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Hybrid protein-polymer shelled microbubbles based on albumin and N-vinyl-2-pyrrolidone copolymer as advanced ultrasound contrast agents

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Abstract

Gas-filled microbubbles have demonstrated long clinical record for contrast-enhanced ultrasound imaging due to the echogenicity provided by gaseous core. Lipids, proteins and polymers were involved in microbubble shell stabilization, affecting agent physicochemical properties. Hence, soft protein shell demonstrates significant contrast capabilities, shortened by low colloidal stability, while rigid polymer shell exhibits prolonged stability, reducing contrast capabilities. To combine advances of each material in one microbubble composition, we have developed a hybrid “protein-polymer” microbubble shell by synthesizing a complex of bovine serum albumin and an amphiphilic copolymer of N -vinyl-2-pyrrolidone and acrylic acid. Hybrid “protein-copolymer” shell composition resulted in fine-tuning of agent physicochemical parameters (concentration, average size, shell thickness), acoustic properties (contrast enhancement, stability), and in vitro biocompatibility. Demonstrated results illustrated the potential of a hybrid "protein-polymer" microbubble composition as advanced contrast agents for ultrasound imaging, combining the benefits of each material included in the shell and precise tuning of agent properties.

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