A Voltage-Activated Phase-Change Agent

Abstract

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We present a voltage-sensitive phase change agent comprising an aqueous emulsion of surfactant-coated liquid perfluorocarbon droplets nested within a negatively charged phospholipid bilayer. The sensitivity to voltage allows, via exposure to an electric field, vaporization - and resultant acoustic activity - of the perfluorocarbon droplets at an ultrasound intensity that is otherwise insufficient to cause vaporization. The result is a phase change agent for which activation depends not on ultrasound intensity but rather on the presence of an electric field. Accordingly, we offer the first enhanced ultrasound contrast agent (Electrast^{TM}) that takes advantage of the electrical activity of the heart and leads to selective activation at a fixed mechanical index (MI). The voltage-sensitive agent activates selectively in the coronary circulation, giving enhanced ultrasound contrast within the myocardium while leaving other regions largely unenhanced. Specifically, in a closed chest swine study, the contrast enhancement between the myocardium and the left ventricle increased by 36.4 dB +/- 0.2 upon injection of a charged, nested PCA formulation at a fixed MI of 0.9 (GE Vivid *i*). Similar enhancement was observed in rats, and the contrast-to-tissue ratio increased by nearly 10 dB at an MI of 0.28 upon exposure to an electric field of 1 V/cm in a tissue-mimicking phantom. Additionally, ultrasound-induced leakage of calcein, a water-soluble fluorescent dye, from a nested, charged PCA formulation more than doubled at a peak negative pressure of 0.5 MPa upon exposure to an electric field of 0.25 V/cm. These results suggest that the voltage-sensitive phase change agent is a candidate for myocardial perfusion imaging.

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