

Digital Pathology uses high-resolution tissue images to diagnose disease. Digitalisation greatly improves access to diagnostic data, eliminates slide loss and degradation. Yet, there are many challenges still to overcome. We present findings from the 2021-25 program 'Metrology for Digital Pathology to improve patient outcomes' conducted by National Physical Laboratory.

Improving reliability of clinical decision making [1,2]

Problematic: Biopsies are used to assess the health of kidneys before transplant. Scoring systems such as Remuzzi score are used to standardize the assessment. Repeated measurements revealed variability in score that can lead to different transplantation decisions for a single kidney (Fig 1).

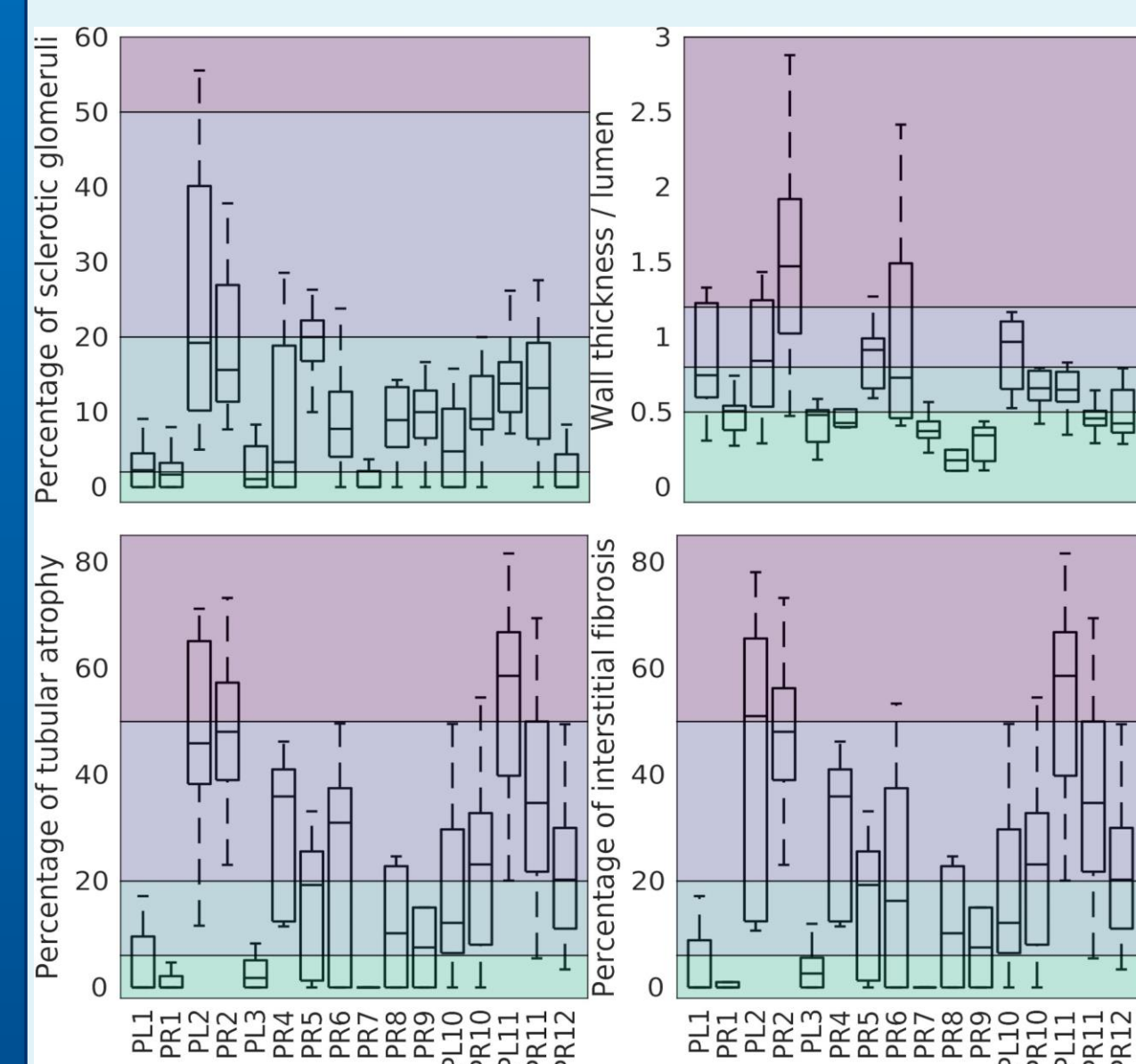


Fig. 1: Variation in diagnostic scores acquired using 250 repeated measurements on 16 kidneys.

