Methods

CT experiments

The imaging protocol was performed on a micro-CT scanner (Hitachi-Aloka, Tokyo, Japan). The phantoms of iodixanol and iobitridol with the same iodine concentration (1.25–40 mM) were scanned for the measurement of their concentrations in the kidneys. The rats (n=8) were anesthetized by 3% pentobarbital sodium through intraperitoneal injection at a dose of 30 mg/kg body weight. After all the animals were in a fully anesthetized state, iodixanol was firstly injected via a catheter into the tail vein, with the injection procedure the same as that for the in vivo MRI experiment. The body temperature was maintained by a hot water bag and supervised by anal temperature detection. Dynamic CT images were acquired during the period of post-injection to 24 minutes, with the following parameters: 1,024 projections, 50 kV, 150 mA, 10 seconds exposure time, FOV =81.5 mm. The total scanning time was approximately 4 minutes. Reconstructed CT images were analyzed using MATLAB, and the CT values (Hounsfield units; HU) were measured in a manually defined kidney ROI. A calibration curve (CT value versus iodine concentration) was derived at 50 kV using phantoms filled with 7 different iodine concentrations ranging from 0.625 to 40 mM. After subtraction from the pre-injection image, ΔHU were calculated to determine the quantitative iodine concentrations. Afterwards, iodixanol was filtrated almost entirely from the kidney at an interval of 2 hours, iobitridol was then injected and the above experiment repeated. Finally, the obtained ratio of iodine concentration was converted into the ratio of exchangeable protons at 4.3 and 5.5 ppm.

