Novel type of 19F MRI contrast agent

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Introduction

Contrast agent (CA) enhanced MRI has wide applications in medical examinations as well as in basic research. Commonly used ^{1}H-CAs in clinical use are based on gadolinium complexes or iron oxide nanoparticles. For answering different medical questions the MRI of other nuclei besides ^{1}H are of interest e.g. ^{19}F. Due to the fact that ^{19}F is absent in normal tissue CAs based on that nucleus lead to a non-ambiguous signal in the ^{19}F-MR image. This work describes the synthesis and the corresponding MR examinations of new types of fluorinated CAs.

Methods

All molecules were prepared in our laboratories and characterized by MRS and mass spectroscopy. MRS were measured at 9.4 T Bruker AMX 400 (^{19}F) and 11.7 T Bruker AMX 500 (^{1}H and ^{13}C).

^{19}F-MRI and additional MRS was preformed using a 7.0 T Bruker Biospec with a homebuilt, double-resonant ^{1}H/^{19}F birdcage-coil using Turbo-Spin-Echo (RARE) as well as Chemical-Shift Imaging (CSI) methods.

Results and Discussion

The skeletal structure of the perfluorinated ligand systems based on NH_2-1B-DTPA [1] Figure 1 shows the synthesized perfluorinated substances F_{17}-1B-DTPA, F_5-1B-DTPA and F_{10}-1B-DTPA. After deprotection of the acid groups F_5-1B-DTPA is water-soluble. In the ^{19}F-MRS the *ortho*-fluorines of the doubly substituted F_{10}-1B-DTPA show a shift to lower field compared to the monosubstituted F_5-1B-DTPA (Figure 3A).

^{19}F-RARE experiments were performed to visualize one isolated resonance line of each fluorinated CA (c.f. Figure 2B) and 3B)). For the RARE experiment with F_{17}-1B-DTPA the resonance line of the CF_3-group (Figure 2A) red) was used. With the perfluorinated aromatic systems the resonance lines of the *ortho*-fluorines were used for RARE experiments. Furthermore, to image all resonance lines at once, ^{19}F-CSI experiments were made to obtain spatially resolved spectral information as well as ultrafast CSI experiments [2] for imaging in short measurement time.

Conclusion and Outlook

We have synthesized three new perfluorinated CAs based on 1B-DTPA and demonstrated their possible application for ^{19}F-MRI. By complexation of the fluorinated ligand systems with Gd^{3+} it could be used as a bimodal CA for ^{1}H- and ^{19}F-MRI.

References

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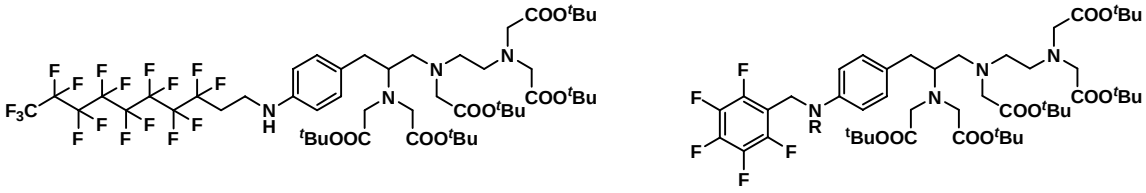

Figure 1: Chemical structures of F_{17}-1B-DTPA, F_5-1B-DTPA and F_{10}-1B-DTPA

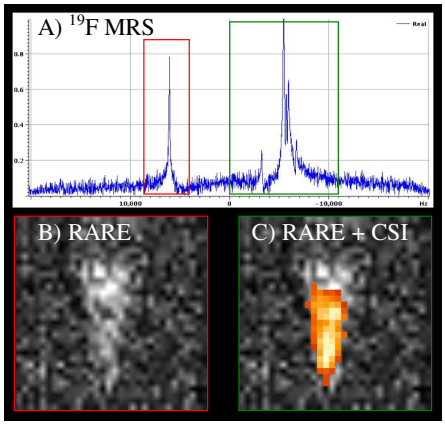

Figure 2: A) ^{19}F-MRS-Image of F_{17}-1B-DTPA.
B) RARE image of the probe
C) Overlay of B and the corresponding CSI image.

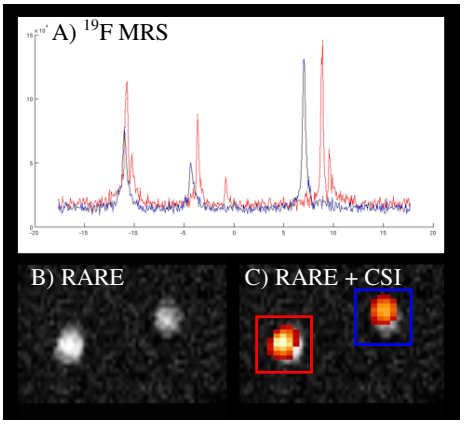

Figure 3: A) ^{19}F MRS-Images of F_5-1B-DTPA (blue) and F_{10}-1B-DTPA (red).
B) RARE image of the probes C) Overlay of B and the corresponding CSI images.