

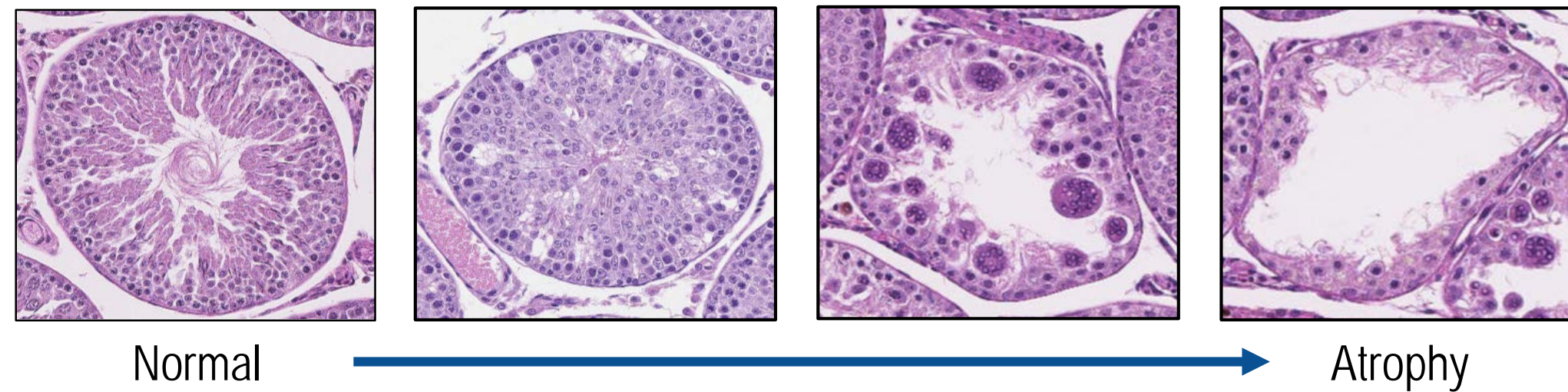
Development of a Novel AI-Based Algorithm for Abnormality Detection in the Testes of Rats

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1 INTRODUCTION AND HYPOTHESIS

- Abnormal male reproductive function contributes significantly to overall human infertility.
- Xenobiotics are an important potential cause of reproductive toxicity.
- Histologic evaluation of the testes in rodents is a best practice for early reproductive safety assessment.
- Hypothesis:** A deep learning artificial intelligence (AI) algorithm will detect common seminiferous tubule lesions in rat testes with high sensitivity and specificity, providing decision support for the pathologist and increasing diagnostic quality and efficiency.



2 METHODS

- Whole slide images (WSI) of testes from rats
- Slides scanned at 40x on a Leica AT2 whole slide scanner
- WSI uploaded to Deciphex Patholytix Preclinical Study Browsers
- Testes annotations for normal and three abnormal classes (degeneration, degeneration/atrophy, atrophy) were performed at 10x magnification
- A convolutional neural network (CNN) model was developed to create AI generated masks
- Qualification at the pixel level using confusion matrices and F1 scores

