Biodistribution of albumin microbubbles functionalized with Photosens photodynamic dye

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**Abstract**

Albumin-based microbubbles have been widely used as ultrasound contrast agents over the decades, while recent attention has been attracted to consider them as drug delivery systems [1]. Recently it was shown that photosensitizers (compounds with photodynamic activity) can be efficiently loaded into the microbubble shell [2] and resulting platform may enhance photodynamic activity [3]. The aim of the study is to explore the biodistribution kinetics of albumin microbubbles modified with commercially available photosensitizer Photosens® using electrostatic coupling. Microbubbles were filled with air (identically to clinically available albumin microbubbles formulation, Albunex) and sulfur hexafluoride (SF6) (to prevent rapid dissolution of bubble gaseous core compared to air-filled agents), resulting in submicron size range of 0.8 ± 0.3 µm and concentrations of 4.8 × 108 MBs/mL and 3.1 × 1010 MBs/mL for air- and SF6-filled agents, respectively. After microbubbles injection into the caudal vein, the fluorescence redistribution kinetics in mice organs was observed *in vivo* within 1 hour period using the IVIS SpectrumCT In Vivo Imaging System (PerkinElmer, Waltham, MA, USA), Photosens® excitation/emission pair of 675/720 nm and Living Image software v.4.7.3. After 1, 10, 30 and 60 min, animals were sacrificed, and their organs (thyroid, kidneys, spleen, liver, lungs, heart, stomach, intestines, appendix), as well as the organs of mice without any injection (used as a control) were imaged *ex vivo*. It was shown that Photosens-loaded microbubbles accumulate significantly in such mice organs as liver, thyroid, and intestines. Increased SF6-filled microbubbles accumulation was observed in lungs, possibly due to longer circulation time of such bubbles over air-filled counterparts. Obtained results demonstrate that proposed photosensitizer-functionalized microbubbles can be used for bioimaging as well as for effective photodynamic therapy.

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**Keywords:** biodistribution, microbubbles, photosensitizer, bovine serum albumin, Photosens, fluorescence tomography.

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