In-line Automated Scan Quality Assessment and Correction for Archival Histopathology Slide Scanning

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Abstract

Background:

Academic medical centers maintain large repositories of histopathology slides for regulatory, clinical and scientific purposes. With the advent of digital pathology, there is increasing interest in digitizing archival slides to meet clinical, educational and scientific needs. However, such interest is often tempered by the significant costs associated with digitization and manual quality review of digitized slides.

Quality is a particularly salient issue when discussing archival scanning, because archives typically contain slides with variation in preparatory technique and differences in stain quality, cleanliness, debris, air bubbles, drying artifacts and other confounders that make high-quality scans difficult to achieve.

Correspondingly, archival scanning may require significant manual intervention (including re-scanning) to achieve acceptable successful quality at high throughput. Such a hands-on approach may be cost prohibitive in many situations, and automated quality assessment tools including those with the possibility for in-line correction of a scan may increase the practicality of archival scanning efforts.

Methods:

With a single human operator, we digitized 23,916 slides over 30 days (approximately 800 slides per day) using a research-use-only 4-head scanning system (nference, Inc). Slides were selected from the Mayo Clinic Pathology Tissue Archive and represented periods ranging from the 1950s to present. No cleaning or other preparatory steps were used to prepare slides for scanning.

Using on-scanner quality models, each slide was annotated in real-time for errors detected in focus, stitching, bubbles and folds, and other detectable errors (see Figure 1).

A subset of images from a quality control slide set (100 well-characterized slides) were also reviewed manually.

