Image-based dosimetry for selective internal radiation therapy (SIRT) using yttrium-90 microspheres

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^{90} Y-loaded microspheres are currently used as a palliative treatment for patients with primary and metastatic solid liver tumors. These microspheres contain radioactive ^{90} Y, which decays via beta-minus transition to ^{90} Zr. While the normal liver receives about 75% of its blood supply from the portal vein, hepatic tumors receive their blood supply almost exclusively from the hepatic artery. Taking advantage of this unique blood flow, radioactive microspheres are injected into the hepatic artery resulting in a preferential distribution to tumor sites within the liver. Studies show that the single best prognostic indicator for patient response is the tumor-to-normal tissue (T:N) activity uptake ratio. However, ^{90} Y emits very few photons its broad bremsstrahlung spectrum leads to diffuse, low resolution images, which are insufficient for accurate T:N quantification. Thus, the first objective was to develop a PET-labeled microsphere as a surrogate for the therapeutic microsphere to provide accurate biodistribution information.

Furthermore, patient outcome is also suspected to be linked to the mean tumor dose and tumor dose volume histogram. Therefore, a second objective was to develop and validate a method to calculate the dose distribution within the tumor and normal liver tissue. Computer software that generates three-dimensional (3D) dose distributions was validated by comparing results to experimental measurements. The novel development of a 3D gel dosimeter will be discussed as well as a new protocol for 2D film dosimetry. Both dosimetry methods were validated but only film provided the desired accuracy.

The overall accuracy of the dose distribution depends on the uncertainty of the ^{90} Y assay, which can extend to 15% at 1σ. Therefore, the third objective was to develop an accurate non-destructive assay of ^{90} Y. To this end, a new ^{90} Y positron branching ratio was measured and a clinically relevant transfer standard was developed.

In summation, this thesis will present a new PET-labeled microsphere for pre- and post-treatment assessment, two new beta dosimetry protocols along with validation studies, a new positron branching ratio for ^{90} Y that led to formation of an accurate non-destructive assay, and the first successful experimental validation of a computer generated internal dose distribution using dose kernel convolution.