Ultrasound On-demand Manganese (III) Porphyrin Microbubbles for Enhanced Ultrasound/ MR Bimodal Tumor Imaging

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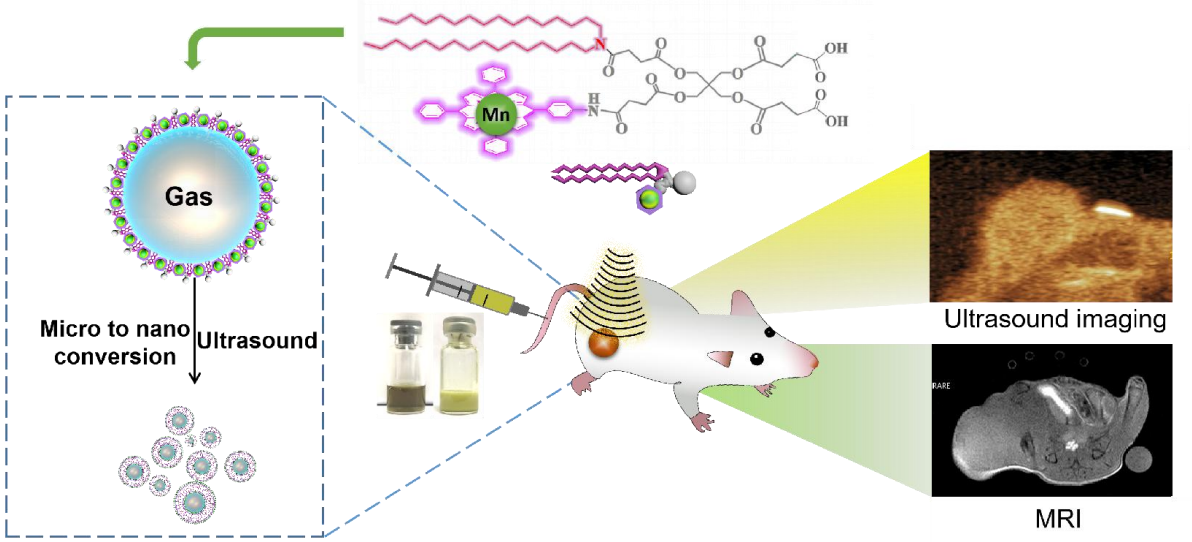
Background, Motivation and Objective

Multimodal imaging integrates different medical imaging modalities to address unmet needs has garnered tremendous interest in recent years. Ultrasound and MR imaging are both noninvasive imaging techniques with their own advantages and limitations. Ultrasound imaging has good temporal resolution while suffers from low sensitivity, meanwhile MRI has good spatial resolution with longer scanning time. Thus a combination of ultrasound imaging and MRI can achieve complementary advantages for a better diagnosis with more information and higher quality images. However, currently there aren't any clinically available US/MRI bimodal contrast agents due to the contradictions on administrated dose differences where US need only a little while MRI require high dose. Therefore, a kind of site-specific delivery strategy for achieving both imaging modality while minimizing unwanted distribution in normal tissues is urgently needed.



Scheme 1. Ultrasound responsive MnP-MBs for MRI and ultrasound biomodal imaging of cancer.

Statement of Contribution/Methods

Manganese (III) porphyrin microbubbles (MnP-MBs) were fabricated by self-assembly from a Mn chelated porphyrin lipid followed by encapsulating inert gas of perfluoropropane. Ultrasound imaging was carried out with a centre frequency of 5.0 MHz (Vinno) and MRI was acquired by the Pharmascan 70/16 US In-vivo MRI system (Bruker, 7.0 T). Exposure ultrasound was conducted at 1.0Mz, 1W/cm^2, 50% duty cycle for 3 min.

Results/Discussion

The as-prepared MnP-MB has diameters around 1.14 um and these microbubbles can be converted into smaller nanoparticles(20-70nm) under ultrasound exposure. The quantified MRI showed that, MnP-MB has a relaxation rate r1 = 1.61 mM^{-1}s^{-1}. Importantly, after intravenous injection, these microbubbles can help to distinguish the tumor precisely by contrast enhanced ultrasound (CEUS). Then low intensity ultrasound can be precisely exposed to the tumor region, where MnP-MBs can undergo micro-to-nano conversion, leading to efficient accumulation of contrast agent in tumor site, achieving remarkable MRI contrast enhancement within 30 minutes at a very low Mn injection dose of 1.65 umol/kg. Therefore, such MnP-MBs based ultrasound enhanced MRI strategy shows great promise for effective US/MRI bi-modal imaging, which will surely appeals to wider interests among biomedical research areas.