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Supplementary Information

MRI Contrast Agent Based on Zwitterionic Metal-chelating Polymer for Hepatorenal Angiography and Tumor Imaging

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Figures

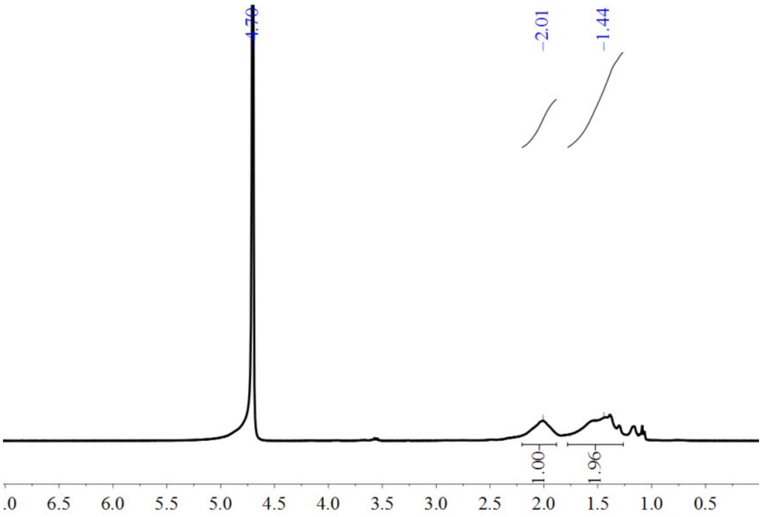

Fig. S1 ^{1}H NMR spectrum of PAA with the numbers of hydrogen atoms determined by integration of the peak areas.

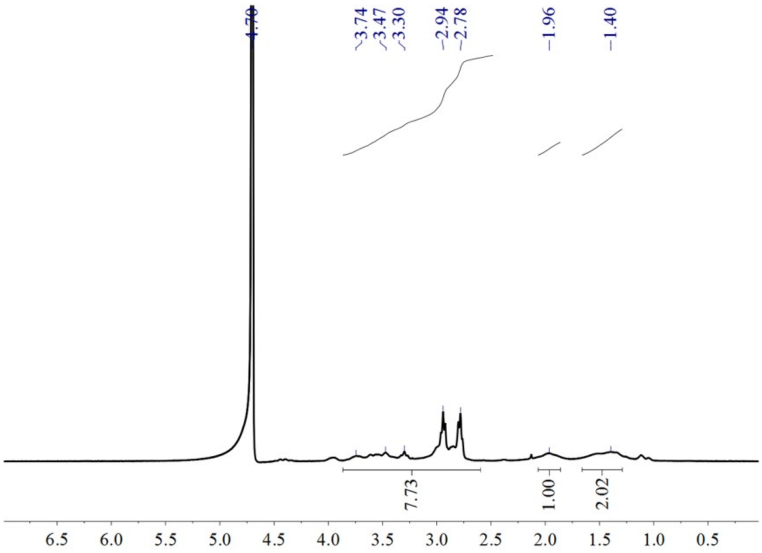

Fig. S2 ^{1}H NMR spectrum of PAA-DET with the numbers of hydrogen atoms determined by integration of the peak areas.

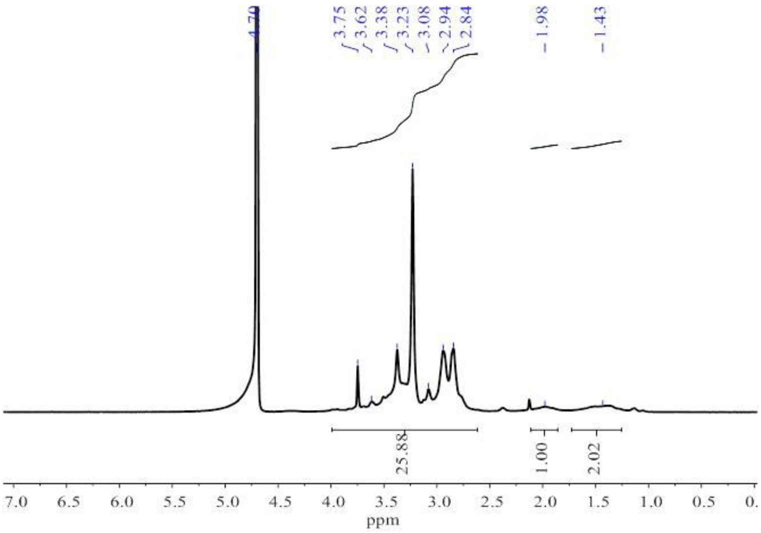

Fig. S3 ^{1}H NMR spectrum of PAA-DTPA with the numbers of hydrogen atoms determined by integration of the peak areas.

