



"Nanobubble Ultrasound Contrast Agents for Cancer Detection and Targeted Drug Delivery."



Application of contrast agents (or microbubbles) in diagnostic and therapeutic ultrasound has grown rapidly during the past two decades. Worldwide microbubbles are used in a broad range of applications including cancer detection and on demand therapy. Due to their shell-stabilized gas core structure their behavior in the ultrasound field permits superb detection at near picomolar concentrations, while their shell facilitates robust functionalization with various targeting entities. Microbubbles are also susceptible to on-demand disruption with higher power ultrasound, making them ideal for drug delivery applications. However, because the agents range in diameter from 1-10 μm , they are confined to the vasculature. This limits their applications in targeted molecular imaging and drug delivery, especially in the cancer arena. For these applications, particles which are highly echogenic yet sufficiently small in size (with a nanoparticle-sized footprint) would enable detection of targets residing beyond the vasculature and could revolutionize the ultrasound imaging field.

To facilitate ultrasound imaging and drug delivery beyond the vasculature, we have formulated a series of nanoparticle-based ultrasound contrast agents (nanobubbles) which possess many of the same benefits as microbubbles but which are also more stable, offer additional cargo space for drug loading and enable simple functionalization all with a footprint approaching 100 nm. The nanobubbles consist of a perfluoropropane (C_3F_8) gas core stabilized with lipids and the surfactant, Pluronic. Additional stabilization with cross-linked N,N-diethylacrylamide also provides a scaffold for drug loading. The nanobubbles, functionalized with a superbly selective, high affinity ligand or antibody, are able to penetrate into the tumor from the vasculature, making them ideal for molecular imaging applications. We are currently developing targeted nanobubbles for early detection of ovarian cancer and for ultrasound-guided biopsy of prostate cancer. The strategy can also be expanded beyond tumor detection and into image-guided therapeutics, since the nanobubbles can bring drug better into the tumor parenchyma. Here, our main application is treatment of liver metastasis from colorectal cancer. Overall, nanobubble-mediated detection and therapy of cancer have the potential to become an exciting alternative direction in cancer management.

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Invitée par Chantal Pichon

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Salle de conférence du CBM