Results:

- statistically significant link between experimental protocol and score (Fig 2), emphasizing the need for standardization.
- most image features vary as much within a single kidney as within the entire population, confirming the need for aggregation scores.
- Remuzzi score did not provide any improvement for discrimination of healthy organs.

Recommendations:

- Using punch biopsy.
- Assessment of 104 μm^2 of tissue to minimise scarring while ensuring a Type I error < 15 % and Type II error < 20 % in glomeruli health assessment.
- Develop virtual staining technics
- Develop colour calibration methods

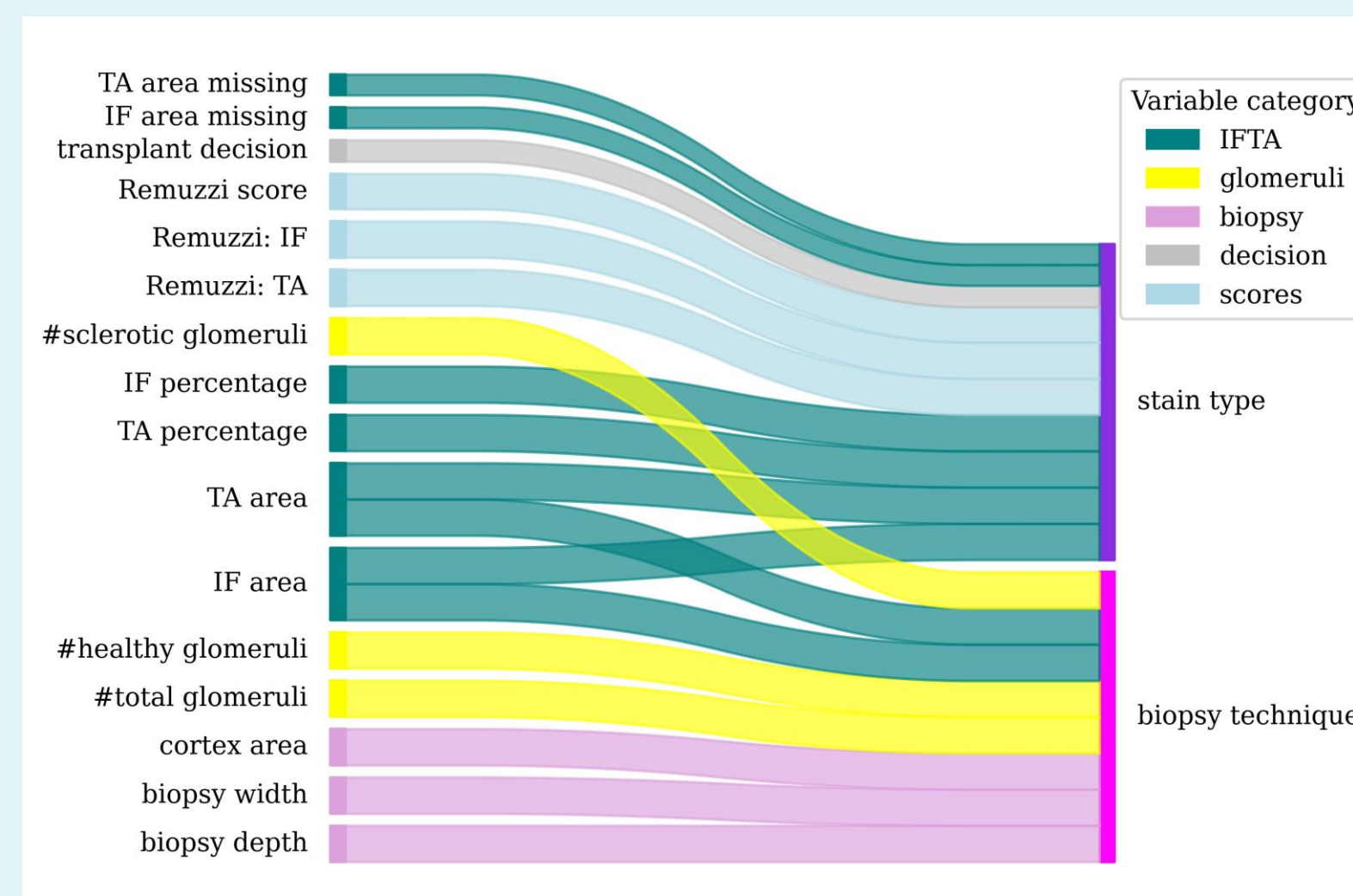


Fig 2: Dependencies between biopsy-related variables found to be statistically significant. TA: Tubular Atrophy, IF: Interstitial Fibrosis

Quality assurance of whole slide images

Whole Slide Imaging (WSI) refers to high-resolution microscopy images of stained tissue slides used in Digital Pathology to diagnose disease and inform treatment. These images can suffer from quality issues, as shown in Fig 3. Quantifying image quality early in the WSI process can inform technicians, pathologists, and Artificial Intelligence algorithms that the diagnostic utility may be limited.