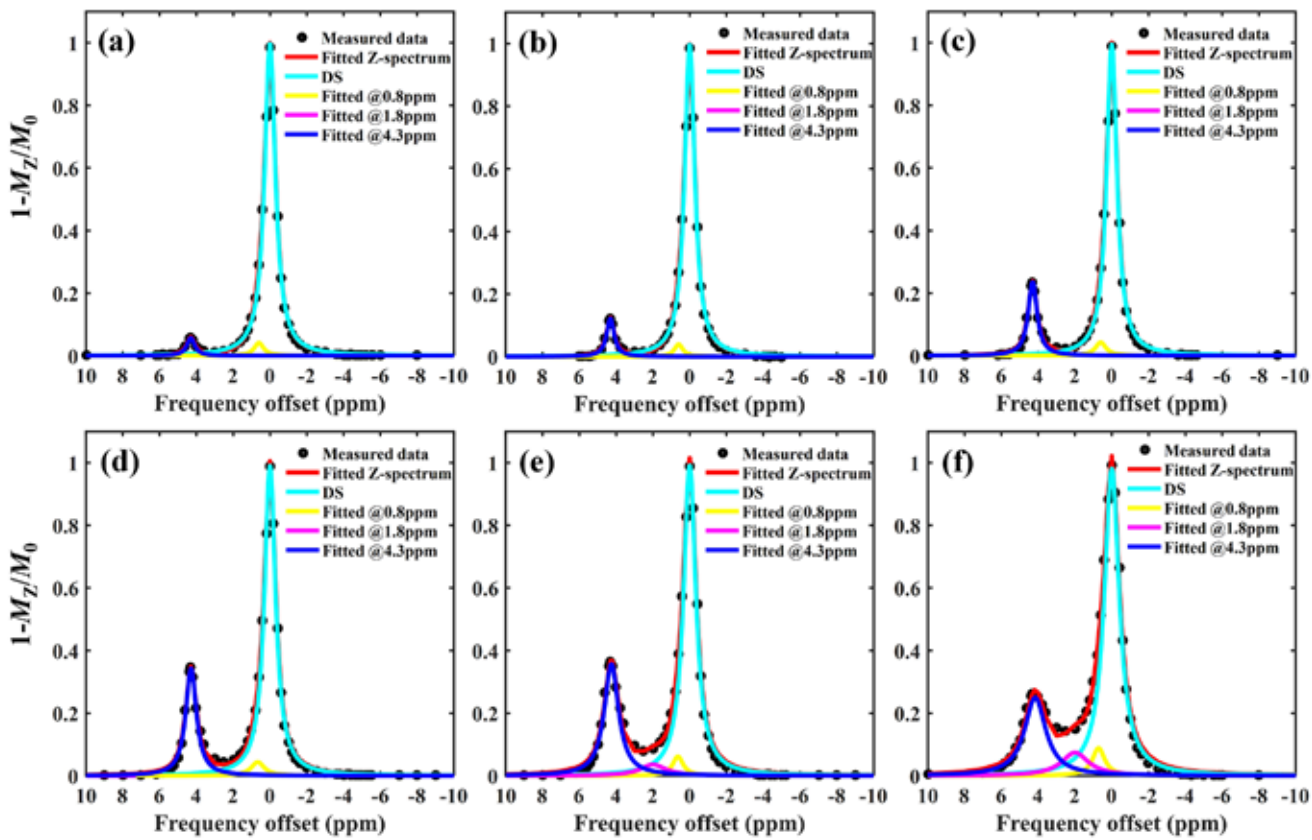

Figure S1 *In vitro* Z-spectra of iodixanol phantom and their fitting results using a four-pool Lorentzian model under the experimental conditions of saturation power =1.5 μT, saturation time =5 s, temperature =37 ℃, agent concentration =30 mM, and different pH values: (A) pH=5.6, (B) pH=6.0, (C) pH=6.4, (D) pH=6.8, (E) pH=7.2, and (F) pH=7.6. DS, direct water saturation.

