In vivo hyperpolarized ^{89}Y studies in a 9.4T animal scanner

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Introduction

Although the gyromagnetic ratio of ^{89}Y is very small, about 20 times smaller than that of protons, the natural abundance of this isotope is 100% and it is a spin-½ nucleus. The *in vitro* longitudinal relaxation times of ^{89}Y in Y^{3+} complexes were recently measured in hyperpolarized solutions and T_1's up to about 500 s were determined [1]. Beyond its exceptionally long T_1 which should provide large time windows for performing *in vivo* measurements, the resonance of ^{89}Y is quite sensitive to its surroundings through its large chemical-shift range, and could hence provide biological and chemical information on the local environment of molecules containing hyperpolarized ^{89}Y. Moreover, the ionic radius and hydration number Y^{3+} are similar to that of Gd^{3+} so yttrium can be substituted for gadolinium in FDA-approved contrast agents such as $Gd(DOTA)^-$. The goal of the present study was to establish the feasibility of enhancing the ^{89}Y polarization in Y^{3+} complexes via DNP using nitroxyl radicals and to detect the *in vivo* ^{89}Y signal in a rat kidney following the infusion of the complexes.

Methods

The yttrium nuclear spins of a glassy frozen 0.4 M $Y(DOTA)^-Na^+$ solution (1:1 D_2O/d_8-glycerol with 50 mM TEMPO polarizing agent) were dynamically polarized for 3 h at 5 T and 1.05 K in a custom-designed polarizer [2,3]. After dissolution, the hyperpolarized solution was blown with He gas into a home-built injection pump through a 6 m long PTFE tube. The pump was placed close to the animal in the scanner 9.4 T magnet. A dual $^1H/^{89}Y$ probe with a 10 mm diameter ^{89}Y surface coil was placed on the rat right flank, on top of its kidney. The injection of 2.2 ml of 25 mM $Y(DOTA)^-$ solution into the femoral vein of a Sprague Dawley rat was started exactly 3 s after dissolution. The infusion lasted for 9 s and the acquisition was launched 1 s after the end of the infusion.

Results and Discussion

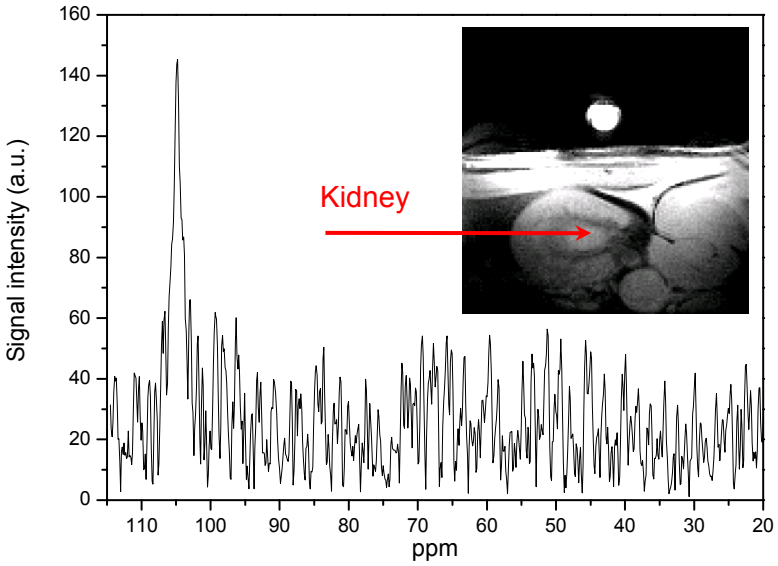

Figure 1. *In vivo* ^{89}Y spectrum measured with a 10^0 adiabatic pulse 1s after the end of the injection of 2.2ml of DNP-enhanced 25mM $Y(DOTA)^-$ solution. The proton image presented in the inset shows the sensitive area of the surface coils used for these measurements.

Consecutive ^{89}Y spectra were acquired at 10 s intervals using adiabatic 10 degree BIR-4 pulses. The first spectrum is shown in Fig.1 along with a proton image showing the location of the surface coil (the white sphere on top of the animal is located in the center of the ^{89}Y coil and contains a 4M solution of YCl_3 in H_2O). A strong signal at the frequency of the $^{89}Y(DOTA)^-$ was detected and the analysis of the ^{89}Y signal time evolution led to the determination of a characteristic *in vivo* decay time of 50±10 s. An *ex vivo* experiment was also performed and, by using the ^{89}Y signal from the sphere as reference, the ^{89}Y enhancement at the end of the infusion was determined to be at least 3250 times thermal.

Conclusions

These results show for the first time the feasibility of *in vivo* detection of hyperpolarized ^{89}Y in biocompatible yttrium complexes. A highly enhanced ^{89}Y polarization can be obtained in $Y(DOTA)^-$ by dissolution DNP using TEMPO as the polarizing agent. The *in vivo* characteristic decay time of the ^{89}Y signal is long and should allow for the study of the complexes' biodistribution. The *in vivo* relaxation mechanisms are not yet clearly understood and the observed *in vivo* decay time was substantially shorter than the one measured *ex vivo* [1]. The effect of the residual TEMPO radical concentration (3mM) in the bolus was likely a strong source of relaxation. Nevertheless, this study demonstrates the potential for MR molecular imaging thanks to the large ^{89}Y signal coupled with its long relaxation time and large chemical shift dispersion.

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