

Blood-flow informed photodynamic therapy improves therapeutic efficacy

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The efficacy of photodynamic therapy (PDT) depends on photosensitizer accumulation and light delivery to a tumor, including to the tumor-supporting vasculature. Subsequent vascular response can be an important component of the treatment effect with rapid decreases in blood flow during light delivery found to correlate with poor PDT outcome in murine studies. This relationship is an expected consequence of ischemia-introduced hypoxia during light delivery that limits the development of damage-creating reactive oxygen species. We posit that blood flow response during PDT can be used in real time to inform the choice of light delivery parameters for treatment.

Diffuse correlation spectroscopy (DCS) was used to measure blood flow continuously in radiation-induced fibrosarcoma murine tumors during Photofrin-mediated (5 mg/kg) PDT. PDT-induced changes in relative blood flow (rBF; i.e. normalized to pre-illumination values) were used in an automated feedback process to modulate illumination fluence rate so as to conserve tumor perfusion. PDT was performed at an initial fluence rate of 150 mWcm⁻², and automatically attenuated to 25 mWcm⁻² when rBF decreased by more than 10% per minute. The light fluence rate was allowed to increase to 150 mWcm⁻² when rBF recovered and exceeded the pre-PDT value. The treatment length was automatically adjusted so that a constant prescribed light dose of 135 Jcm⁻² was delivered. Long-term tumor response (i.e., time-to-a-400 mm³ tumor volume) and treatment length were compared between mice treated with blood flow-informed PDT to those treated at a constant light fluence rate of 150 mWcm⁻² or 25 mWcm⁻². Improved PDT efficacy was observed using blood-flow informed light delivery.

A noninvasive system for real-time monitoring of tumor blood flow during PDT was successfully used to adjust light delivery in an automated fashion. The ability to measure and modulate tumor physiologic properties in clinical applications of PDT will provide a means for personalized delivery of treatment.