Microscale Histology-Informed Minipig Salivary Gland Model for Preclinical Radiopharmaceutical Dosimetry

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Introduction

Radiopharmaceutical treatment (RPT) of castration-resistant metastatic prostate cancer using agents tagged with prostate-specific membrane antigen (PSMA) has shown improved outcomes through selective targeting of prostate tumor tissue. PSMA is however expressed in many other tissues including the salivary glands. For many PSMA-tagged RPT agents, the salivary glands are considered a dose-limiting organ due to the incidence of deterministic tissue effects like xerostomia. Minipigs are widely used in preclinical pharmaceutical studies, but no model has yet been developed to represent the microstructures of the minipig salivary glands. The purpose of this study is to develop a 3D model of parotid gland ductal and acinar structure which will support radiation dosimetry as it relates to salivary gland toxicity in radiopharmaceutical therapies.

Methodology

- A parotid gland model has been constructed based on literature values taken from salivary gland imaging studies.
- H&E-stained minipig histology slides of the parotid gland have been used to inform branching ductal network microanatomy.
- A physiological arborization algorithm has been used to model separate branching networks for the salivary ducts, arteries, and veins.
- The duct network model has been exported to polygon mesh format and refined using the 3D modeling software *Blender* before being converted to tetrahedral-mesh format for dose calculations.
- Monte Carlo radiation transport simulations are being conducted on the parotid model using the Particle and Heavy Ion Transport code System (PHITS) to model dose distribution from radionuclide uptake in source regions

Results

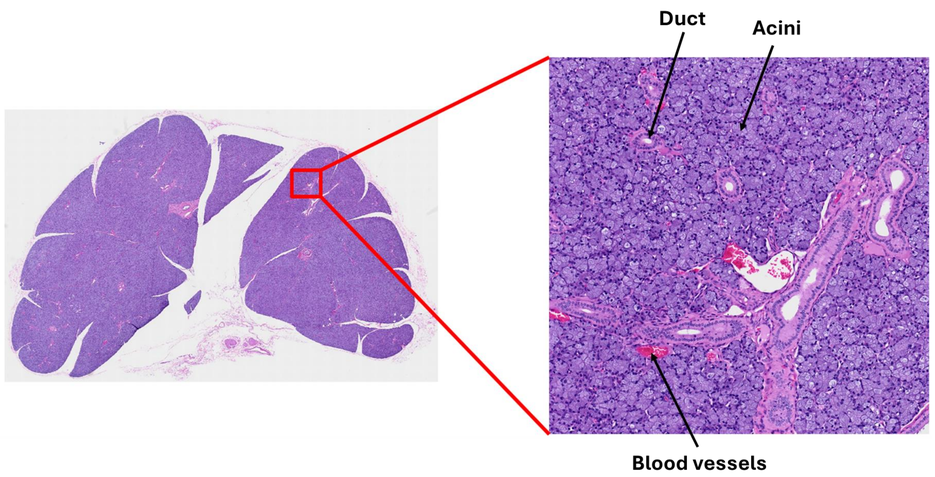

Figure 1: Digitized H&E-stained histological image taken from a minipig parotid gland featuring ducts, blood vessels, and acini.

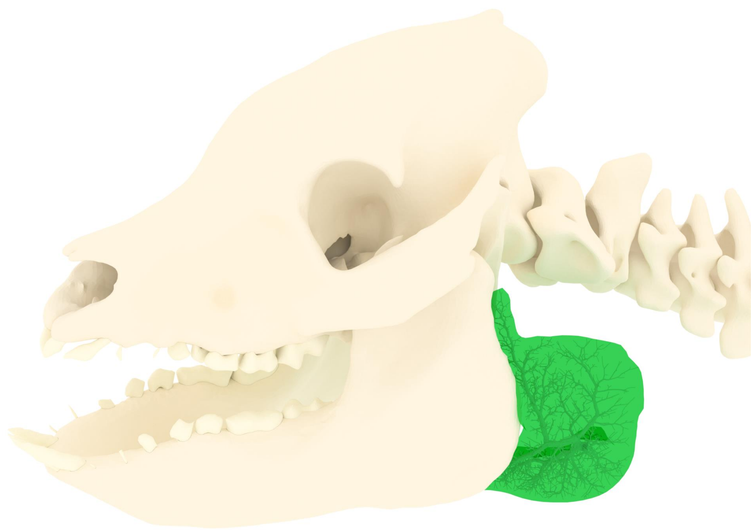

Figure 2: Rendering of the branching duct system shown in the minipig parotid gland.

Conclusion

The present study has developed a microscale model of the minipig parotid gland, comprised of branching networks for salivary ducts and blood vessels, and a space representing acinar cells and other connective tissues. Radiation transport simulations in the Particle and Heavy Ion Transport code System (PHITS) Monte Carlo code have been implemented toward computing S-values for select radionuclides that have been shown to cause toxicity in salivary glands. Absorbed fraction plots for monoenergetic electron sources show significant differences between a fully homogenous parotid and a model with defined microstructures. This work will provide accurate predictions of dose-response in healthy salivary gland tissue and allow for more informed clinical decision making.

Future Work

- Continued Monte Carlo simulations to complete dose calculations for all relevant glands and radionuclides
- Calculation of specific absorbed fractions (SAFs) and radionuclide S-values

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