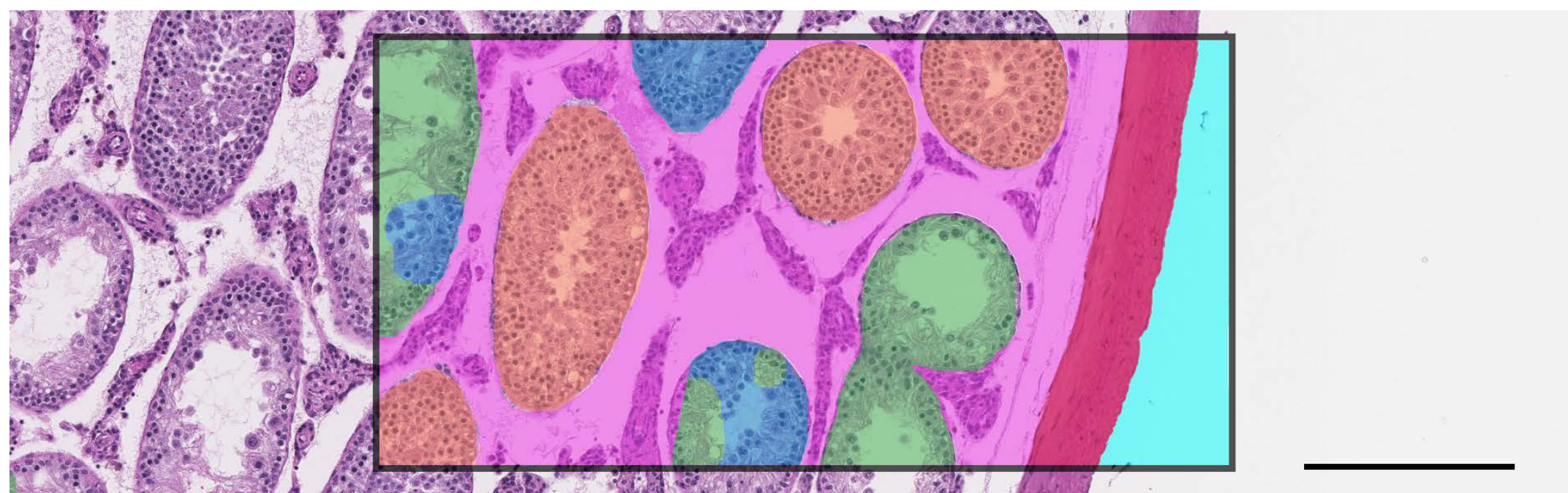


Figure 1. Full tile annotation of rat testes and seminiferous tubules: background (light blue), capsule (red), degeneration (orange), degeneration/atrophy (dark blue), atrophy (green). H&E, Bar = 250 μm.

3 CONFUSION MATRIX AND F1 SCORES

Confusion Matrix

| Actual \ Predicted | Background | Degeneration, Seminiferous Tubules | Capsule | Interstitial | Seminiferous Tubules | Atrophy, Seminiferous Tubules | Degeneration/Atrophy, Seminiferous Tubules |
|--|------------|------------------------------------|---------|--------------|----------------------|-------------------------------|--|
| Background | 99% | 0% | 0% | 1% | 0% | 0% | 0% |
| Degeneration, Seminiferous Tubules | 0% | 80% | 0% | 1% | 16% | 0% | 4% |
| Capsule | 26% | 0% | 67% | 6% | 1% | 0% | 0% |
| Interstitial | 8% | 1% | 1% | 88% | 1% | 0% | 1% |
| Seminiferous Tubules | 0% | 9% | 0% | 2% | 89% | 0% | 0% |
| Atrophy, Seminiferous Tubules | 0% | 0% | 0% | 2% | 0% | 74% | 24% |
| Degeneration/Atrophy, Seminiferous Tubules | 0% | 13% | 0% | 0% | 0% | 3% | 83% |

Confusion Matrix 1. Confusion matrix of rat testes algorithm. Confusion matrices help the trainer visualize algorithm tissue class identification discrepancy.

| Seminiferous Tubule Lesion Classes | Latest F1 score |
|---|-----------------|
| 1. Atrophy, Seminiferous tubules | 0.87 |
| 2. Degeneration, Seminiferous tubules | 0.72 |
| 3. Degeneration/Atrophy, Seminiferous tubules | 0.78 |

Table 1. F1 scores for rat seminiferous tubule lesion classes and algorithm. F1 scores harmonize the mean of specificity and sensitivity.

4 RESULTS AND DISCUSSION

- The CNN model identified normal testicular structures, including seminiferous tubules and interstitium with approximately 90% accuracy.
- The model accurately identified abnormal tissue classes, including degeneration, degeneration/atrophy, and atrophy, with 80%, 83%, and 74% accuracy, respectively.
- All class F1 scores exceeded the minimal acceptable performance level of 0.70.
- Conclusion:** A novel CNN detects common seminiferous tubule lesions in rats.
- Discussion:** The algorithm confusion is predominately between abnormal tissue classes and the identification overlap is on a pixel level. As the intended use of this algorithm is as a screening tool for pathologists, the confusion and overlap would not interfere with abnormality detection. To avoid false negatives, algorithm sensitivity needs to approach 100%. This high algorithm sensitivity results in expected false positives.