https://dx.doi.org/10.21037/qims-21-1229

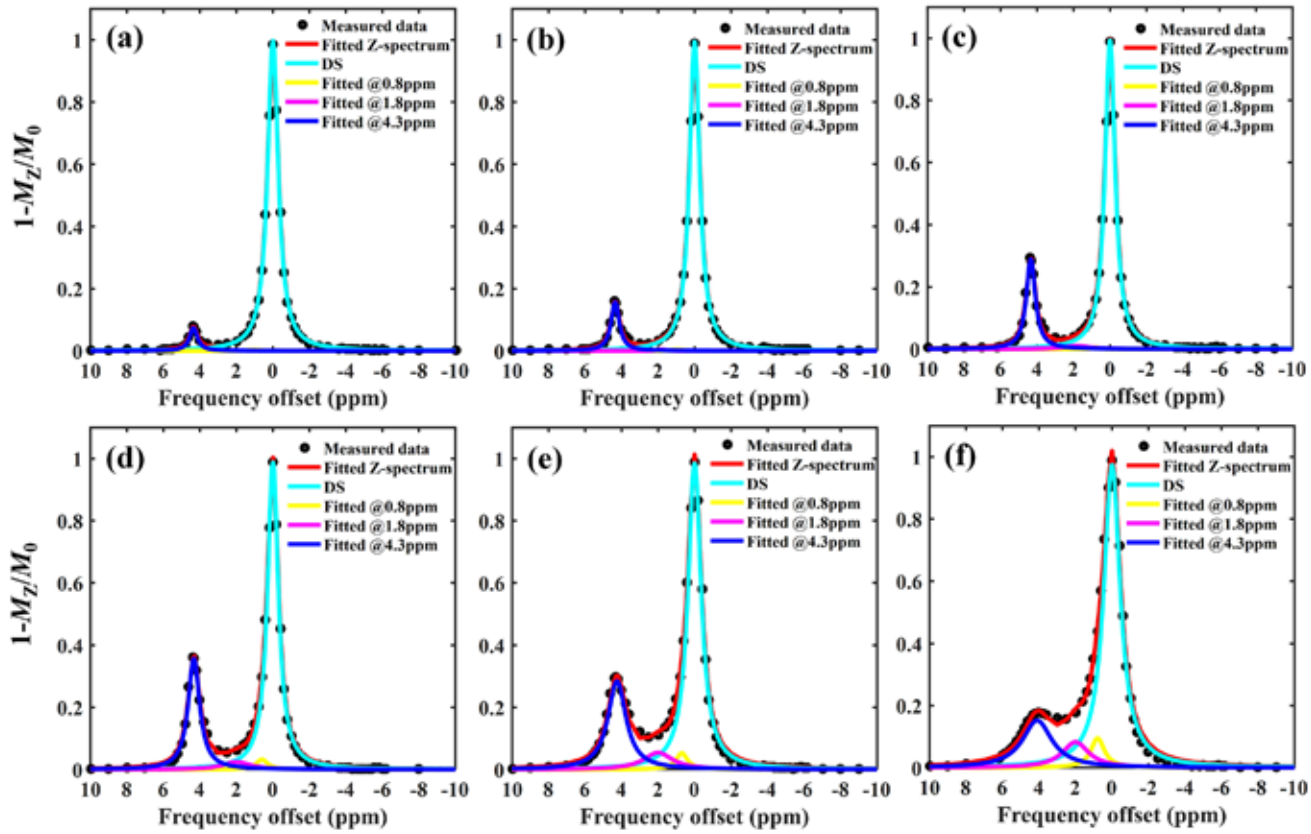

Figure S2 *In vitro* Z-spectra of iohexol phantom and their fitting results using a four-pool Lorentzian model under the experimental conditions of saturation power =1.5 μT, saturation time =5 s, temperature =37 ℃, agent concentration =60 mM, and different pH values: (A) pH=5.6, (B) pH=6.0, (C) pH=6.4, (D) pH=6.8, (E) pH=7.2, (F) pH=7.6. DS, direct water saturation.

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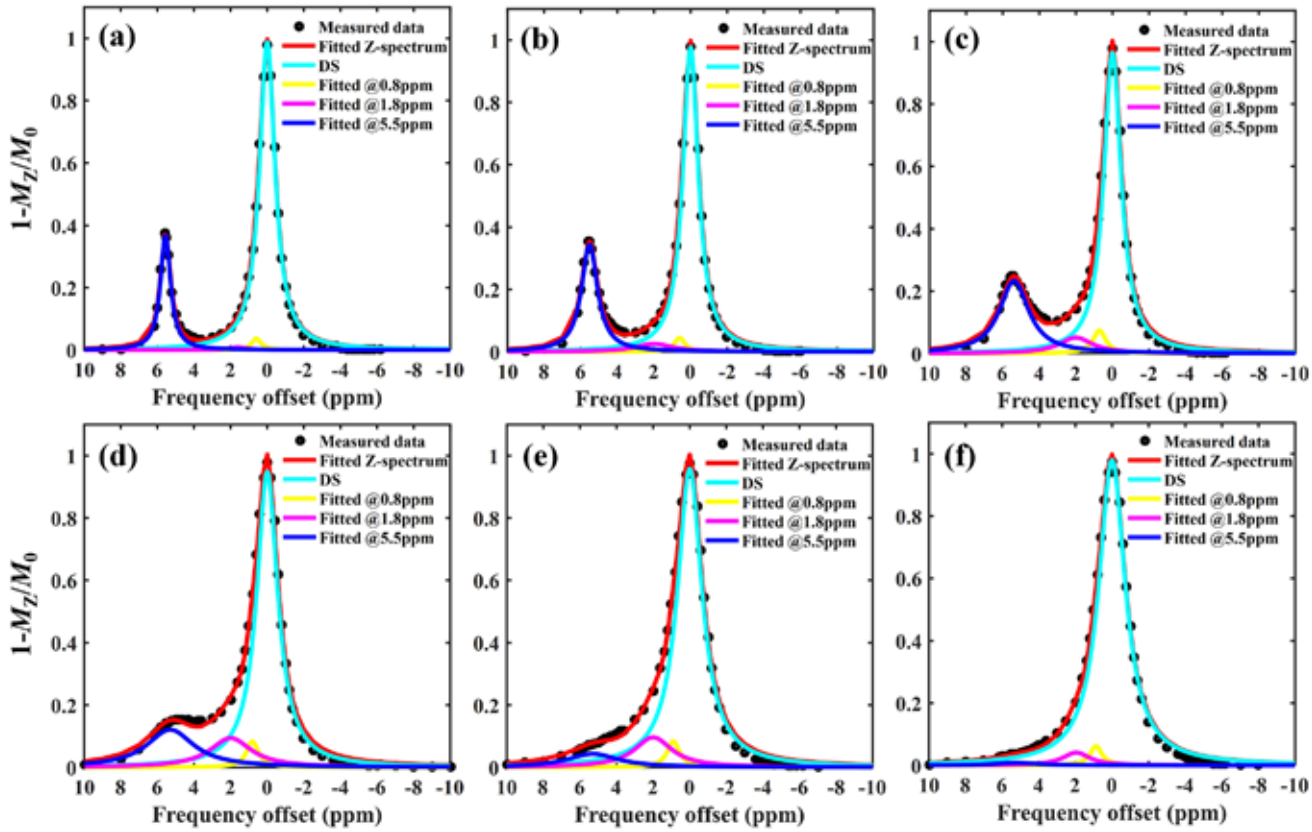

