Novel CE-IVD certified deep learning clinical workflow for quality control, diagnosing, and grading of prostate cancer core needle biopsies

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Background

- Prostate cancer is the most commonly diagnosed cancer in men. Incidence rates continue to rise.
- Each case consists of multiple biopsy cores, which must be diagnosed and graded for cancer by a pathologist.
- This represents a large clinical workload where multiple cases are reported daily.

Objectives

- Develop a clinically validated diagnostic and grading deep learning algorithm for the automated reporting of prostate cancer in H&E stained tissue sections of core needle biopsies.
- Develop a deep-learning and automated AI-based quality control algorithm to remove artifacts found in whole slide images from downstream diagnostic and grading analysis.

Methods

HALO Slide QC 2.0

The AI algorithm was trained using 1984 annotations across 254 H&E stained WSI from more than 9 tissue types and 2048 annotations from synthetically generated out-of-focus images. Annotations were generated from the following artifacts: Air bubble, dust/debris, folds, out-of-focus, pen marker. The output of the algorithm is binary: Tissue or Artifact. Test data was comprised of 49 WSI H&Es sourced from the open source TCGA database. The algorithm was tested across 375 annotations (tissue and artifact).

HALO Prostate AI

Two AI algorithms were trained with over 870,000 training patches obtained from expert annotated H&E stained prostate tissue section WSIs sourced from TCGA (n=450) and the University of Cologne (n=200). One classifier was trained for the detection of cancer and the other was trained for Gleason grading. The cancer diagnostic classifier was tested against 4973 biopsy samples from 3 cohorts and using 2 separate scanners (Table 1). The ground truth for cancer diagnosis comprised of expert pathologist slide level diagnoses. The Gleason grading classifier was tested on 2 cohorts digitized using a single Hamamatsu scanner (Table 2). The ground truth for Gleason grading was reported as a consensus score calculated by the average quadratic kappa scores from 10 globally distributed pathologists.

Results

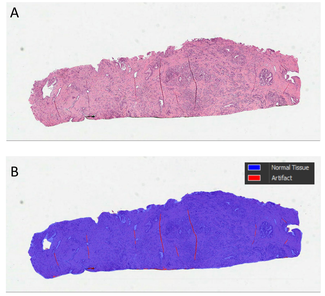

Figure 1. A. H&E stained prostate biopsy. B. Artifact detection by HALO Slide QC 2.0.

HALO Slide QC 2.0: Artifact detection

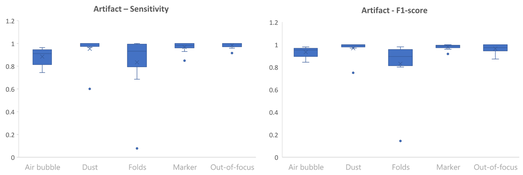

Figure 2. Results of HALO QC AI reported from a 49 WSI test cohort.

HALO Slide QC 2.0 showed a high sensitivity, and F1-score when validated across a test cohort of images (n=49) sourced from TCGA and across all artifacts that it was trained to detect: Air bubble, dust/debris, folds, pen marker and out-of-focus tissue.

HALO PROSTATE AI: Cancer detection

HALO Prostate AI returned high negative predictive value (>99%), sensitivity (97.1-98.3%), and specificity (92.4-97.0%) for cancer diagnosis after analyzing the 4,973 digitized biopsies from the three independent cohorts.

VALIDATION RESULTS: CANCER DETECTION

Cohort	Cores Analyzed	Scanner	Accuracy	Sensitivity	Specificity	Negative Predictive Value
1*	2,280	Hamamatsu	93.5%	97.5%	92.4%	99.2%
2**	2,022	Hamamatsu	93.7%	98.3%	92.0%	99.3%
3**	671	Leica	97.0%	97.1%	97.0%	99.0%

*University Hospital Cologne, **Landesklinikum Wiener Neustadt

Table 1. Cancer detection validation results.

HALO PROSTATE AI: Gleason Grading

For Gleason grading, HALO Prostate AI returned an average quadratic kappa statistic of 0.7 and 0.8 respectively across the two independent test cohorts.

GLEASON GRADING VALIDATION

9x Board-Certified GU Pathologists

1x Board-Certified General Surgical Pathologist

Cohort	Cores Analyzed	Average Quadratic Kappa	
		AI	Pathologist Range
1*	235	0.8	0.64 - 0.82
2**	165	0.7	0.65 - 0.75

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Table 2. Gleason Grading validation results.

HALO Prostate AI

The CE-IVD marked HALO Prostate AI algorithm analyzes all appropriate case slides automatically and notifies pathologists of cases with suspected findings directly in their native workflow. The algorithm provides comprehensive analysis including tumor size, cancer detection and localization, as well as Gleason Grading.

HALO Prostate AI is deployed through Indica Lab's CE-IVD marked HALO AP® platform which provides a fully validated and automated end-to-end clinical workflow.

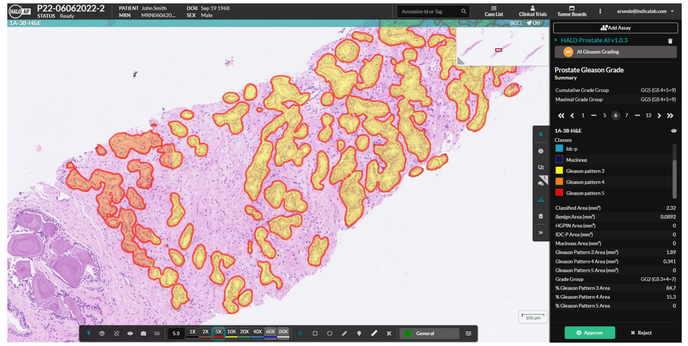

Figure 3. The HALO Prostate AI user interface within Indica Labs' HALO AP® software.

Conclusions

HALO Prostate AI demonstrates high clinical accuracy for the diagnosing and grading of prostate cancer on independent cohorts of patients that represent the full spectrum of prostate cancer histological subtypes and grading, as well as disease precursor and benign diagnoses.

HALO QC AI can allow the triaging and alerting of slides containing a high level of artifact within a digital pathology workflow as well as excluding the artifact region from downstream analysis by subsequent image analysis algorithms.

Regulatory Compliance

HALO Prostate AI and HALO AP® are CE-marked for *in-vitro* diagnostic use in Europe and For Research Use Only in the USA.

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