Automated Scan Error Detection

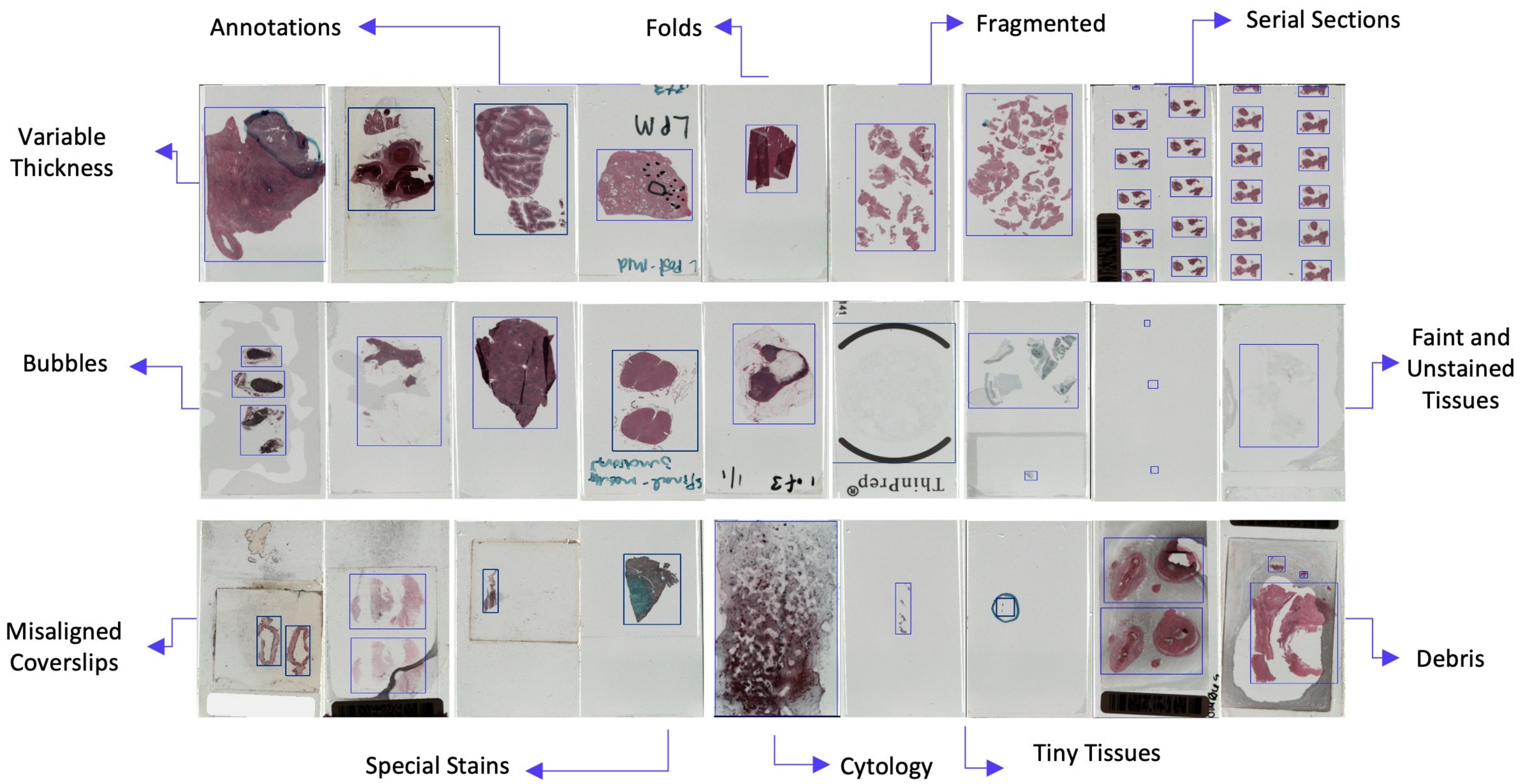


Figure 1. Detectable Features: In-line feature detection was capable of annotating and/or abstracting: 1) areas of variable tissue thickness and/or focus variation, 2) existing hand-written slide annotations, 3) tissue folds, 4) tissue fragmentation, 5) serial sections, 6) bubbles, 7) faded or unstained tissue, 8) misaligned coverslips, 9) special stains, 10) cytology preparations, 11) small or minute tissue fragments, 12) artifacts or debris, and 13) tile stitching artifacts.

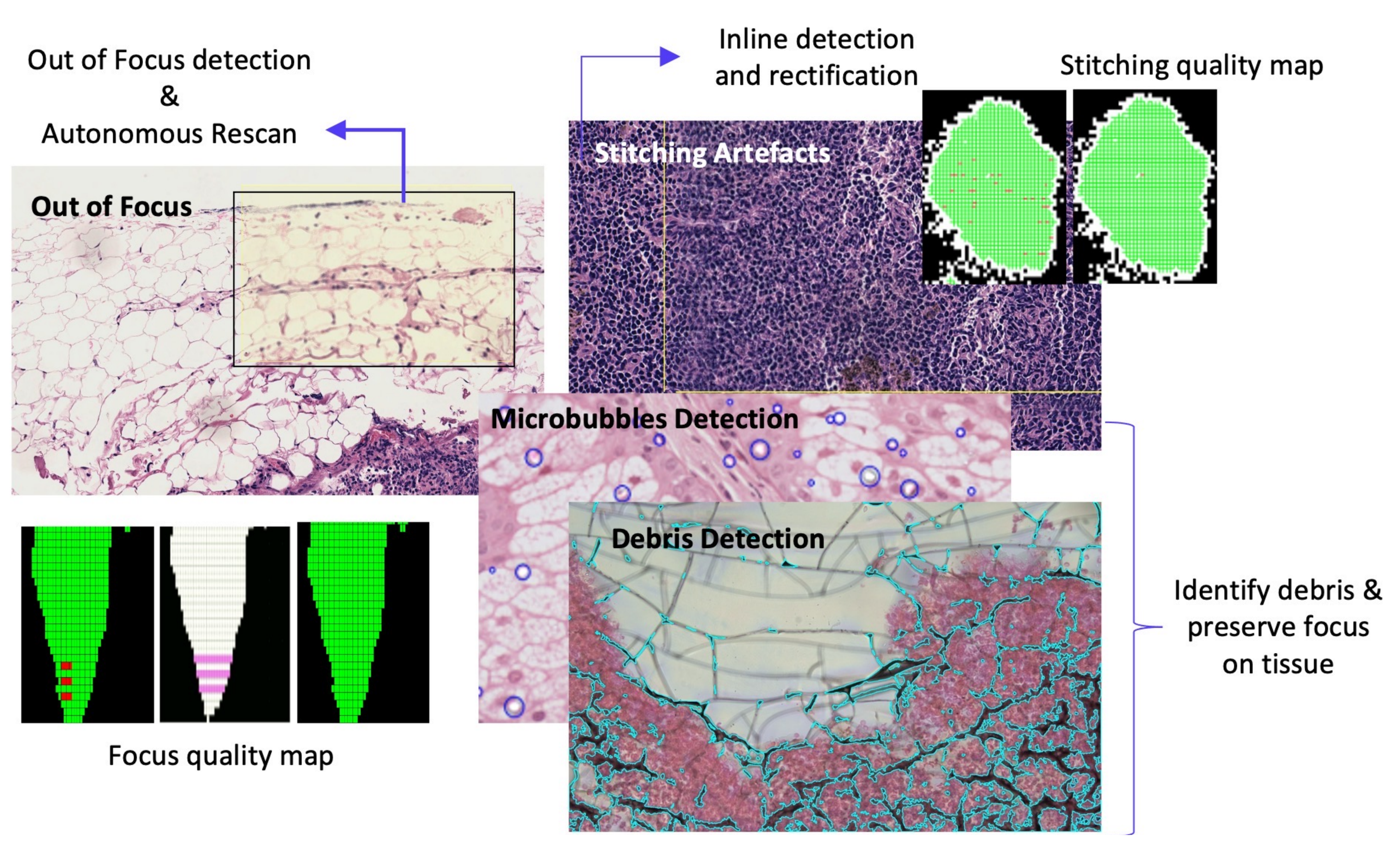
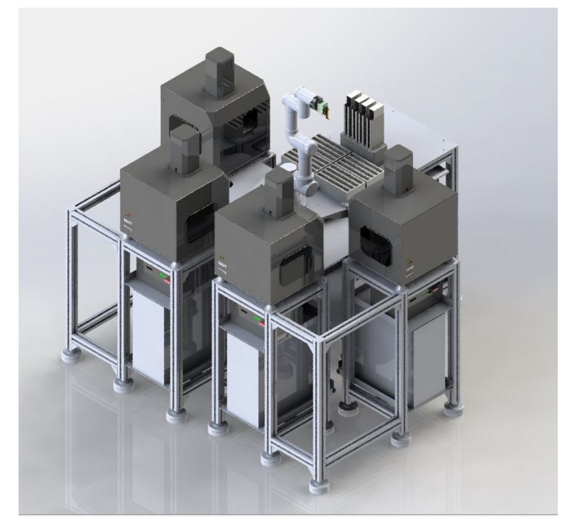


