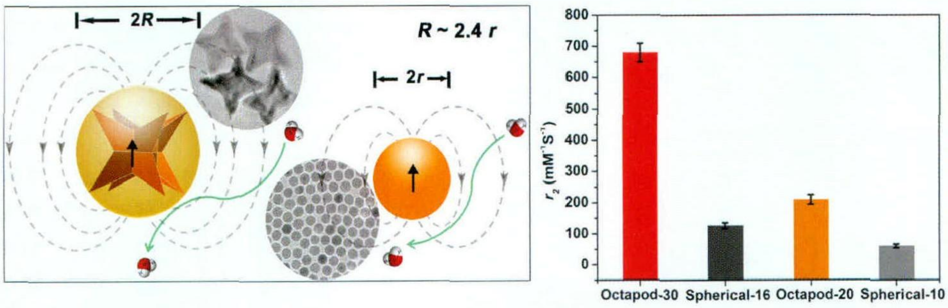
High-performance iron-oxide-based MRI contrast agents

Magnetic nanoparticles are attracting extensive interest for their ability to enhance the magnetic resonance contrast effect. Spherical superparamagnetic iron oxide (SPIO) nanoparticles (e. g., Feridex and Resovist) have been developed as T_2 negative contrast agents for magnetic resonance imaging (MRI) in clinical use due to their biocompatibility and ease of synthesis. However, the relatively low transverse relaxivity (r_2) and poor performance of spherical SPIO nanoparticles as T_2 contrast agents have hampered their clinical applications. It is of urgent need to develop new T_2 contrast agents with high relaxivity for high-performance MRI diagnosis. Based on the quantum mechanical outer sphere theory, the T_2 relaxivity is highly dependent on both the saturated magnetization (M_s) and the effective radius of typically superparamagnetic core. The strategies of making iron oxide nanoparticles with high M_s values based on size-growth control and metal-doping have been widely exploited. Funded by NSFC and MOST, a team of investigators led by Prof. Gao Jinhao at Xiamen University reported a novel strategy to strongly increase T_2 relaxivity by tuning the effective radius of magnetic core through morphology control, which is recently published in *Nature Communications* (**2013**, 4: 2266).

Researchers successfully synthesized octapod-shaped iron oxide nanoparticles by introducing chloride ions in the reaction system under thermal decomposition condition. The octapod SPIO nanoparticles (edge length of 30 nm) exhibit an ultrahigh r_2 value ($\sim$679.3 $mM^{-1}s^{-1}$), which is approximately 5.4 times larger than that of spherical SPIO nanoparticles. With the same geometric solid volume, the octapod nanoparticles have much larger effective radia than the spherical nanoparticles by about 2.4 times under an external magnetic field B_0. Moreover, the octapod morphology results in a significantly more inhomogeneous induced magnetic field than the spherical one. Compared with the conventional SPIO nanoparticles, the octapod iron oxide based nanoparticles and synergistically enhanced T_1-T_2 dual-modal gadolinium-embedded iron oxide nanoparticles (*Advanced Materials*, **2012**, 24: 6223) are much more effective contrast agents for *in vivo* MRI and small tumor detection, which holds great promise for highly sensitive, early stage, and accurate detection of cancer in the clinic.



It turns out that by increasing the effective radius and local field inhomogeneity of the magnetic core, the octapod iron oxide nanoparticles exhibit an incredibly high T_2 contrast enhancement effect. The controlled synthesis of octapod iron oxide nanoparticles is facile, highly reproducible, and amenable to scale up, thereby rendering these novel iron oxide nanoparticles promising T_2 contrast agents for MRI. This new strategy of achieving extremely high T_2 relaxivity of iron oxide nanoparticles by increasing the effective radii of iron oxide cores rather than the M_s values is believed to be critically important in developing highly sensitive second-generation contrast agents for MR imaging, especially for the early and accurate diagnosis of liver cancer in patients. Moreover, the controllable synthesis of novel octapod iron oxide nanoparticles, together with other morphologies, certainly facilitates the applications of magnetic nanoparticles in data storage, hyperthermia treatment, and magnetically guided drug delivery.