Digital Biopsy for Glomerular Ultrastructural Measurement in TEM Images

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The glomerular filtration barrier is vital to normal kidney function. Transmission electron microscopy (TEM) images visualize its cross-sectional ultrastructure, which consists of the sieve-like glomerular basement membrane (GBM) and podocyte foot processes. Proteinuric kidney diseases (PKD) are associated with filtration barrier morphological changes, which are observed experimentally and clinically in terms of GBM width and foot process width (FPW) measurements. Current TEM image measurement is performed manually as no fully automated solution exists. This limits research into PKD mechanisms and therapeutics with its labor intensiveness and operator bias. We developed an automated tool to measure input TEM images from a dataset of wild type (WT, n=5) and PKD model (ILK cKO, n=5) mice. A U-Net semantic segmentation model was trained on the dataset and corresponding manually annotated GBM masks. First, the segmentation model identifies GBM in input images. Next, these GBM segmentations enter an image processing algorithm that estimates GBM width and FPW. In our validation study on the dataset, resulting segmentation accuracy was strong relative to existing literature. The estimated mean GBM width and FPW measurements closely matched manual measurements for WT but differed significantly for ILK cKO animals. Measured GBM width and FPW were significantly wider for ILK cKO than WT mice, which aligns with known morphology. These results suggest our tool performs comparably to manual measurement on healthy tissue and can distinguish healthy from pathological samples. Our tool provides high-throughput, objective morphological analysis for research, and in the future could potentially facilitate clinical PKD diagnosis.