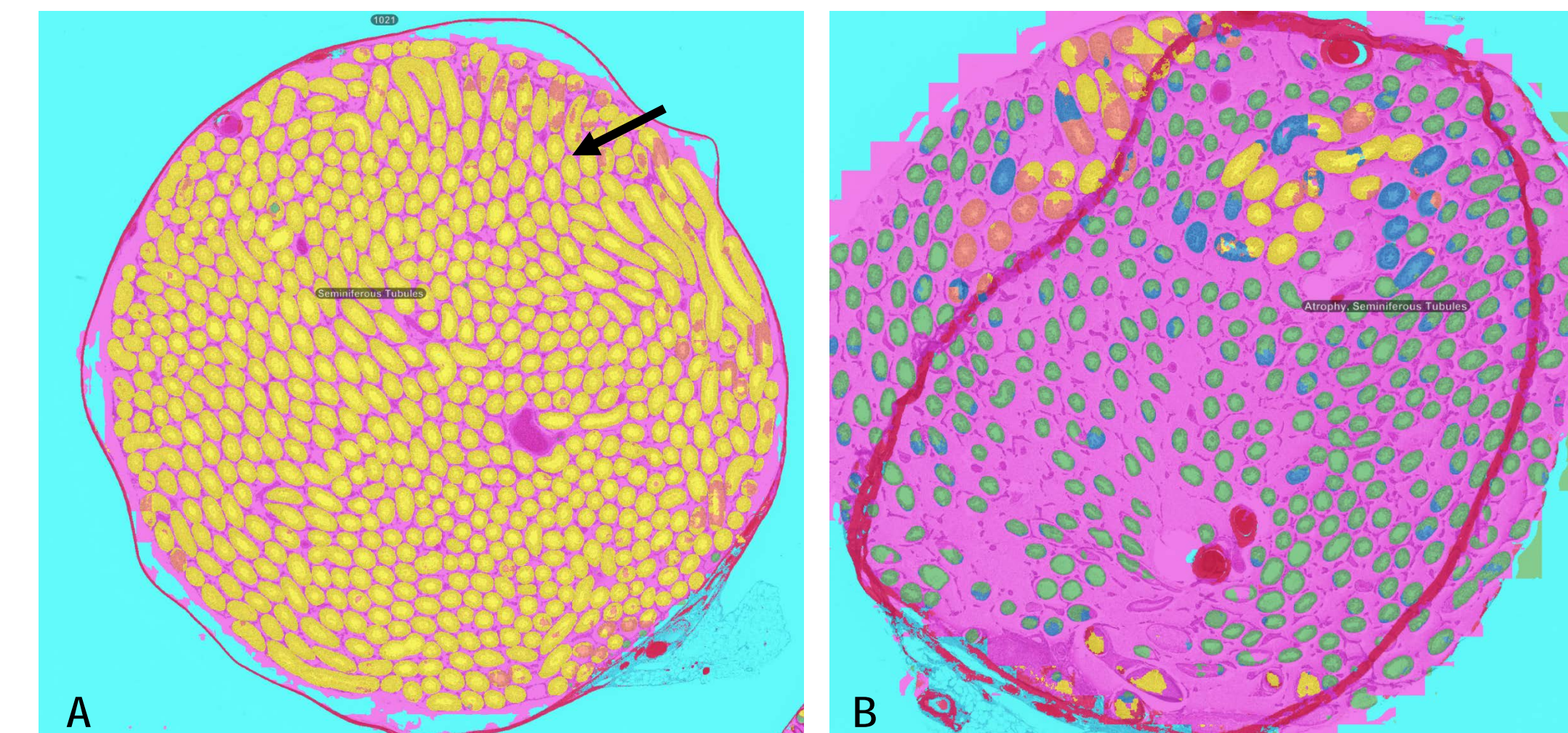


Figure 2. AI generated masks, rat testes. A) Normal seminiferous tubules (yellow) with a small area marked as potentially seminiferous tubular degeneration (orange) in the rete testes (arrow), a known spontaneous change. B) Spontaneous age-related testicular atrophy in this rat highlighted to pathologist by DL algorithm. Normal seminiferous tubules (yellow), degeneration (orange), degeneration/atrophy (blue), and atrophy (green) are highlighted.

Next steps: Qualification of the testes model using unseen slides and comparing algorithm performance to an expert annotator, not involved in initial training.