

Evaluation of Expert vs Trained Reader Interpretation of The Vaginal Health Assessment Tests in Gynecology Patients with Vaginitis

Ashley Deer¹; Joe DeGroot²; Tayce Jacques¹, Haley Keene¹, John Kearney²; Kent Murphy²; Nitika Pentakota¹; Paushaly Sau¹, Yongjian Yu²; Peggy Robinson²; Jim Mahaney¹

Edward Via College of Osteopathic Medicine, Blacksburg, VA¹, Caza Health, LLC, Earlysville, VA²

CONTEXT AND OBJECTIVE

- Vaginal infections are one of the most presented complaints by female patients.
- Artificial intelligence (AI) based diagnostics** have the potential to improve accuracy for vaginitis testing while providing more prompt results compared to NAAT.
- Caza Health has developed the DayZ™ Vaginal Health Assessment Assay (VHA) which combines AI-driven automated scanning microscopy with immunofluorescence antibody cocktails to detect bacterial vaginosis (BV), candida vaginitis (CV), and trichomonas vaginosis (TV) (Figure 1 and 2).
- Analysis of 200 (out of 400 planned) vaginal swab samples from symptomatic participants have demonstrated algorithm accuracies of 86% for BV, 83% for CV, and 94% for TV compared with expert human interpretation.
- Because DayZ™ VHA results will be interpreted by readers with varying levels of expertise in clinical practice, standardized image-reading training has been developed to accompany assay deployment.

Objective: This multi-reader study evaluated the ability of trained novice readers to interpret DayZ™ VHA results compared with expert ground truth, assessed the effectiveness of the proposed training, and examined inter-reader variability.

THE DayZ™ VAGINAL HEALTH ASSESSMENT

- Vaginal swab samples were obtained from participants with symptomatic vaginitis and asymptomatic participants (controls). All participants were at least 18 years of age and provided informed consent.
- Exclusion criteria:** use of oral antibiotics in the last 14 days, use of vaginal products, vaginal douching, or vaginal intercourse within the previous 24 hours.
- Two swabs were collected from each participant:
 - Swab 1:** used for wet mount microscopy and related tests in accordance with standard clinical care for diagnosing vaginitis.
 - Swab 2:** used for the DayZ™ VHA test and analysis.
- The nCyte AI algorithm produced a set of images from the sample to be used to identify and quantify targets of interest in the sample. All images were evaluated by an expert human reader, and the results were compared to the DayZ™ System findings and data from the standard-of-care diagnosis of BV/TV/CV using wet mount microscopy and/or NAAT, all correlated with the results of the physical exam and Amsel Criteria for each participant. The results of this analysis provided the “ground truth” data, which was used to verify the accuracy of the DayZ™ VHA test method. **Images from this data set were used in the current reader study, which seeks to evaluate a training program for novice readers in evaluating DayZ™ VHA test results compared to ground truth data.**

MATERIAL & METHODS

Caza Health provided 19 archive files, containing a total of 13,750 individual images from the current data set of DayZ™ VHA test results for this reader study. The image files contained no information about the research participant or the clinical diagnosis, or any information about the AI algorithm assignment of target images.

- Five readers in this study received one-on-one training on the DayZ™ VHA immunofluorescence method, the images produced by the system and criteria for assessing the images which was documented in a simple training manual.
- During the training session, readers were evaluated one-on-one with the trainer to successfully identify each target species. The same training image file was used by all five readers and was not included in the data set.
- Each image file to be evaluated contained putative target species identified by the AI algorithm: **200 possible clue cells, 25 possible yeast pseudohyphae, and 25 possible trichomonads.** For each potential target species, the reader clicked a “Yes” or “No” check box for species identity, which was tabulated within each file as it was read.
- Completed files by each reader were uploaded to Caza Health for analysis, which compared the results of individual readers for each target species and to results to the ground truth.

