INTRODUCTION
To date, the use of whole slide imaging for diagnostic cytology has been primarily used for research and teaching purposes. There are many potential benefits of digital cytology and several publications have compared the accuracy of digital review versus microscope review showing no significant difference in accuracy across the two mediums. However, several challenges make the existing digital cytology solutions impractical for current clinical use:
1. Focusing capability: Due to the 3D nature of cytology, scanning a single layer will result in many of the cells being out of focus. However, scanning multiple focal layers and allowing for fine focus, significantly increases the file size, time required to scan the slide and leads to screening dissatisfaction. Merging multiple focal layers into a single layer decreases the file size and presents all cells in focus.
2. Screening a Whole Slide Image (WSI): Digitally screening the entire cell spot of a ThinPrep Pap slide is cumbersome and less efficient than manually screening a glass slide. Providing a gallery of diagnostically relevant images from the WSI has the potential of maintaining high quality and improving screening efficiency.

This study is a preliminary investigation into whether these galleries of cell images and associated WSI with merged focus will provide sufficient image quality for cytotechnologists (CTs) to accurately and efficiently make a diagnosis on ThinPrep Pap Test slides that have been digitized.

METHODS
Two hundred and fifty ThinPrep Pap Test slides with previously verified diagnoses were selected for inclusion in the study (Table 1). Slides were scanned on a digital scanner at the equivalent of 40x magnification (0.25 um/pixel) over 14 focal planes. The focal stack was then merged into a single focal layer of optimal focus (Figure 1).

Twenty-four diagnostically representative objects from each case were selected and presented at 10x magnification in a gallery along with the WSI (Figure 2). An additional 24 relevant objects were also available if the CTs wanted to see more objects like the ones presented in the original gallery. All cases were viewed on a 27 inch high definition monitor.

Fifteen CTs each reviewed 250 cases digitally. Participants had an average of 23 years of experience as a cytotechnologist (range of 10 - 43 years). None had any prior experience reviewing cytology cases digitally. CTs were trained on the platform but did not receive any digital cytology training. CTs were instructed to make the diagnosis from the gallery if possible. The full WSI was also available for review if needed. The diagnosis was entered into the embedded form.

In this study, false positives are defined as any negative (NILM) cases that are called ASCUS+. False negatives are defined as any positive cases (ASCUS+) that are called NILM. The overall false positive rate was 12.3% and overall false negative rate was 3.3%. Rates per CT are shown in Figure 5.

RESULTS
Overall concordance of the digital review compared to the reference glass diagnosis can be found in Figure 3. Figure 4 shows the proportion of agreement for each diagnostic category with respect to the truth diagnosis.

DISCUSSION
This pilot study examined whether merging multiple focal planes of digital ThinPrep Pap Test slides and presenting diagnostically relevant cells in a gallery would provide sufficient detail to accurately and efficiently diagnose ThinPrep Pap cases.

The concordance of digital diagnosis compared to the reference glass diagnosis was 86.4%. The concordance on ASCUS+ cases was over 90% and the false negative rate was 3.3%. This suggests that the CTs were able to make the diagnosis accurately using the gallery of diagnostically relevant cells from a WSI with merged focal planes. There were an average of 19 gallery clicks per case, suggesting that the tiles were not big enough on their own to render a diagnosis and that the cell spot is required. However, as evidenced by the low number of mouse clicks within the cell spot, the CTs in this study used the cell spot only to see the gallery object larger and in context but did not fully screen the WSI.

The concordance on NILM cases was 87.5%. Ninety-five percent of the NILM overcalls were called ASCUS. This is consistent with previous research that suggests that the ASCUS rate may increase with the introduction of new technology until the cytotechnologist gains experience and confidence. In this study, CTs received training on how to use the digital system but were not trained on any additional diagnostic criteria specific to digital. The expectation is that the ASCUS overcalls would decrease over time.

In this study, the average time to complete a case was 101 seconds which is more efficient than previous studies examining the time required to make a diagnosis. This preliminary study suggests that it is possible to screen digital ThinPrep Pap Test slides efficiently and with high concordance with the reference glass diagnosis with a gallery of diagnostically relevant tiles. One limitation of this study is that there was no direct comparison to glass diagnosis from each CT.

REFERENCES