AbstractID: 13949 Title: Imaging the biological structure and characteristics of model tumors using optical computed transmission and emission tomography

Purpose: To obtain the first co-registered high resolution 3D images of an intact xenograft tumor showing (i) the vasculature network labeled with an absorbing vasculature contrast agent, and imaged with optical-CT (ii) the distribution of red-fluorescent-protein (RFP) constitutively expressed by viable tumor cells, and (iii) the distribution of green-fluorescent-protein (GFP) endogenously expressed by tumor cells exhibiting HIF-1 transcription (hypoxia-inducible-factor).

Method and Materials: An in-house prototype optical-CT/ECT system was constructed incorporating specialized optics to facilitate accurate parallel beam tomographic imaging. Both transmission imaging (optical-CT) and emission imaging (optical-ECT) can be performed on the same sample, enabling very accurate multi-modal image registration. A 4T1 tumor cell line with double fluorescent reporter labeling (GFP and RFP as described above) was grown in a window chamber (under IACUC approved protocol). The tumor was first imaged in-vivo, with an epi-fluorescent microscope. A tail vein injection of vascular contrast was then administered, and the tumor removed from the window and optically cleared, in preparation for optical-CT/ECT imaging.

Results: Comparison of the in-vivo window chamber images with post clearing images revealed consistent areas of fluorescent signal but, importantly, new areas of signal were visible in the cleared images where signal had been obscured by overlying structures in the in-vivo images. All 3 biological characteristics (vasculature, viable tumor-sub-volume, and HIF-1 expressing sub-volumes) were successfully imaged, and accurately co-registered, enabling detailed analysis of inter-relationships using overlay images. Quantitative metrics were derived from the images, including viable-tumor-volume=10.5mm3, GFP-hypoxic sub-volume=2.6mm3, vessel-volume =1.7mm3, and hypoxic ratio=0.25.

Conclusion: High resolution multi-modal 3D co-registered images can be acquired with optical-CT/ECT techniques from optically cleared tissue samples. The unique capabilities of these techniques to image relatively large un-sectioned samples offers a new low-cost way to investigate biological processes and inter-dependencies in whole samples.

Conflict of Interest (only if applicable):