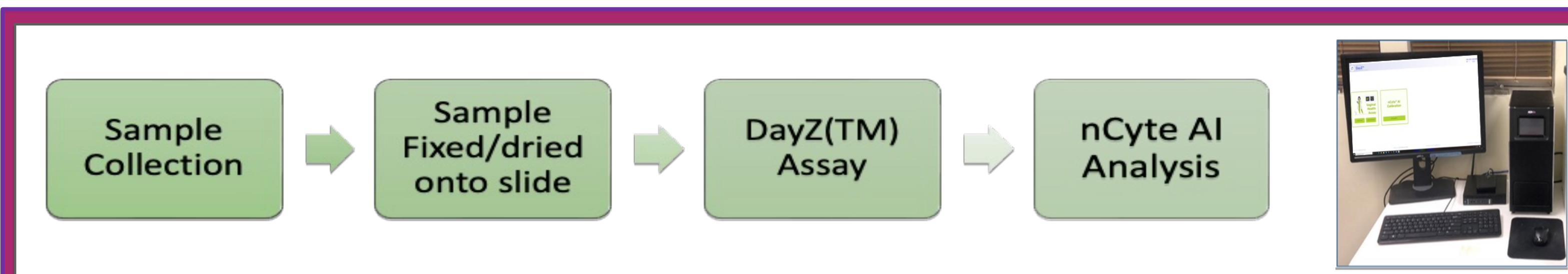


Figure 1: Workflow using the DayZ™ System. Sample is collected using a swab, placed onto a glass microscope slide and fixed/dried onto the slide. The slide is then stained using a cocktail containing fluorescent-labelled antibodies (DayZ™ Assay) and analyzed in the DayZ™ Artificial intelligence (AI)-driven optical scanning instrument.

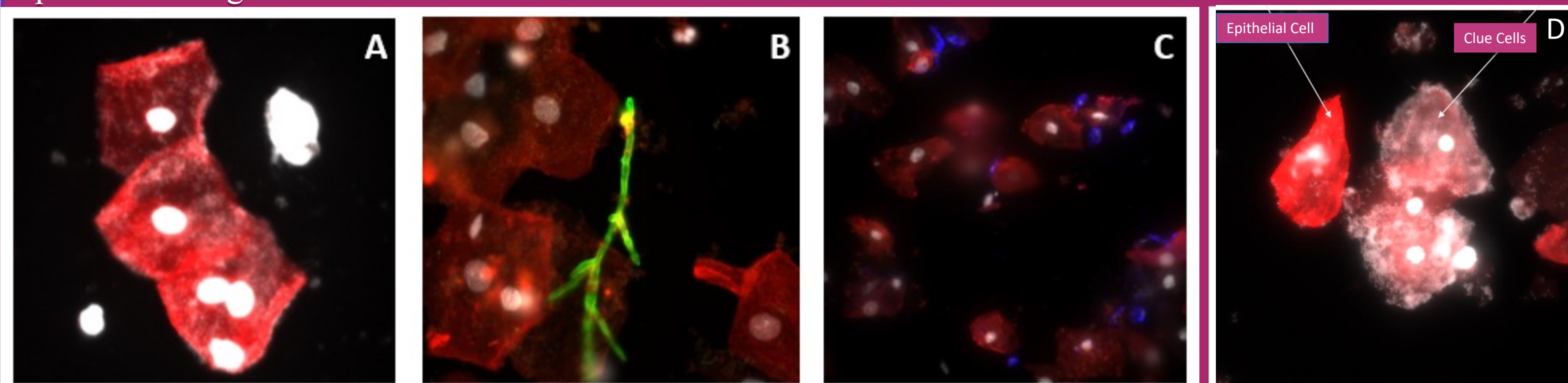


Figure 2: High Resolution Reference Training Images from the DayZ™ System. **A.** A cluster of 3 clue cells, which are vaginal epithelial cells (stained red) with white nuclei and the presence of small white bacteria covering at least 50% of the cell surface, indicative of bacterial vaginitis. **B.** A pseudohyphae strand (stained green), indicative of a candida vaginitis yeast infection. **C.** Trichomonas vaginalis (stained blue), the parasite and causative agent of Trichomoniasis. **D.** Comparison of a normal vaginal epithelial cell (left) with two clue cells (right) from a clinical sample image.

