. Since Guardant's product launch, it maintains a 99.8% availability rate and delivers results with 99.9% reliability.

Deployment of integration

Since deployment of Lunit SCOPE PD-L1 22C3 within the Guardant Galaxy suite, users have seen a 98% concordance rate for NSCLC TPS and 94% concordance rate for pan-cancer CPS versus manual pathologist evaluation.

CONCLUSIONS

Automated clinical workflows integrating AI algorithms with IMS and LIMS can be used in clinical practice to simplify and strengthen pathology workflows. This integration serves a dual purpose: to simplify complex processes and to reinforce the accuracy and efficiency of diagnostics. Importantly, the configuration of these workflows can be designed to leverage the potential of AI while prioritizing ease of use and minimal disruption to pathologists' daily routines. By seamlessly integrating with existing systems, these workflows enhance rather than replace the invaluable expertise and decision-making capabilities of the pathologist.

The practical application of this integration in a real-world clinical setting highlights its immediate relevance and utility within today's healthcare landscape. As the demand for accurate and timely diagnostic insights continues to grow, this integration demonstrates the potential and utility of AI in the clinic today.

FUTURE DIRECTIONS

We plan to link to Lunit analysis results from within HALO AP's slide tray to allow pathologists even faster access to AI algorithm results.

CONTACT INFORMATION

To learn more about Guardant360 TissueNext™, contact clientservices@guardanthealth.com
To learn more about Lunit SCOPE PD-L1, contact contact@lunit.io.
To learn more about HALO AP, contact info@indicalab.com.

REFERENCES

1. Choi S, Cho SI, Ma M, et al. Artificial intelligence-powered programmed death ligand 1 analyser reduces interobserver variation in tumour proportion score for non-small cell lung cancer with better prediction of immunotherapy response. Eur J Cancer. 2022;170:17-26. DOI: 10.1016/j.ejca.2022.04.011
2. Jung HA, Park KU, Cho S, et al. A Phase II study of nivolumab plus gemcitabine in patients with recurrent or metastatic nasopharyngeal carcinoma (KCSG HN17–11). Clin Cancer Res. 2022;28(19):4240-4247. DOI: 10.1158/1078-0432.CCR-22-1238

Regulatory note: *HALO AP® is CE-marked for in-vitro diagnostic use in Europe and the UK. HALO AP is For Research Use Only in the US and is not FDA cleared for clinical diagnostic use.*