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Small Scale Modeling and Dosimetry for the Salivary Gland: Application to 177Lu- and 225Ac-PSMA Therapy

Objectives: Salivary gland toxicity is a quality of life concern in radioiodine treatment of thyroid cancer and more recently has become a concern for radiolabeled-PSMA therapy of prostate cancer. Clinically observed toxicity is inconsistent with absorbed doses (AD) to the salivary glands calculated by absorbed fraction methods, even considering the alpha-particle RBE. Small scale anatomical modeling and activity apportionment, the macro-to-micro methodology, has been proven to reconcile discrepancies between whole organ AD values and clinically or pre-clinically observed toxicities for alpha-particle renal toxicity.

Methods: Uptake in the salivary glands has been shown to be primarily confined to the epithelial striated ducts where PSMA is expressed. Dimensions of typical striated duct cells were obtained from the literature. Based on the fraction of occupancy of these cells within the salivary glands (5.1 %), striated cells were placed randomly in gridded spheres of increasing size representing the salivary glands and was used to simulate decay of activity in these cells. The GEANT4 Monte Carlo was used to simulate decays for both 177Lu and 225Ac in the striated ducts. The absorbed dose .was calculated to both striated cells and acinar cells, which make up 60 % of the salivary glands. Dose volume histograms of these two cell types were obtained as a function of salivary gland size as was the ratio of average striated duct AD and acinar cell AD to whole organ AD.

Results: The grid-based Monte Carlo results showed a ductal cell AD to salivary whole organ AD ratio of 5.1 –5.3 for 177Lu and 13.4 –13.8 for 225Ac dependent on salivary gland size (5 - 25 ml). This suggests an average salivary gland dose threshold of ~ 0.45 Gy for 225Ac, assuming an RBE of 5, and a threshold of ~5.8 Gy for 177Lu.

Conclusions: This is a significant step in quantifying the discrepancy between clinically observed toxicity and predicted toxicity based on whole organ AD values using small scale dosimetry, which has been shown to explain similar discrepancies in different cases, particularly alpha-particle dosimetry. This study shows that while the salivary glands may be considered as parallel organs for external beam radiation, the physiology for activity uptake means that for radiopharmaceutical therapy, they have a more complex structure.

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