AbstractID: 9065 Title: Assessment of early vascular response to anti-angiogenic therapy in a murine model using acoustic radiation-mediated multimodal optical spectroscopy

Purpose: To investigate the efficacy of using acoustic radiation force (ARF) combined with optical spectroscopy to assess early effects of anti-angiogenic therapy on changes in oxy-hemoglobin saturation in a human glioblastoma xenograft model.

Method and Materials: Pilot experiments were carried out with nude mice bearing human U87 glioblastoma xenografts. Acoustic field intensities were generated using a focused transducer operating below the FDA diagnostic ultrasound limits. During each experiment, ultrasound was administered for 5-second bursts, with 55-second relaxation periods between bursts and a total of five bursts per data collection per tumor position. A broadband light source was used for tissue illumination; diffuse reflectance spectra were collected from the tumor using an optical probe and a room-temperature spectrometer. Baseline measurements were taken on Day-0 before injecting a VEGF blocker drug to the mice. After drug administration, multimodal ARF-optical measurements were taken each day at the same locations of each tumor for 4 consecutive days (Day1–4).

Results: Preliminary results revealed that the mean values of the spectroscopic signals reflecting oxy- vs. deoxy-hemoglobin concentrations increased over a period of 4 days, which suggest an increase in oxygen level over time during treatment with the VEGF blocker in the tumor tissue. On Day-2, post-ischemic reactive hyperemia was highly significant, a phenomenon previously observed in normal vasculature only, which suggests that the drug effects on blood vessel normalization were most significant at this treatment time-point. On Day-4, the multimodal ARF-optical signal starts to display the behavior of flow stasis in benign vessels, which corresponds to the expected schedule of the drug on vessel normalization.

Conclusion: This is the first pilot study to demonstrate the feasibility of using multimodal imaging to monitor and assess early changes of blood vessel normalization due to anti-angiogenic therapy. Ongoing experiments are being carried out for further mechanistic investigation.