Construction of Histology-Based Three-Dimensional Minipig Renal Cortex Model for Preclinical Dosimetry

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Introduction

Radiopharmaceutical therapy (RPT) delivers radionuclides to tumors, but because much injected activity clears renally, the kidney is considered a critical dose-limiting organ. Alpha emitters are promising for their high linear energy transfer, but due to alpha particles' very short range, accurate dose estimation demands microscale anatomical models. Minipigs are used in preclinical dosimetry for their human-comparable physiology; however, no microscale renal cortex model exists, limiting dosimetric translation to humans.

Purpose: To construct histology-based 3D microscale models of the minipig renal cortex — resolving glomeruli, Bowman's capsules, and proximal and distal convoluted tubules — across cortical depths in female and male animals (target 3–4 each, 6–8 total) to support Monte Carlo dosimetry of alpha- and beta-emitting radiopharmaceuticals.

Methodology

Two hundred serially-sectioned H&E-stained renal cortex images were obtained from a 6-month-old female micro-Yucatan minipig (5 µm sections, 2.74 µm pixel size) and aligned by landmark-based rigid registration. Whole renal corpuscles were segmented with a human-tissue deep-learning autosegmentation algorithm from the University of Florida Histology Laboratory. Because it imperfectly captured minipig anatomy, its outputs were manually corrected and used to fine-tune a minipig-specific model that segmented corpuscles across all sections. A subset of these corpuscles was manually partitioned into glomerulus and Bowman's capsule to train a second model differentiating the two across all sections. Labels were converted to 3D surface meshes and repaired in Blender. An in-house Python routine filled the remaining 1 × 1 × 1 mm³ volume with proximal and distal convoluted tubules, using morphometric parameters from the histology (tubule radius ≈ 18 µm; proximal ≈ 37% and distal ≈ 14% of cortical volume). The assembled model was converted to a tetrahedral mesh and implemented in the PHITS Monte Carlo code, where electron and alpha specific absorbed fractions (SAFs) will be computed.

Results

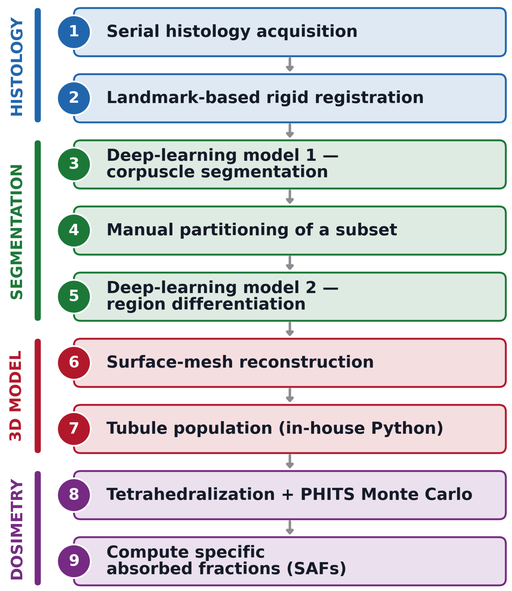

Figure 1: Workflow

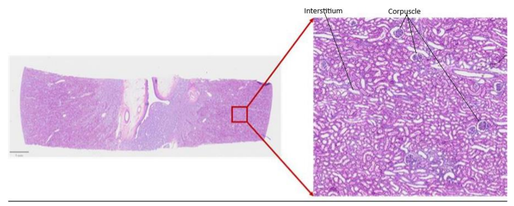

Figure 2: H&E Histology of the Minipig Renal Cortex

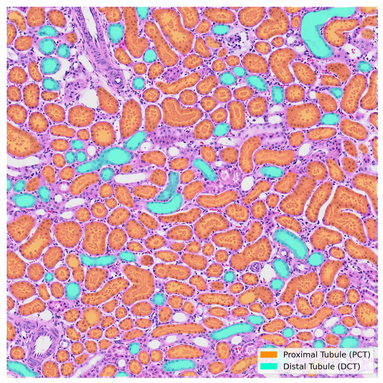

Figure 3: Reconstructed Convoluted Tubules (PCT & DCT)

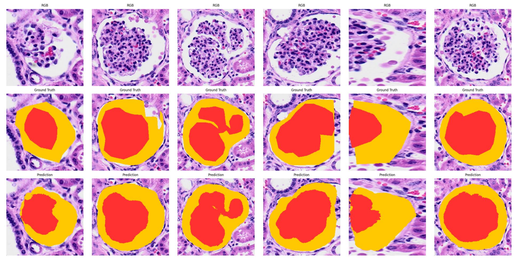

Figure 4: Deep learning model to segment Bowman's capsule and glomerulus

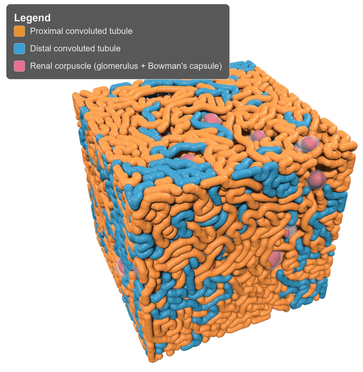

Figure 5: Final 3D Model

Conclusions

- The first histology-based 3D microscale model of the female micro-Yucatan minipig renal cortex was successfully constructed in polygonal-mesh format.
- The model explicitly resolves glomeruli, Bowman's capsules, and proximal and distal convoluted tubules within a 1 mm³ volume, and was tetrahedralized to compute electron and alpha SAFs.

Future Work

- Build additional depth-dependent female and male cortex models (target 3–4 each) to capture cortical-depth and inter-subject variation, then compute SAFs and radionuclide S-values across the full series with statistical analysis.
- Port the workflow to the mouse kidney and train a deep-learning segmenter to reduce manual annotation for future models.

Funding

- Supported by NCI Grant P01 CA272222 and a P01 grant with Johns Hopkins University (JHU).

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