^{19}F-CEST: Studying binding kinetics and applying to molecular MR imaging

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Chemical exchange saturation transfer (CEST) is an MRI contrast mechanism that enables the detection of low concentration solutes via the transfer of their magnetization to the bulk (high concentration) nuclei, from which the MRI signal is derived. Using ^{1}H (of ^{1}H2O) as the bulk nucleus, CEST MRI has been used in a wide range of applications. The combination of CEST and heteronuclear NMR opened a new avenue for the design of MRI sensors, since it exploits the benefits of both methodologies, i.e., (i) the amplification effect of the CEST mechanism, and, because of the use of heteronuclear spins; (ii) the large Δω (several hundreds of ppm for non-proton spins); (iii) the high sensitivity of the obtained Δω to the local environment; and (iv) the lack of background signal. Here we show the principles used for the design of novel fluorinated platforms for ^{19}F-CEST MRI and their potentiality to be used for in vivo molecular imaging. We show the rational design of fluorinated-sensor for maximizing both the specificity and the sensitivity for the detection of Zn^{2+}, which is crucial for wide range of biological processes in both health and disease. We also demonstrate the ability to use host-guest supramolecular systems as platforms for ^{19}F-CEST with the potential to be used for monitoring multiple targets using single ^{19}F-agent in a “multicolor” fashion. The combination of fluorinated agents (i.e., chelates, molecular guests, etc.) together with the saturation transfer-based approaches for MR may be extended to study binding kinetics in a wide range of dynamic systems. This combination can provide valuable information that could contribute dramatically to an understanding of the dynamicity of supramolecular systems and may result in an interesting role for host-guest interactions in molecular MRI.