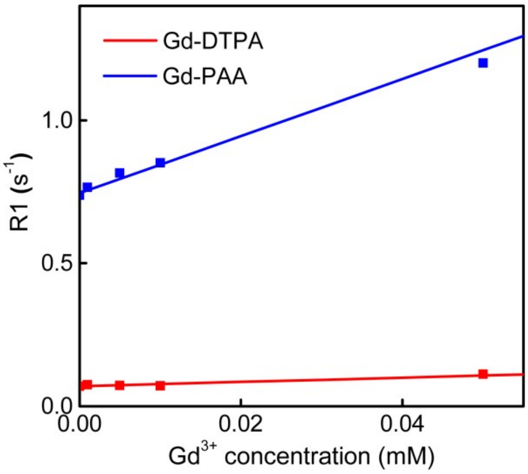

Fig. S4 The experimental data in the range of 0-0.05 mM (solid square points) and the corresponding theoretical fittings (solid lines) of the relaxation rate R1.

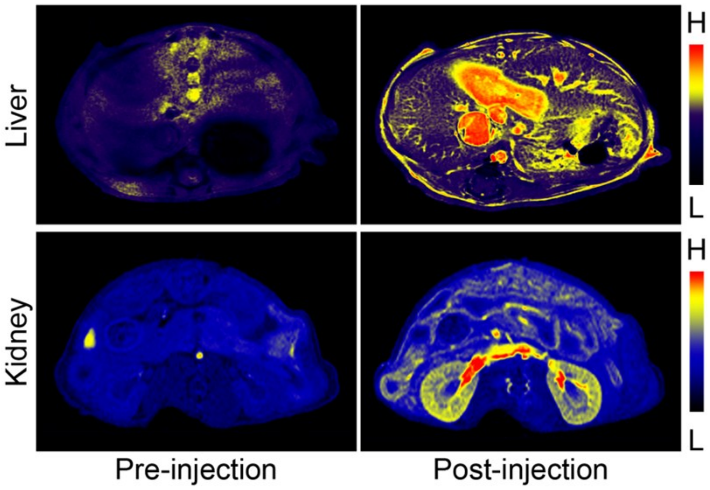

Fig. S5 MR imaging for hepatic vessels with pseudocolor received pre and postinjection of Gd-PAA.

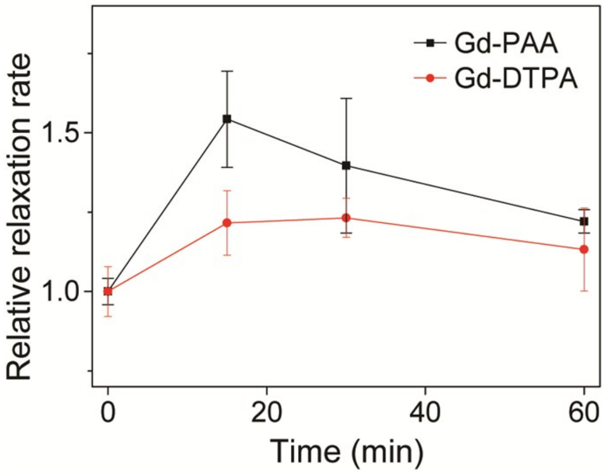

Fig. S6 Temporal evolution of relative relaxation rate R1 of tumor region before and after administration.

