In vivo quantitative photoacoustic imaging of targeted Lipo-JICG

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Background, Motivation & Objective

Photoacoustic (PA) imaging is a powerful preclinical tool; however, currently available contrast agents lack sufficient PA-signal-generation ability for deep imaging, or their absorbance spectra overlap with hemoglobin, reducing *in vivo* imaging sensitivity. Our contrast agent is based on antibody-targeted liposomes loaded with J-aggregates of indocyanine green dye (Lipo-JICG). This agent delivers a strong, narrow absorbance at ~890 nm, where it can be readily unmixed from hemoglobin, as well as enhancement of the PA signal due to dye-aggregation-mediated increases in thermal gradients and peak absorbance. This study uses the iThera inVision PA imaging system to quantitatively assess targeted Lipo-JICG in an ovarian cancer model.

Statement of Contribution/Methods

Ten athymic nu/nu mice were injected with SKOV3 ovarian cancer cells in the left ovary. Once tumors reached an MRI-confirmed 5 mm^2 **(D)**, mice were PA imaged at 730, 760, 780, 800, 830, 890, 910, 920 nm, with 15-frame averaging, and at five time-points: pre-injection, and immediately, 30 min, 1 hour, & 24 hours post-injection. Mice were injected with either targeted (a-FRα) or non-targeted (a-RG16) Lipo-JICGs. The left kidney was used as a common fiducial to co-register between PA and MR images. Chromophore unmixing was performed for oxy-/deoxyhemoglobin and Lipo-JICG with different wavelength combinations to maximize the ratio of CNR and acquisition time (i.e., cost function) between pre- and 1-hour-post-injection images (intratumoral ROI determined by 800-nm image and MRI). To improve quantification accuracy, an SNR-regularized, FEM-based fluence correction model **(B,C)** was applied to account for local fluence variations and mitigate the water-pathlength-bias at longer wavelengths.

Results, Discussion & Conclusions

From the cost function **(A)**, optimal wavelengths were found to be 730, 760, 780, 800, 830, 890, & 920 nm. Arterial SO_2, expected to be ~100%, was estimated to be 86% without correction and 93% after surface-fluence correction. Lipo-JICG intratumoral contrast increased by a factor of 2.6 after surface-fluence correction **(E,F)**. Improved quantification of targeted Lipo-JICG may allow for quantitative assessment of treatment response over time, which can lead to improved treatment strategies.