Feasibility of Mapping Transient Tumor Hypoxia using *in situ* Activation PET Imaging: A Simulation Study

**Purpose:** To determine the feasibility of quantifying transient tumor hypoxia using *in situ* activation PET imaging.

**Material & methods:** A $^{64}$Cu-ATSM autoradiography image of rat tumor, reported previously [1], was digitized and used to quantify heterogeneous tumor hypoxia regions, as shown in Fig 1. Micro-vessel densities (MVDs) were mapped from the image based on regional uptake of $^{64}$Cu-ATSM. The corresponding MVDs map (Fig 2a) was input to a reaction diffusion model [2] to simulate a steady state oxygen tension ($pO_2$) map (Fig 2b). The $pO_2$ map was input to the Ten Haken model [3] to simulate an *in situ* activation PET image (Fig 2c), using photon beam energies of 20-50 MeV. This “total” activation image includes both mobile and immobile $^{15}$O. An image of *in situ* activated mobile $^{15}$O (Fig 2d) was produced by subtracting the fast decay portion from the overall decay curve. Finally, the $pO_2$ map and *in situ* activated mobile $^{15}$O PET image were thresholded and compared. All simulations were performed in 2D for a vasculature size of 20 cm$^2$ using MATLAB 2007b.

**Results:** A threshold value of 5 mmHg was used to define the hypoxia fraction (HF) on the $pO_2$ map (Fig 3a). A threshold value of 63% of the mean image intensity on the *in situ* PET image was used to define the HF on the mobile $^{15}$O image (Fig 3b). Both maps demonstrate comparable hypoxia distributions. The calculated HF or hypoxic regions to the overall tumor-bearing vasculature ratio was found to be similar, with 0.178 on the $pO_2$ map and 0.157 on the mobile $^{15}$O image.

**Conclusions:** Although a more accurate method to threshold the activation map needs to be established, the *in situ* activation approach to quantify tumor transient hypoxia is feasible. Additionally, a relationship between activity and mmHg needs to be established.

**References:**