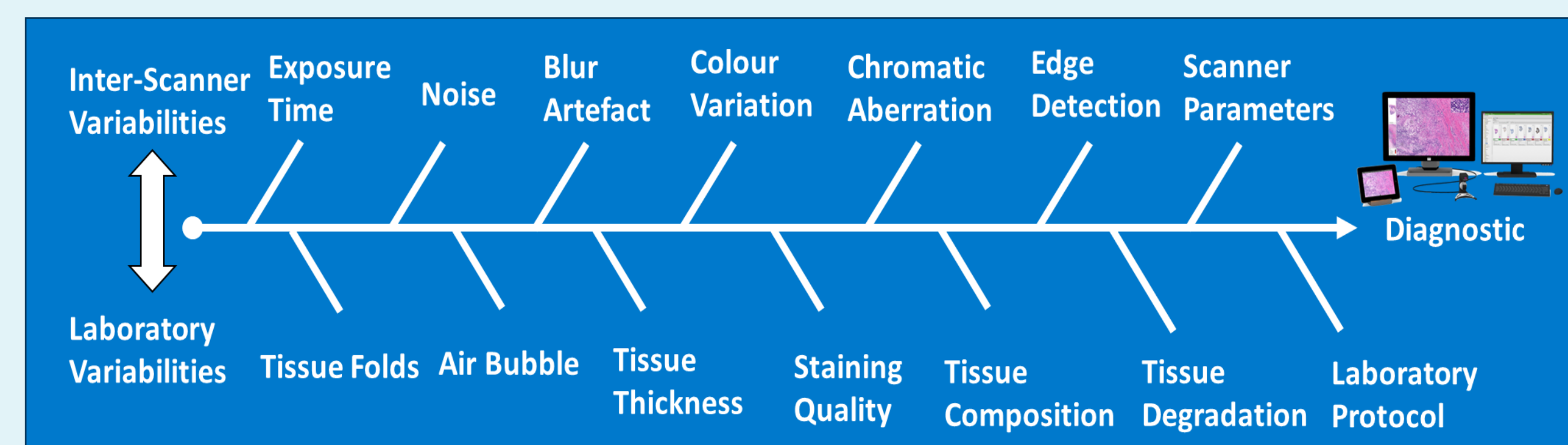


Fig 3: Sources of variation in Whole Slide Imaging

Solution:

- We designed and implemented a software (Fig 4) to provide image quality metrics
- The software provides both no-reference metrics (defined from the test image itself) and full-reference metrics (defined by comparing the test image to a reference image)
- Metrics can be applied to batches of images. Population diagnostics and quality assessment of an image relatively to a population can be derived.
- These metrics assess a range of quality characteristics. When combined, they provide both a general idea of quality, and a specific notion of where each image's quality falls short

