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Comparative Analysis of Nanoscale Ultrasound Contrast Agents

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ABSTRACT

Current ultrasound contrast agents utilize microbubbles as a blood pooling agent, but the size inhibits access to small capillaries. The development of nanoscale ultrasound contrast agents can enter small capillaries of tissues and aid in the detection of diseased states. However, current nano-formulations are flushed from the body over a short period of time. We developed a nanoscale ultrasound contrast agent with increased circulation time to allow for better detection of diseased states in the microvasculature of the body. Characterization (zeta potential, size, echogenicity and stability) and pharmacokinetic analysis were conducted on three nanoscale formulations: 1) Liquid based Bovine Serum Albumin (BSA)- Perfluoropentane (PFP), 2) Gas based Lipid -L61 Pluronic, and 3) Gas based L61-Pluronic with Polyethylene Glycol (PEG). Characterization was conducted using Dynamic Light Scattering (DLS) and Nanoparticle Tracking Analysis (NTA). Echogenicity testing was performed using ultrasound imaging (Vevo2100) in vitro with a tissue phantom. The concentration, frequency response, and bubble stability were evaluated. The BSA-PFP, L61, and PEG L61 formulations had mean sizes of approximately 300 nm, 250 nm, and 330 nm respectively ($n = 6$). Images taken on the high frequency ultrasound system revealed that the L61 nanobubbles had higher signal intensity. Stability of the different formulations was measured over 2 hours. Nanobubble intensities decreased overtime, except the BSA-PFP bubbles, most likely due to being liquid-derived. Future in vivo studies will be conducted for circulation times in an animal model. Utilization of these formulations could lead to targeting of proteins in the body through modified nanobubble formulations.

KEYWORDS

Nanobubble, Ultrasound, Nanodrop, Contrast, Pharmacokinetics