Figure S3 *In vitro* Z-spectra of iobitridol phantom and their fitting results using a four-pool Lorentzian model under the experimental conditions of saturation power =1.5 μT, saturation time =5 s, temperature =7 ℃, agent concentration =120 mM, and different pH values: (A) pH=5.6, (B) pH=6.0, (C) pH=6.4, (D) pH=6.8, (E) pH=7.2, (F) pH=7.6. DS, direct water saturation.

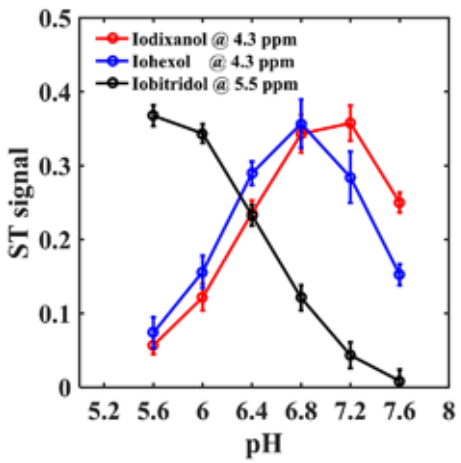

Figure S4 Quantified ST signals from amide protons of iodixanol and iohexol located at 4.3 ppm and iobotridol at 5.5 ppm, respectively. ST, saturation transfer.

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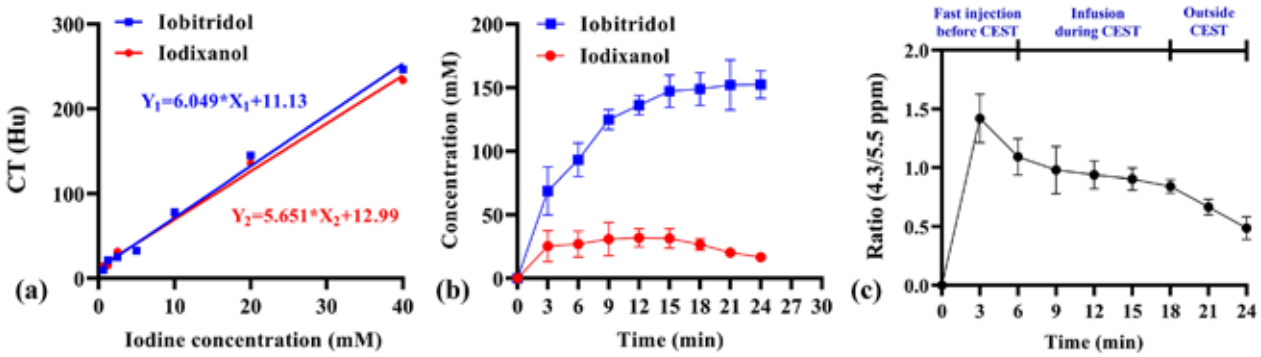

Figure S5 The ratio variation of two nonequivalent amide protons at 4.3 ppm and 5.5 ppm in a rat kidney during the period of the CT experiment. (A) The calibration curve of CT value versus iodine concentration in phantoms; (B) the dynamic changes of iodixanol and iobitridol concentrations in rat kidney after successful injection of two agents; (C) the calculated ratio between two nonequivalent amide protons. CT, computed tomography; CEST, chemical exchange saturation transfer.

https://dx.doi.org/10.21037/qims-21-1229