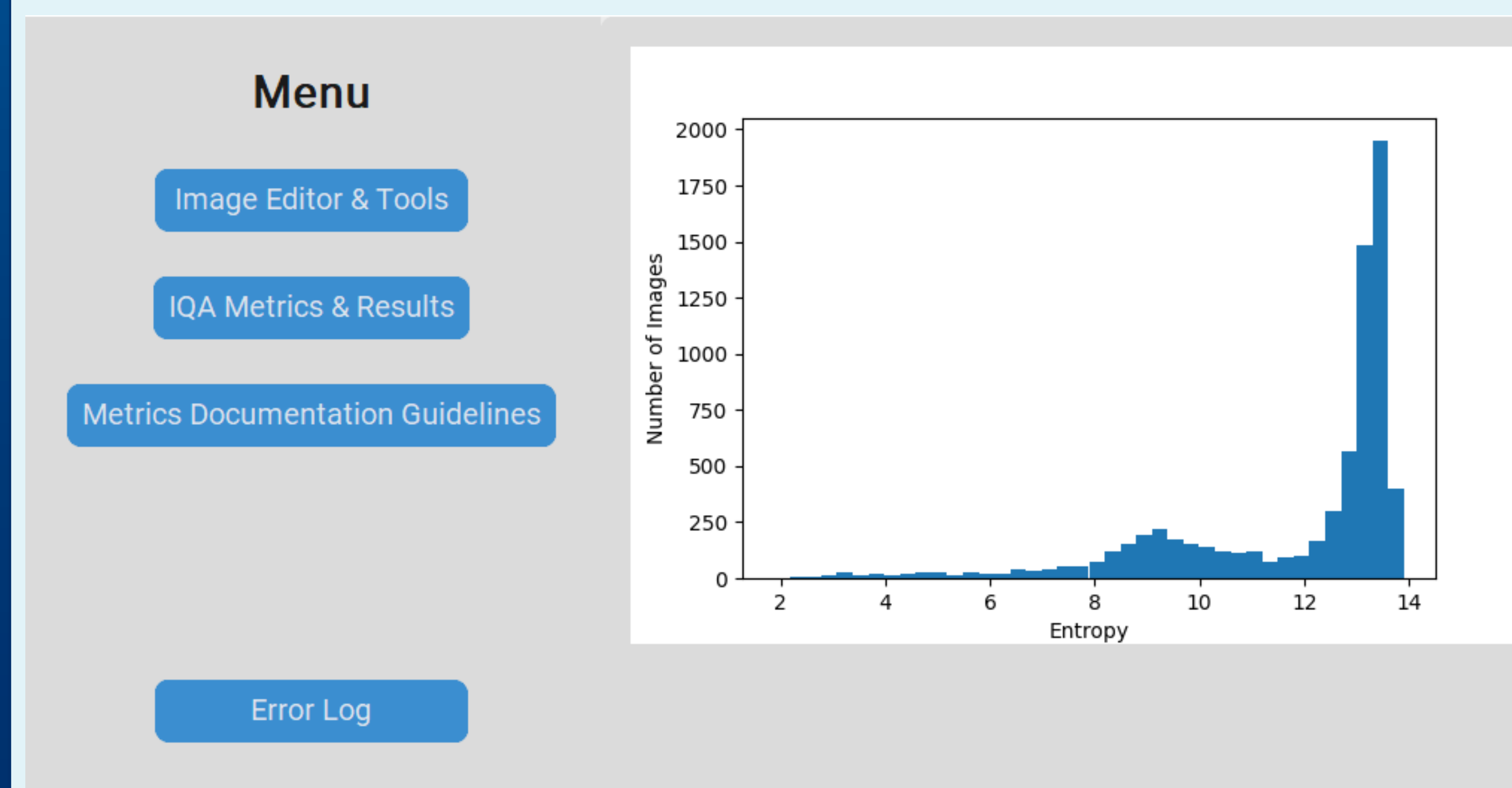


Fig 4: Screenshot of in-house image quality assessment software

Colour calibration to reduce uncertainty

Method:

- A tissue slide and two calibration objects were scanned in five scanners across four laboratories.
- Inter-scanner colour differences were quantitatively described.
- We designed and implemented a new method (Fig 5) for colour cross-calibration based on Optimal Transport and kernel regression.
- This dataset was then used to test and validate this method.