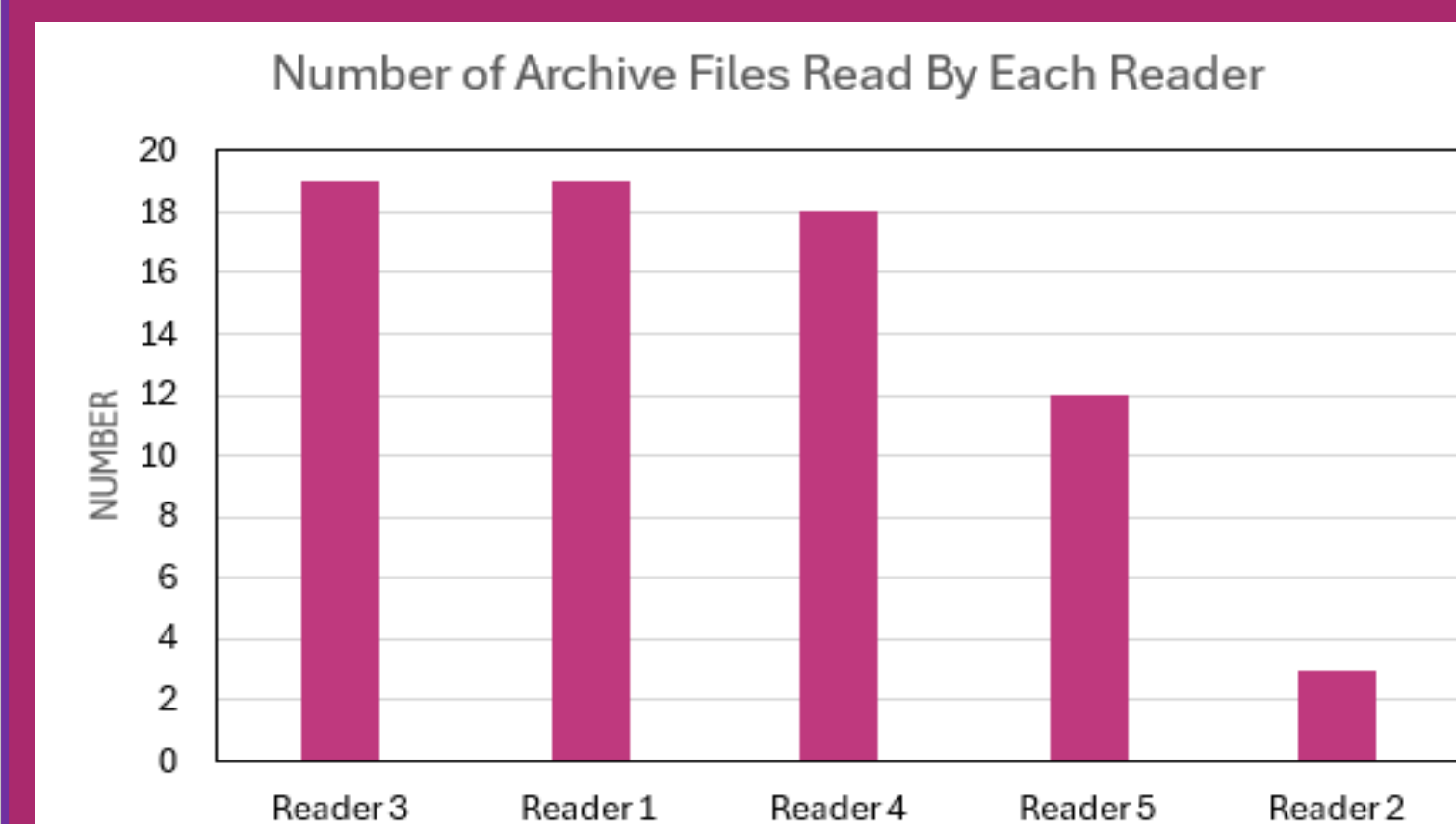


Figure 3: Number of Archive Image Files Read by Reader. 5 readers were provided access to 19 archive image files from Caza Health. Readers evaluated files in any order as time permitted, with each file requiring approximately one hour to complete. Although the number of files read varied by reader, all 19 files were reviewed, resulting in a total of 17,750 images evaluated.

