NOVEL STEALTHY Gd(III)-DOTA/POLYMER CONJUGATES FOR MAGNETIC RESONANCE IMAGING (MRI)

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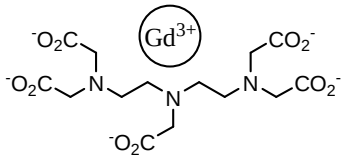
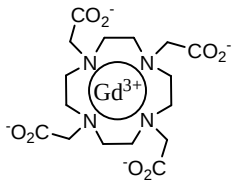
Magnetic resonance imaging (MRI) is a routine diagnostic tool in modern clinical medicine. MRI has many advantages as a diagnostic imaging modality. It is noninvasive, delivers no radiation, and has excellent (submillimeter) spatial resolution. Some Gadolinium(III) complexes are commonly used to enhance the contrast between adjacent tissues when the resolution/sensitivity of MRI is too low. Because free Gd^{3+} is very toxic in doses required for MRI, Gd(III) is chelated by poly(amino-carboxylate) such as diethylenetriamine pentaacetic acid (DTPA; scheme 1) or 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA; scheme 2)).



Scheme 1



Scheme 2

Although DTPA/Gd^{3+} and DOTA/Gd^{3+} are water soluble, they have a very short circulation lifetime in blood, a low molecular weight and a short rotational time that make the contrast poor. To enhance the contrast, the Gd^{3+}/complex doses have to be increased.
In order to increase the sensitivity of the technique, while not increasing the concentration of the contrast agent, we were investigating different strategies to improve (i) the circulation lifetime in blood, (ii) the relaxation rate of Gd(III) (and consequently, the contrasting efficiency) and (iii) the targeting of the contrast agent. This presentation aims at reporting how a multifunctional (co)polymer can be designed and exploited for improving the contrasting ability and bioavailability of gadolinium-based complexes.