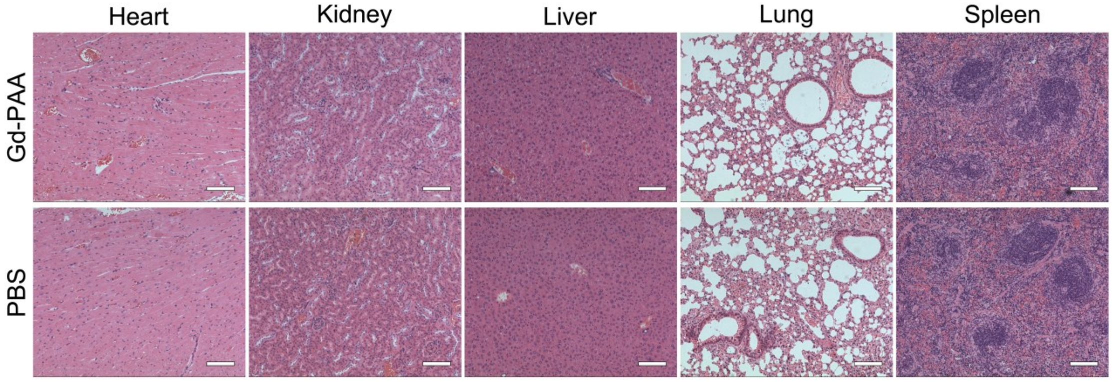

Fig. S7 H&E stained tissue slices of major organs extracted from mice 40 days after receiving Gd-PAA and 1 × PBS buffer solution, respectively. The scale bars embedded correspond to 50 μm.

Relaxivity Calculations

The enhancement of Gd-PAA on r_1 compared with Gd-DTPA is mainly attibute to inner-sphere contribution, which can be expressed as equation 1.

$$r^{IS} = \frac{q/[H_2O]}{T_{1M} + \tau_m} \qquad (1)$$

Where q is the number of water molecules directly coordinated with Gd^{3+}, which can be considered the same for per Gd in Gd-PAA and Gd-DTPA. T_{1M} and τ_m is the T1 relaxation time and residency time of coordinated water molecules in inner sphere. For water in the inner-coordination sphere where the residency time of them is long enough to be correlated with the metal complex, $T_{1m} \gg \tau_m$, thus r^{IS} can be approximately simplified to equation 2, which depends inversely on T_{1m}. T_{1m} is given by equation 3.

$$r^{IS} = \frac{q/[H_2O]}{T_{1M}} \qquad (2)$$

$$\frac{1}{T_{1M}} = \frac{2}{154\pi} \frac{\mu_0 \gamma_H^2 g_e^2 \mu_B^2 S(S+1)}{r_{MH}^6} \left(\frac{3\tau_C}{1 + \omega_H^2 \tau_C^2} \right) \qquad (3)$$

Accordingly, T_{1m} is governed by a number of parameters: the gyromagnetic ratio of the proton (γ_H), the electronic g-factor (g), the Bohr magneton (μ_0), the spin quantum number (S) of the corresponding metal ion, the proton Larmor frequency (ω_H), as well as the metal (Gd^{3+} in currently work)-proton distance (r_{MH}) and the correlation time (τ_C), the time constant for the fluctuating magnetic dipole. As indicated by the equation 3, τ_C becomes the deciding factor of the r_1 value, which is a fastest process that characterizes the magnetic dipole fluctuation, as shown in equation 4.

$$\frac{1}{\tau_C} = \frac{1}{\tau_R} + \frac{1}{T_{1e}} + \frac{1}{\tau_m} \qquad (4)$$

Where τ_R is the rotational correlation time of the contrast agent, T_{1e} characterizes the electronic T_1 relaxation process. Notably, the residency time of the water in the inner-sphere (τm) is usually long compared to the τ_R. For Gd^{3+}, the electronic T_{1e} increases with the square of the applied magnetic field and is much longer than τ_R at 3 tesla fields. Therefore for Gd-DTPA and Gd-PAA contrast agents, the τ_C that describes relaxation for inner-sphere water can be approximated as the τ_R, which can be expressed as equation 5

$$\tau_R = \frac{4\pi\eta a^3}{3k_B T} \quad (5)$$

Where η is the dynamic viscosity, k_B and T are the Boltzmann constant and temperature, and a represents the hydrodynamic radius of the contrast agent. Obviously, a for Gd-PAA molecule is much larger than the single Gd-DTPA molecule, which indicates that Gd-PAA has a longer rotational correlation time τ_R. Therefore, Gd-PAA presents a much higher r_1 than Gd-DTPA.

These above theoretical results explain the reason why the molar longitudinal relaxation rate r1 of Gd-PAA is much higher than that of Gd-DTPA.