AbstractID: 11142 Title: Influence of Oxygen Tensions and Tissue Optical-properties on Optical Reporter Genes

Purpose: To quantify the effects of oxygen concentrations on optical reporter genes imaging methods, by modeling the influence of oxygen tensions on reporter protein signal generation activity as well as the propagation of reporter fluorescent and bioluminescent photons from locations within tissues to measurement apparatus. **Method and Materials:** A reporter gene construct composed of *Renilla* luciferase and monomeric red fluorescent protein was modeled using analytic techniques. Previous *in vitro* work was performed to measure the imaging signal produced by this construct when exposed to reduced oxygen levels. The relationship between the luminescent intensities and different oxygen levels was studied for the reporter gene. The setup depicted in the model consisted of a point source with a fixed amount of reporter protein and oxygen at depth in tissue. The bioluminescent signals as well as fluorescent signals upon illumination by a pencil beam source were modeled for this setup using Michaelis-Menten enzyme kinetics and photon diffusion theory. **Results:** The model developed produced results that agree well with the *in vitro* measures of bioluminescent and fluorescent reporter activity. The relative fluorescent and bioluminescent signals can be combined to infer the oxygenation of the sample, although this relationship varies with depth in tissue. **Conclusion:** This work indicates that the adverse effect of oxygen tensions on bioluminescent report activity can be modeled by enzyme kinetics, which provides insight into forming methods to differentiate reporter expression from activity based on optical measurements. This technique could then be applied towards quantitating measurements from reporter genes constructs including hypoxia-driven expression schemes. This study also shows that, to a first order approximation, fluorescent signals can be used as a control for bioluminescent measurements since the fluorescent reporter activity does not vary substantially under different low oxygen levels.