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Acoustic properties of multifunctional nano/microbubbles used in ultrasonography and ultrasound-mediated chemotherapy

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Multifunctional nano/microbubbles were developed that combine properties of drug carriers, ultrasound imaging contrast agents, and enhancers of ultrasound-mediated drug delivery. At room temperature, the formulations comprised perfluoropentane (PFP) nanodroplets stabilized by biodegradable diblock copolymers. The nanodroplets converted into nano/microbubbles upon heating or ultrasound irradiation. The acoustic properties of the droplets and corresponding bubbles depended on the type of the bubble stabilizing copolymer. Two different copolymers were tested, poly(ethylene oxide)-co-poly(L-lactide) (PEG-PLLA) and poly(ethylene oxide)-co-polycaprolactone (PEG-PCL). For the same quantitative composition, the PEG-PLLA-stabilized bubbles demonstrated higher inertial cavitation threshold and coalescence propensity than PEG-PCL-stabilized bubbles. Nanobubble tendency to coalescence is advantageous for using PEG-PLLA bubbles as tumor-targeted contrast agents.On the other hand, a lower cavitation threshold for PEG-PCL-stabilized bubbles is useful for ultrasound-mediated drug delivery. The drug doxorubicin (DOX) was localized in the bubble walls; it was released from the bubbles in response to sonication by therapeutic ultrasound, which resulted in a significant degree of drug tumor-targeting and effective tumor chemotherapy.