Validating an Al-based Analytic Tool for IHC Staining QA: Precision Studies of The Digital Pathology Pipeline

Omar Z. Baba, MD¹; Dhananjay Chitale, MD¹; Kyle Perry, MD¹; Nilesh Gupta, MD¹; Wargeaux Schmidt, MLT¹; Danielle Pirain², Henrik Høeg²; Mateusz Tylicki²; J. Mark Tuthill, MD¹ and the set th **1** Pathology and Laboratory Medicine Department, Henry Ford Health, Detroit, Michigan, United States **2** Visiopharm, Denmark

Introduction

Standardization of immunohistochemistry (IHC) staining quality assurance (QA) is critical for diagnostic accuracy. Pathologists currently assess stain quality subjectively, comparing control sections to patient tissue. Qualitopix (Visiopharm, Denmark), a cloud-based artificial intelligence (AI) platform for IHC staining QA, uses quantitative analysis for scoring cell lines-derived, stained and digitized control slides. To establish the reliability of Qualitopix, we conducted a study to validate the precision of the digital pathology (DP) pipeline consisting of the scanners and the image analysis algorithms used.

Methodology

Glass slides were produced from two 4-core standardized cell-line blocks (Histocyte Laboratories, Newcastle, England) of increasing intensities, with epitopes for estrogen receptor (ER) and progesterone receptor (PR), stained using Ventana Benchmark Ultra and scanned on DP 200 and Ventana iScan HT scanners (Roche, Basel, Switzerland). Using AI, Qualitopix detects cells in digital slides and reports their staining intensity as a numerical H-score (0-300, divided by 3 to get a %). See Figure 1. Intra-scanner precision (Figure 2) and Inter-scanner comparison (Figure 3) studies were performed.



Figure 1: (A) Typical workflow for using Qualitopix for QA in IHC. (B) Pipeline for analyzing images of cell lines cores on Qualitopix. (C) ER an PR 4-core cell line blocks structure with annotated Qualitopix- calculated core-specific average numerical H scores (reported in %), using the DP 200 scanner.



Figure 2: Calculating percent coefficient of variation (%CV) for intra-scanner repeatability studies to determine precision of DP+AI pipeline. (A) 3 ER and 3 PR slides were scanned 40 times each, on DP 200 scanner (Roche), followed by numerical analysis on Qualitopix. (B) Similarly, 10 ER and 10 PR slides were scanned 10 times each, on Ventana iScan HT scanner (Roche), followed by numerical analysis on Qualitopix.



Figure 3: (A) Inter-scanner comparison of Qualitopix scores between DP 200 and Ventana iScan HT (Roche) for 50 ER and 50 PR. (B) Intraclass correlation coefficient at 99% confidence interval was calculated using R.





ICC (0-1)	<0.5	0.5-0.75	0.75-0.9	>0.90
Interpretation of correlation	Poor	Moderate	Good	Excellent

You Can't Improve What You Don't Measure...

- Al based IHC QA sets the stage for an overdue transition from a subjective, qualitative, variable and episodic at best, to an objective, quantitative, standardized, and continuous approach.
- Validating the Digital pathology pipeline including the Whole slide imaging scanner(s) and AI tool is a vital pre-requisite step before implementation. Our studies have demonstrated a highly precise and reliable assay within and across 2 scanners.

Questions?

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Results



Figure 4: Intra-scanner repeatability studies (see Figure 2) results in average %CV showing overall highly tight precision of DP+AI pipeline, for ER and PR on both the DP 200 scanner and the Ventana iScan HT scanner. (A) Average %CV for 40 repetitions of 3 ER and 3 PR (B) slides, scanned on DP 200 scanner (Roche), followed by numerical analysis on Qualitopix. (C) Average %CV for 10 repetitions of 10 ER and 10 PR (D) slides scanned on Ventana iScan HT scanner (Roche), followed by numerical analysis on Qualitopix.



Figure 5: Inter-scanner comparison studies (see Figure 3) comparing Qualitopix scores obtained by scanning slides on DP 200 scanner (Roche) vs Ventana iScan HT scanner (Roche) for both ER (A) and PR (B). Intraclass correlation coefficient calculations are shown for each core. Inter-scanner studies between DP and HT indirectly assessed time variation as well since they were completed several months apart.

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Contact us at : obaba1@hfhs.org & mtuthil1@hfhs.org