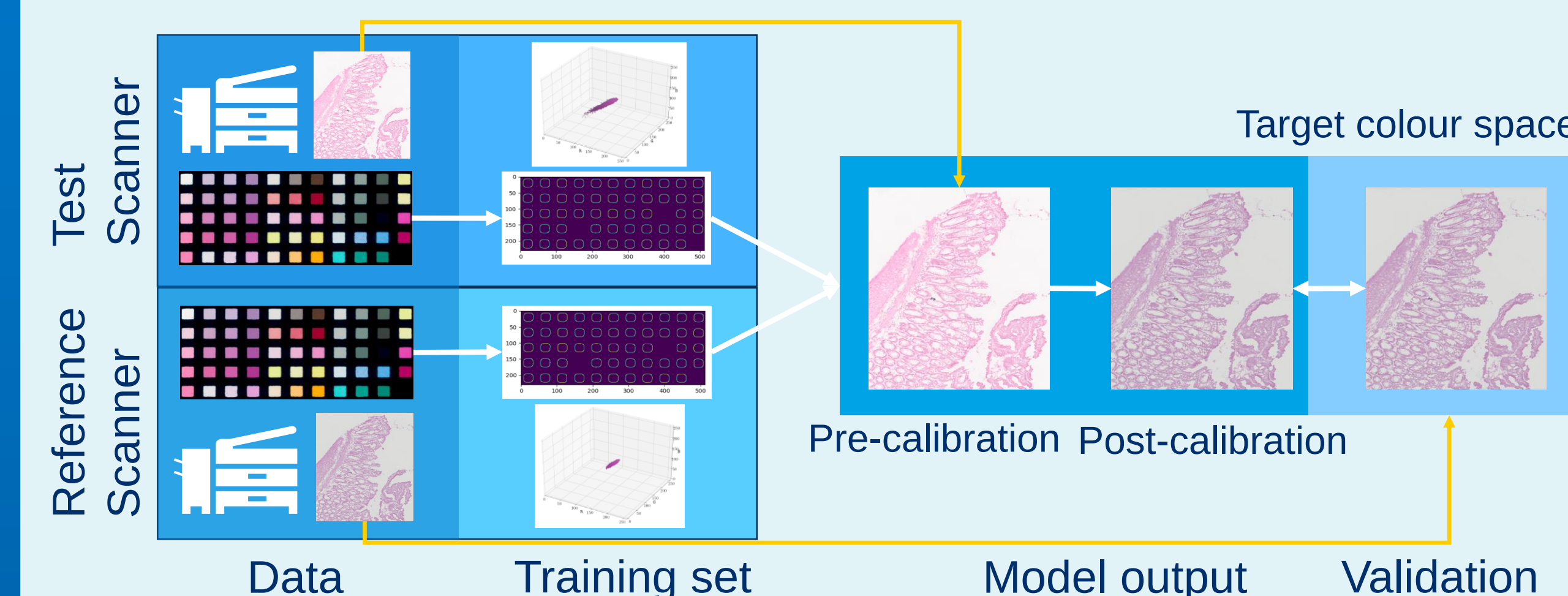


Fig 5: Graphical representation of the colour calibration method

Results (Fig 6)

- Scalable method (100 Mega pixel in 2 minutes on nVidia P100).
- The method provides GUM-compliant uncertainty quantification.
- Our method allows an average 10 % reduction in colour palette differences.

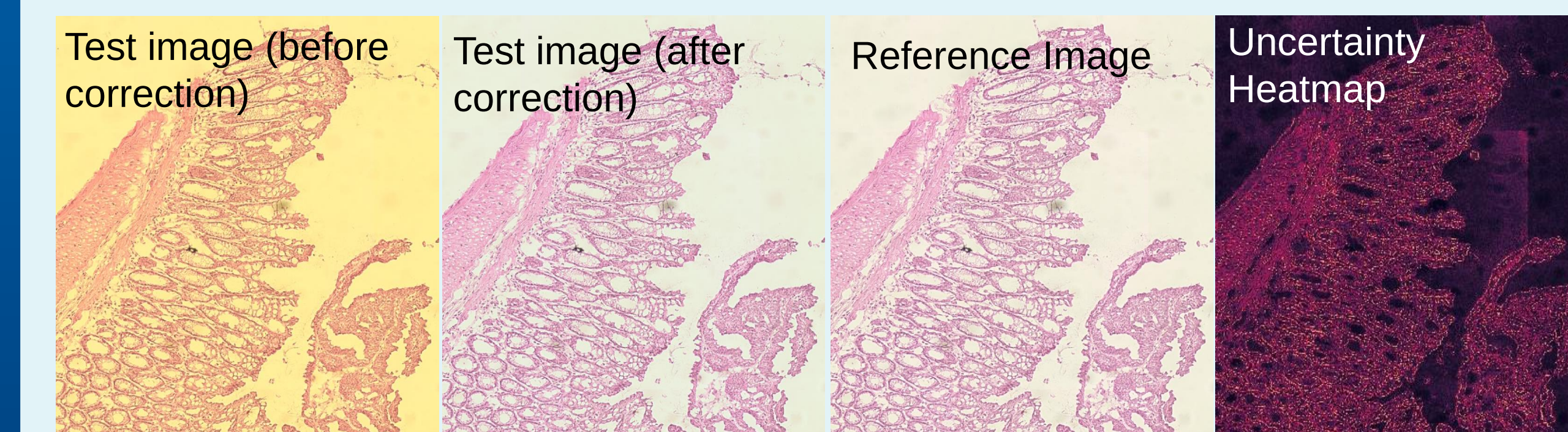


Fig 6: Illustration of the performance of the colour calibration method

Bibliography

- [1] Loizeau, Xavier, et al. "Quantifying measurement uncertainty in renal transplant biopsy assessment." (2024): 1458491.
- [2] Ayorinde, John OO, et al. "Measurement Matters: A Metrological Approach to Renal Preimplantation Biopsy Evaluation to Address Uncertainty in Organ Selection." (2024): e1708.

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