Development of Ultrasmall Core-shell Silica Nanoparticles for ^{19}F Magnetic Resonance Imaging

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Magnetic Resonance Imaging (MRI) is one of the most applied imaging technologies benefiting from its deep tissue penetration, high special resolution, and non-radioactivity. ^{19}F MRI is an especially powerful tool for bio-imaging benefiting from its negligible background.

Our laboratory has previously developed a multifunctional ^{19}F MRI contrast agent, fluorine accumulated silica nanoparticle for MRI signal enhancement (FLAME) (Figure 1a)[1]. FLAME is a kind of nanoparticles (NPs) with core-shell structure that combines of liquid core accumulated of perfluoro-15-crown-5-ether (PFCE) and silica shell that has diameter around 100 nm (Figure 1b). FLAME was expected to be applied for diagnosis of tumor via enhanced permeability and retention (EPR) effect. However, the tumor targeting effect of FLAME was not satisfactory because FLAME is also distributed into liver and accumulated after two weeks. The reason of long-term liver accumulation was considered to be related with size of NPs. It has been reported that smaller size of NPs significantly induces tissue permeability[2]. Therefore, this research aims to develop ultrasmall ^{19}F MRI nanoprobe with reduced size distribution.

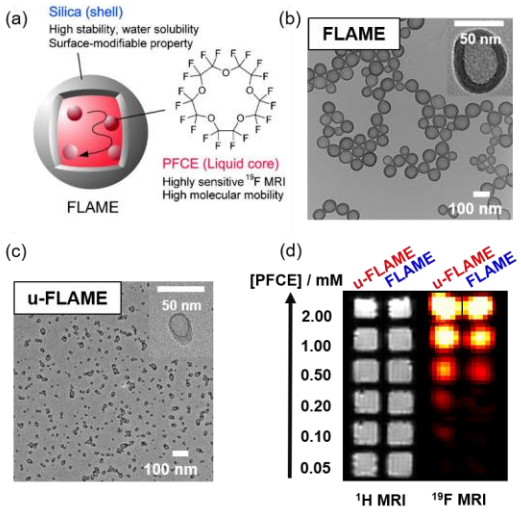

Figure 1. (a) (b) Schematic and TEM image of FLAME; (c) TEM image of u-FLAME; (d) Phantom ^{19}F MRI of u-FLAME and FLAME.

Herein, we introduce the development of ultrasmall FLAME (u-FLAME) NPs. u-FLAME were synthesized via a one-pot method that avoid the increase of nanoemulsion size. u-FLAME obtains similar core-shell structure with FLAME and had a size distribution approximately at 30 nm (Figure 1c). u-FLAME was also proved to have MR sensitivity that is comparable with FLAME (Figure 1d). Finally, *in vivo* experiment was conducted to evaluate the application potential of u-FLAME.

[1] Matsushita, H. *et al*., *Angew. Chem. Int. Ed*., **2014**, *53*, 1008-1011. [2] M. G. Bawendi *et al*., *Angew. Chem. Int. Ed*., **2010**, *49*, 8649-8652.