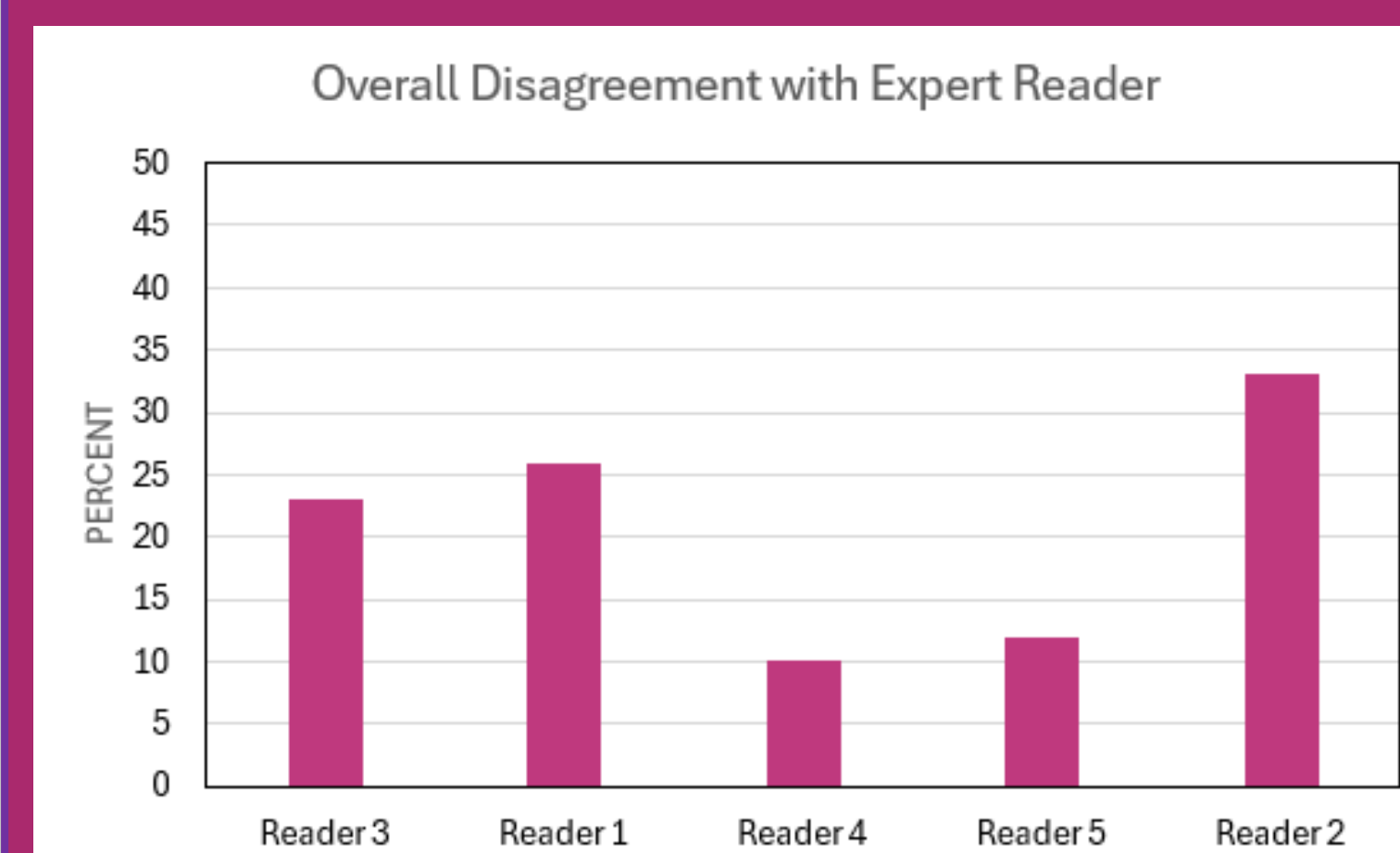


Figure 4: Discordance between Individual Readers and the Expert Reader (ground truth). Readers reviewed all target images within each file and classified each as present (“yes”) or absent (“no”) for clue cells, yeast pseudohyphae, or trichomonads. **Overall reader discordance with the expert reader was 21%** and did not correlate with the number of image files analyzed, suggesting that disagreement was driven more by individual image interpretation than by reading volume or experience.

