

Development of Core-shell Silica Nanoparticles for *in vivo* ^{19}F MRI

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Magnetic resonance imaging (MRI) is one of the most well-established clinical imaging techniques, known for its high sensitivity, deep tissue penetration, and non-invasive, radiation-free nature. ^{19}F MRI, in particular, is a powerful tool for *in vivo* imaging, allowing for the tracking of specific cells and enzyme activities in deep tissues, all in a background-free modality.

Our laboratory has developed FLAME (Fluorine-Accumulated Silica Nanoparticle for ^{19}F MRI Enhancement), a novel ^{19}F MRI nanoprobe enabling *in vivo* ^{19}F MRI^{1,2}(Figure 1a, b). FLAME features a core-shell structure, in which liquid perfluorocarbon is encapsulated within a silica shell. This design provides the probe with high ^{19}F MR sensitivity and enhanced surface modifiability. However, despite these advantageous properties, the delivery efficiency of FLAME to cancer tissues remains suboptimal. Instead, FLAME demonstrates long-term accumulation in the liver and spleen following administration in mice. This inefficiency is believed to be influenced by its size, as modified FLAME nanoparticles can reach up to 200 nm. Consequently, developing smaller-sized nanoprobe is deemed necessary to improve delivery efficiency.

Herein, we introduce the development of ultrasmall FLAME (u-FLAME) nanoparticles. u-FLAME was synthesized via a one-pot method that prevents an increase in nano-emulsion size. Surface modification with carboxyl groups was achieved through a co-condensation approach to produce u-FLAME-COOH (Figure 1c). *In vivo* experiments demonstrated the rapid clearance of u-FLAME-COOH from the liver (Figure 1d).

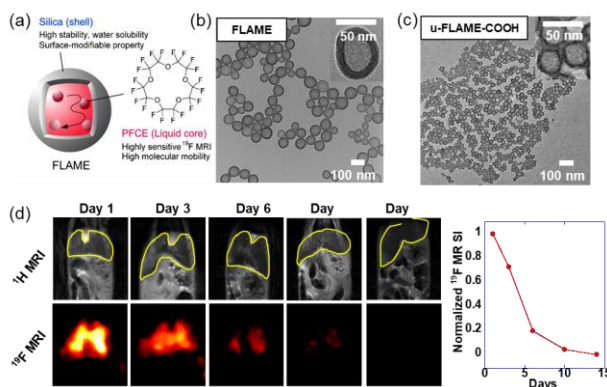


Figure 1. (a) (b) Schematic and TEM image of FLAME; (c) TEM image of u-FLAME-COOH; (d) ^{19}F MRI of u-FLAME-COOH.

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