

**Purpose:** The feasibility of delivering deliberately heterogeneous dose distributions based on biological image data is related to transformations that map the image data to dose prescription values, which is currently unknown. We created optimized dose distributions that were based on four possible image-to-dose-prescription transformations to determine their delivery feasibility.

**Materials and Methods:** Tomotherapy photon dose calculations were performed for a canine with a nasopharyngeal tumor using the Convolution/Superposition algorithm. Linear, square root, quadratic, and Gompertz transformations between the standard uptake values (SUV) from  $^{61}\text{Cu}$ -ATSM PET images and the prescriptions were implemented to yield weighted distributions of prescribed dose boosts in regions of expected radio-resistant hypoxic cells. Maximum dose boosts were constrained to reflect clinically realistic whole tumor doses and constant normal tissue doses. Optimized heterogeneous dose distributions were found by minimizing a voxel-by-voxel quadratic objective function in which all tumor voxels were given equal importance weightings.

**Results:** The planned non-uniform dose distributions founded on hypoxia maps display variability between preservation and resolution of biological heterogeneities. Whereas the linear transform preserved the SUV distribution with similar heterogeneities in the prescription, the square root and quadratic transforms softened or sharpened heterogeneities in respective prescriptions. The square root dose plan matched its prescription well due to shallow dose gradients but failed to resemble the hypoxia map, while the quadratic plan poorly matched its prescription due to steep gradients but resembled the PET scan. The linear planned dose distribution matched both its prescription and the biological image fairly well.

**Conclusions:** Simple transformations investigate the importance of knowing given prescriptions exactly to deliver non-uniform dose distributions from biological images. Transformations that blur heterogeneities lead to dose distributions that match their prescriptions coupled with loss of conformality to the PET images. Those preserving heterogeneities lead to less well-matched distributions but do conform to the scans.