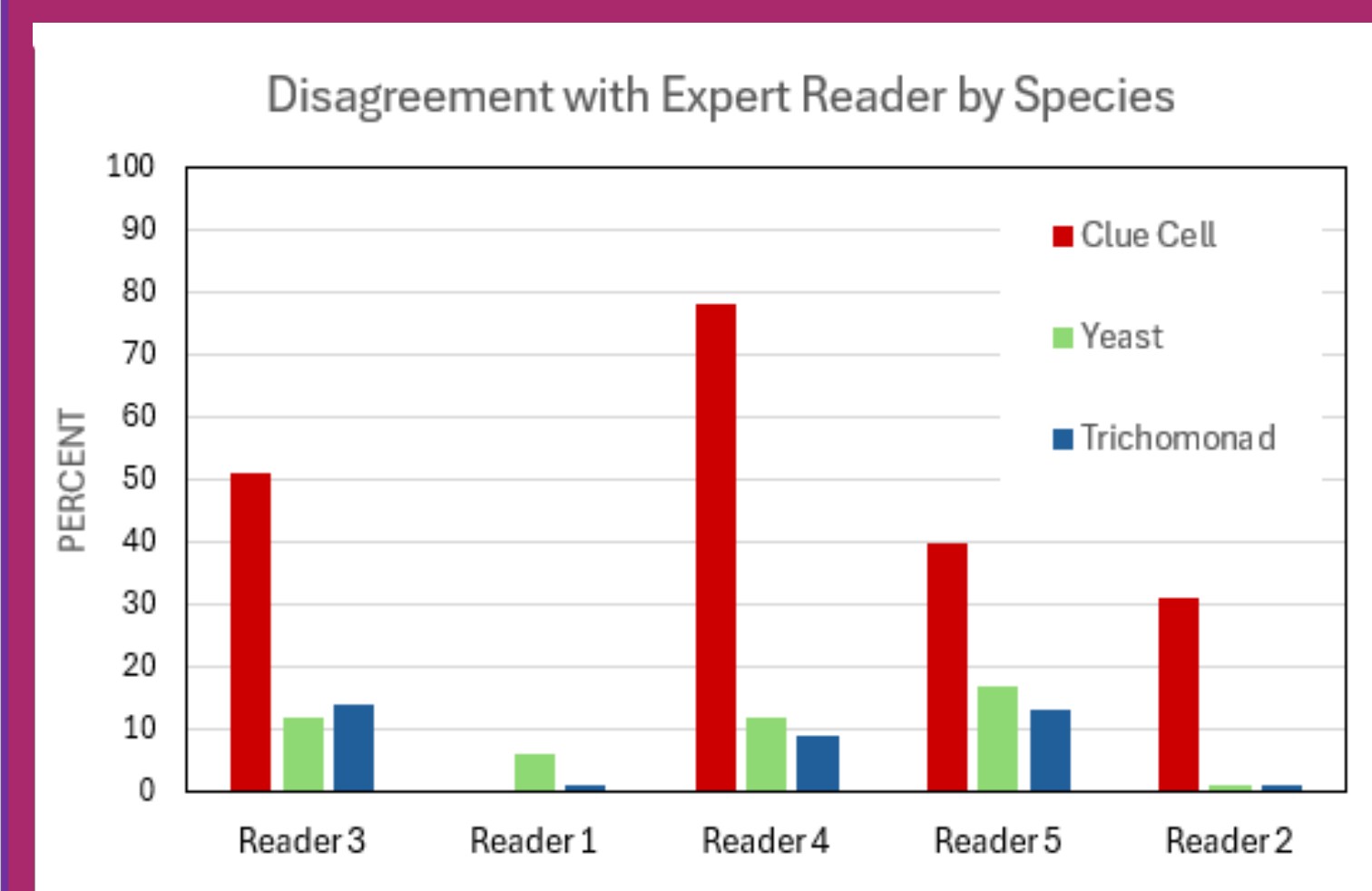


Figure 5: Discordance between Individual Readers and the Expert Reader by target species. The data suggest that yeast pseudohyphae (Figure 2B) and Trichomonads (Figure 2C) are more easily identified in the images than are clue cells (Figure 2A). CV or TV is defined as finding one or more of these species in all images read. In contrast, BV is defined as 20% or more clue cells found within all epithelial cells in the image. Therefore, the observed variation in identifying clue cells among the individual readers compared to the expert reader for this population of target species indicates improved training for the identification of clue cells is needed.

RESULTS

- Figure 3 shows each of the five readers independently evaluated between three and nineteen image files. The readers as a group read all available files, and there were at least three independent reads for each individual image file. Image reading for the project is ongoing.
- Figure 4 shows the average discordance between reader and ground truth for all images read did not correlate with reader experience (i.e., the number of files read, Figure 3).
- Figure 5 shows readers had the most difficulty correctly identifying clue cells (Figure 2A,D) compared to ground truth. In contrast, readers had more success identifying pseudohyphae (Figure 2B) and trichomonad (Figure 2C) targets in the image files compared to ground truth. Unlike epithelial cells, yeast and trichomonads are not native to the vaginal microbiome, such that seeing either of these species in a sample image is a positive affirmation. Clue cells are epithelial cells (native to the vaginal biome) that have 20% or more cell surface area covered with bacteria (Figure 2A,D). Therefore, the reader examined each target epithelial cell and visually estimated bacterial coverage for that cell, to make the assignment as a clue cell or not. This resulted in significant variability between the readers and with ground truth.

SUMMARY/CONCLUSIONS

- The DayZ™ Vaginal Health Assessment System is in development as a near point of care instrument to provide physicians with improved vaginal biome data for the assessment and treatment of vaginitis.
- This study is providing key information to enhance training effectiveness for end-point users, including providing clearer definitions of clue cell characteristics and how to identify clue cells more accurately versus normal epithelial cells.
- Going forward, the project will develop and improve training modules and methods, to enhance easy start-up of the DayZ™ VHA System when deployed in a clinician practice.

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