Figure 2. Feature Maps and Automated Correction: Select features, including focus and stitching, are abstracted to tile-based feature overlays. The feature overlays provide an “at a glance” snapshot of slide quality and can also be integrated into a numeric quality metric (if desired) to drive in-line or downstream quality control activities. In our testing, we used real-time on-scanner out-of-focus assessment to provide an automated trigger for autonomous rescan of the image with an increased density of focus points. While use of this quality control feature increased scanning time of out-of-focus scan slides by 3-6 seconds, it provided a significant improvement in 1st scan acceptability without human (manual) intervention.

Scanning Process

Figure 3. High Throughput Cluster: Scanning was accomplished using a research use only cluster of 4 single slide line scanners using 40X zoom with 0.26 µm/pixel scan resolution. The 4 scanners are fed by an automated robotic arm from a single common slide tray. Each scanner is independent of the others and can complete scanning (or re-scanning as necessary) without disrupting the operation of its cluster partners.



Scanning features:
The scanners capture dynamic Z-stacks of each scan area and utilize Z-stacks to perform real-time focus assessment and continual refinement of the optimal focal plane. Real-time focal quality assessment allows for in-line quality control and autonomous re-scanning as needed. The scanners render final images as DICOM objects with lossy-compressed JPEG2000 pixel data.

Case Study
Large bubble on a slide

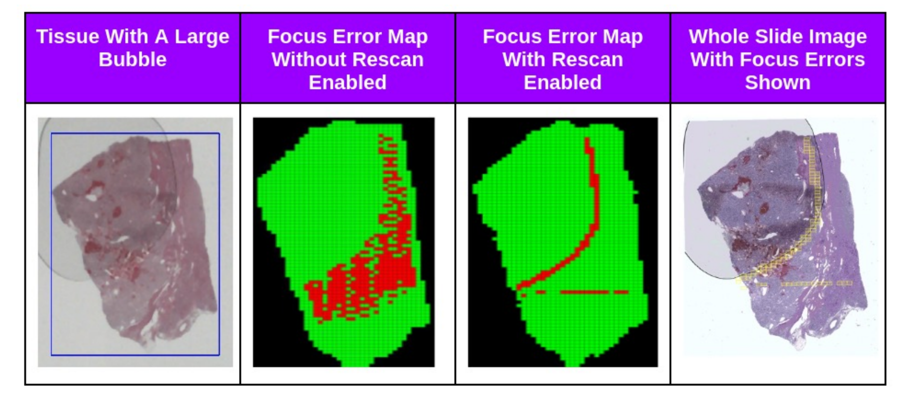


Figure 4. Quality assurance example: Automated in-line error detection initiates automatic re-scan to correct most errors at a tissue level without human intervention

Outcomes

- The system was able to successfully scan 99.4% of archival test slides. In total, 177 slides were rejected for scan quality. The most common reason for scan failure was inability to establish a tissue plane due to faint tissue, debris or protruding labels (n=137).
- Post-scan focus errors were detected algorithmically in 4035 slides (17%), with 4.21% of slides impacted over greater than 1% of the slide pixel area. Similarly, post-scanning stitching errors were algorithmically detected in >1% of pixel areas regions in 2.68% of slides.
- Manual review of 100 slides verified algorithmically detected errors. In rare instances (n=3), manual review detected focus, stitching or other errors that were not flagged by automated review.

Conclusions

- In-line quality assessment allows for rapid recognition of quality defects in scanned archival tissue slides.
- Autonomous focus assessment can ameliorate focal defects while the slide is still on the scanner, potentially saving significant resources in manual review and slide handling.
- Algorithmically detected errors were verified in manual review, suggesting a high specificity in the error detection algorithms.
- Rare undetected focus & stitching artifacts detected during manual review suggests potential further improvements in algorithm sensitivity are possible.

References

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3. A quantitative approach to evaluate image quality of whole slide imaging scanners. Shrestha et al., 2016