Deep Learning based Spermatogenic Staging Assessment for Hematoxylin & Eosin (H&E) stained sections of Wistar Rat Testes

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OBJECTIVE

- To propose an automated solution for identification of the 14 stages of spermatogenesis cycle in digital images of Hematoxylin and Eosin (H&E) and Periodic Acid Schiff (PAS) stained sections of Wistar rat testes.
- To examine the accuracy and precision of the proposed solution, comparing the results with manual staging done by expert pathologists.

INTRODUCTION

In preclinical toxicology studies, spermatogenic staging by histopathology is considered to be a sensitive method to detect toxicologic effects on male reproductive system. For better visualization of histological features, in addition to H&E, PAS stained slides need to be analysed. However, the complexity of testicular histology, close association of various germ cells, and overlapping features among adjacent stages make manual evaluation challenging, time consuming and subjective.We propose a faster and evidence-based automated method to identify the 14 stages of spermatogenic cycle in whole slide images of Wistar rat testes.

MATERIALS

- Training dataset of 10 and validation dataset of 3 H&E and PAS stained whole slide images of Wistar rat testes
- Leica SCN400 & Nanozoomer XR (Hamamatsu) scanners for image acquisition

METHODS

- Segmentation of seminiferous tubules by training a customized variant of Resnet and UNet based deep learning architecture on 1200 tiles of size 512 x 512 at 10x magnification taken from the training data set.
- Mapping of segmented tubules from 10x to 40x for accurate segmentation of various germ cells relevant for characterizing the different stages of the tubules.
- Germ cells used for staging are Elongated Spermatids (ESp), Spermatocytes (Spc), Round Spermatids (RSp), Residual bodies (RB), Meiotic bodies (MB), Spermatogonia (Spg).
- Detection of germ cells using a customized variant of ResNet based deep learning architecture.
- Tubules in stages 2/3 and 4/5 grouped together due to closely overlapping features.
- Classification of individual tubules into respective stages using a rule based classifier.
- Algorithm was validated on 3 H&E and PAS stained rat testes slide images and the results were verified by pathologists.

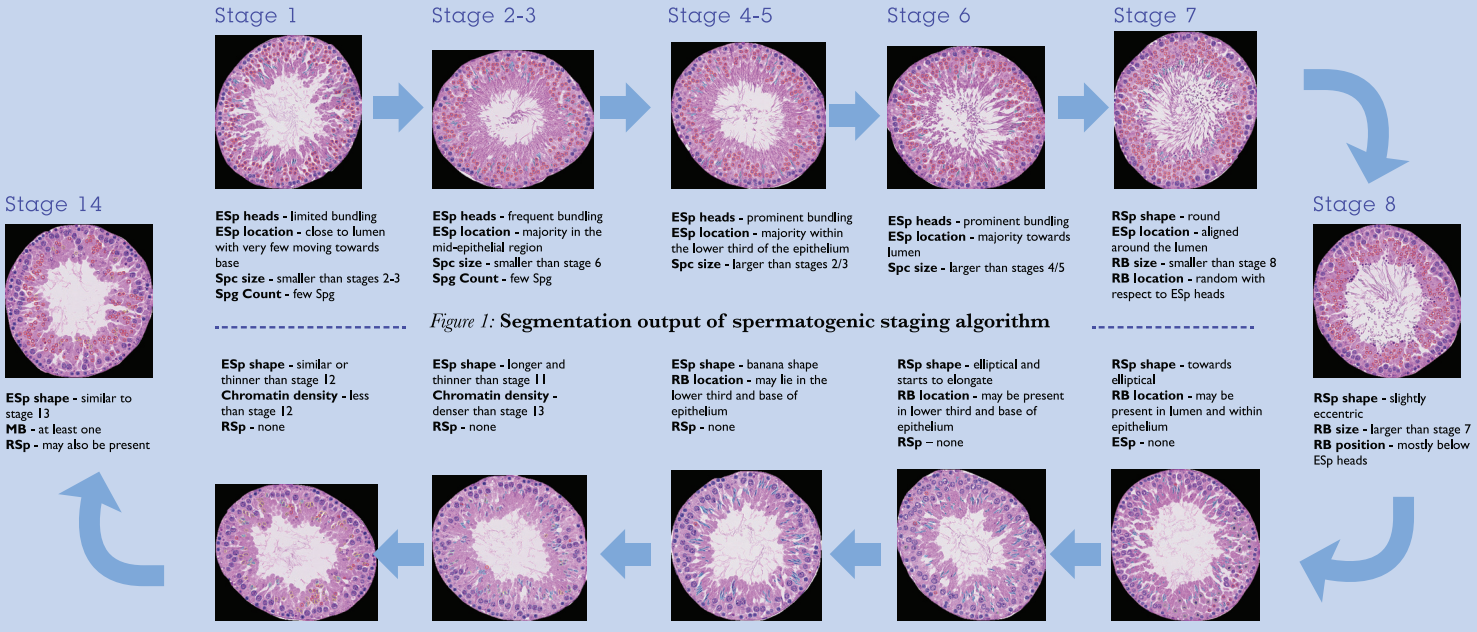


Figure 1: **Segmentation output of spermatogenic staging algorithm**

RESULTS

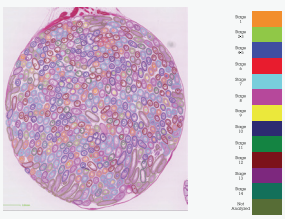
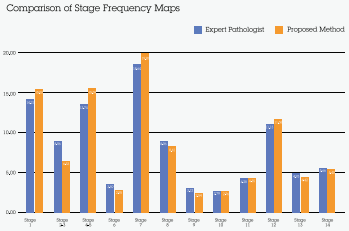


Figure 2: **Results of spermatogenic staging algorithm**



Through all the stages, the algorithm showed the following values of average accuracy and precision respectively:

STAIN	AVERAGE ACCURACY	AVERAGE PRECISION
H&E	82.88%	82.94%
PAS	80.91%	83.66%

Table 1: **Validation of spermatogenic staging algorithm**

CONCLUSIONS/FUTURE DIRECTIONS

- The proposed algorithm provides objective, accurate and precise spermatogenic staging with rapid turnaround.
- It eliminates the need of preparing an additional PAS stained slide.
- This algorithm can potentially be developed as an effective evaluation tool in male reproductive toxicology studies.

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