Over recent years, a range of vascular-modulating therapeutics have enjoyed success in the preclinical suppression of tumor growth. Clinical responses, however, have been limited by the onset of systemic side effects such as hypertension. Preclinical in vivo cancer models have arguably lacked the appropriate application of reliable biomarkers with which to detect and contrast subtle structural changes, for example vascular “pruning” (d’Onofrio et al 2010), in both tumor-associated and systemic vascular beds. Additionally, there has been a poor understanding around the complex phenomena of drug-induced systemic toxicities, in the presence or absence of certain tumor types (Hadjiandreou et al 2014).

This presentation will introduce a novel solid-tissue biomarker of vascularity, incorporating immunohistochemistry and image analysis. This can be used preclinically, with a range of xenograft and explant models, in order to determine the level of intra-tumoral vascular regression (efficacy), and compare this to the extent of organ-associated vascular rarefaction (toxicity). Preliminary data, concerning the effects of tumor burden upon systemic vascular bed resistance, and the potential modulation of toxicity, will be put forth.

Understanding these concepts may provide insight into how to stratify patients for treatment with vascular-modulating agents and predict the risk of clinical toxicity, based upon likely therapeutic indices and tumor status.

References:
