SUPPORTING INFORMATION

Gd^{3+}:DOTA-modified 2-Hydroxypropyl-β-Cyclodextrin/4-Sulfobutyl Ether-β-Cyclodextrin-based Polyrotaxanes as Long Circulating High Relaxivity MRI Contrast Agents

Yawo A Mondjinou[1], Bradley P Loren[1], Christopher J. Collins[1], Seok Hee Hyun[1], Asher Demoret[1], Joseph Skulsky[1], Cheyenne Chaplain[1], Vivek Badwaik[3], and David Thompson[1,2,3]*

[1]Department of Chemistry, [2]Weldon School of Biomedical Engineering, and [3]Center for Cancer Research, Multi-disciplinary Cancer Research Facility, Bindley Bioscience Center, Purdue University, 1203 W. State Street, West Lafayette, IN 47907

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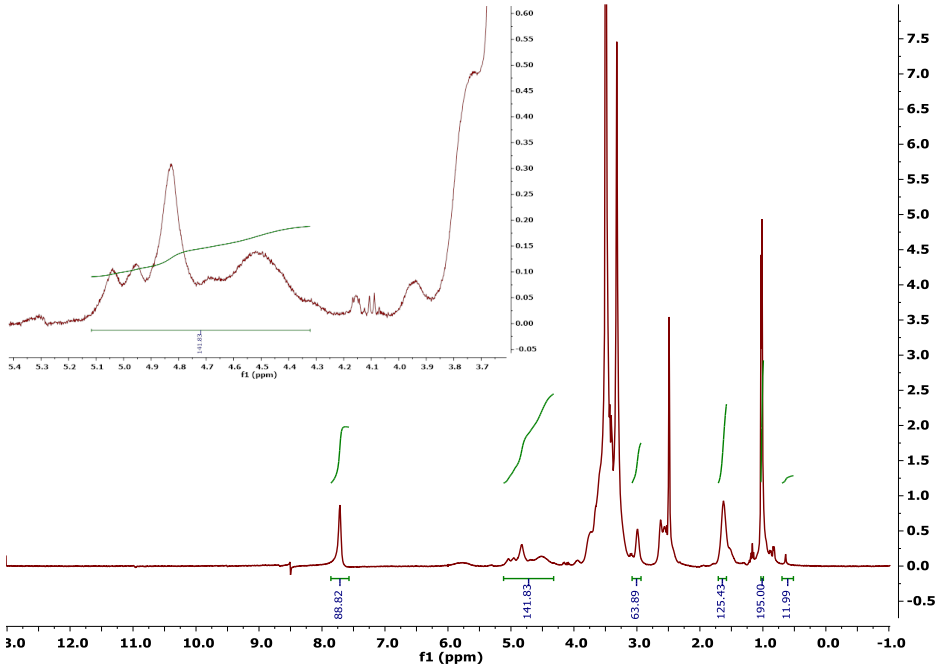


Figure S1. 400 MHz ^{1}H NMR of HPβCD/SBEβCD F127 in DMSO-D_6, 25 °C.

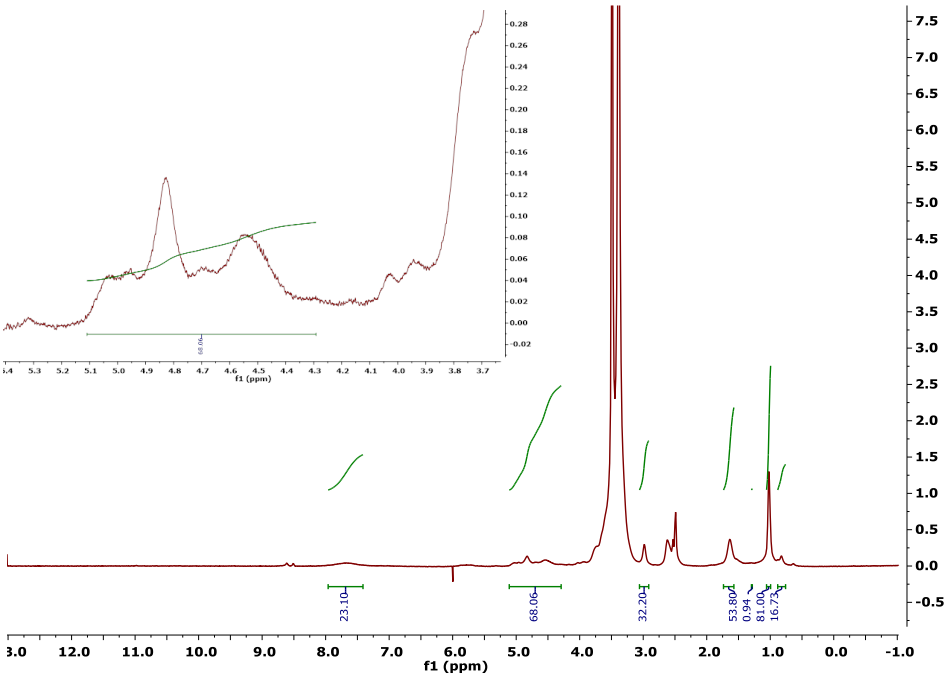


Figure S2. 400 MHz ^{1}H NMR of HPβCD/SBEβCD F68 in DMSO-D_6, 25 °C.

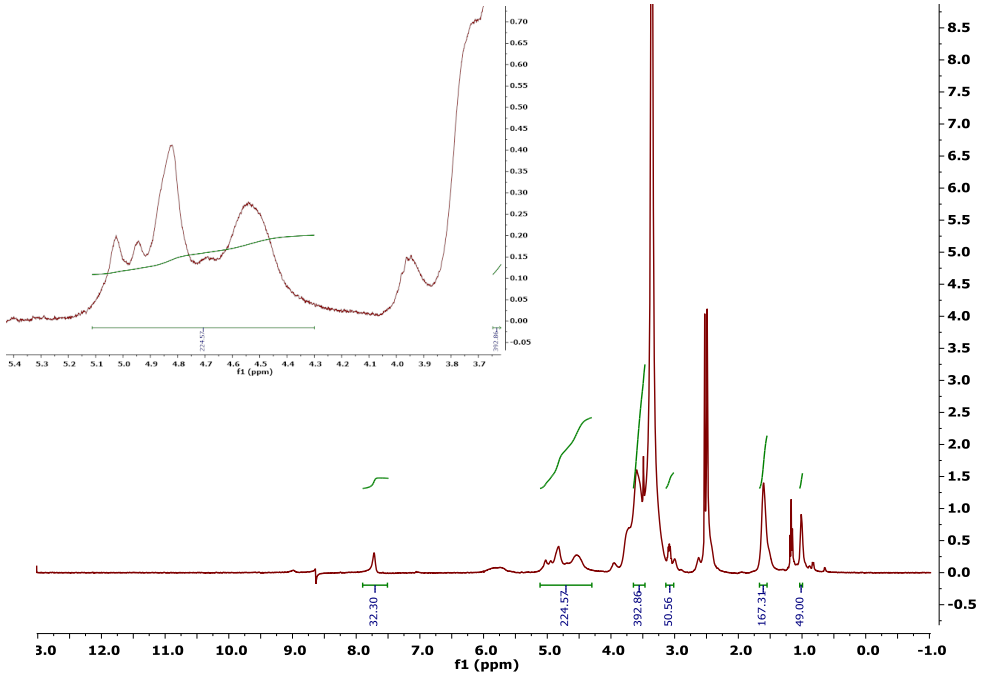


Figure S3. 400 MHz ^{1}H NMR of HPβCD/SBEβCD L35 in DMSO-D_6, 25 °C.

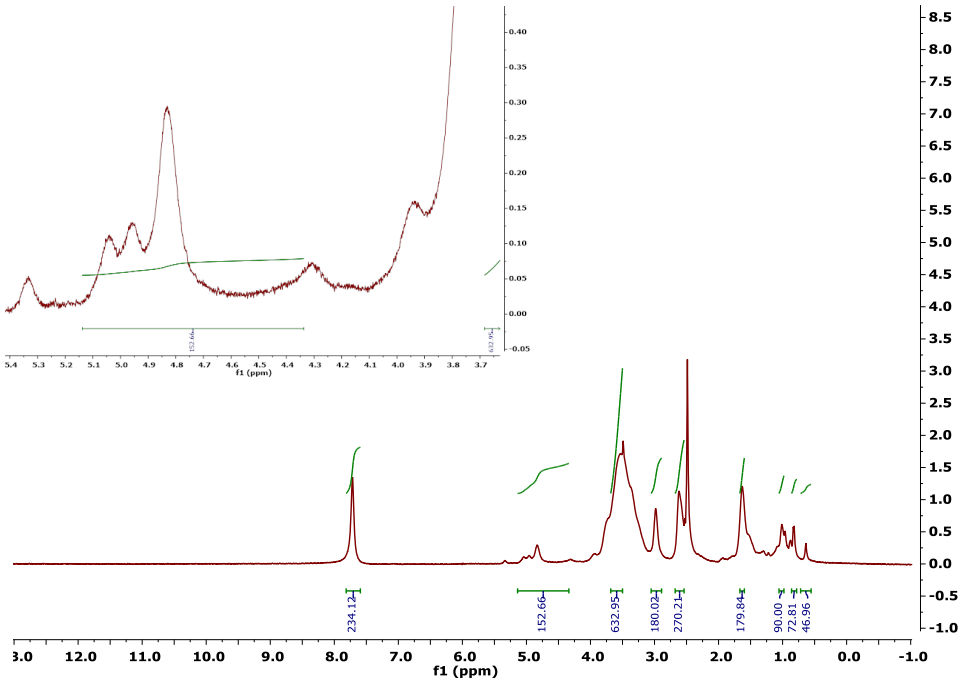


Figure S4. 400 MHz ^{1}H NMR of HPβCD/SBEβCD L64 in DMSO-D_6, 25 °C.

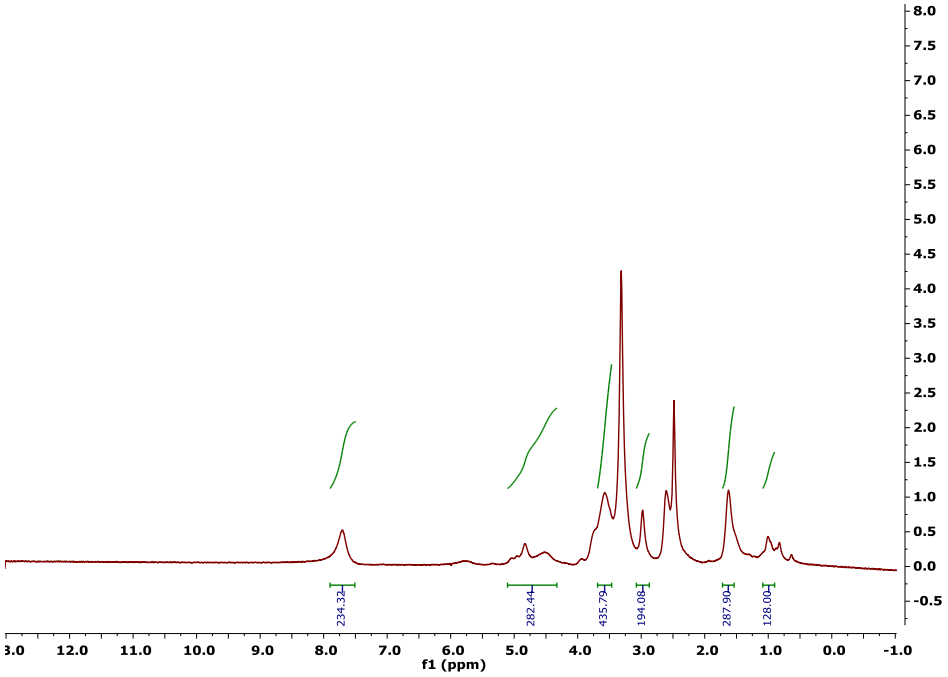


Figure S5. 400 MHz ^{1}H NMR of HPβCD/SBEβCD L81 in DMSO-D_6, 25 °C.

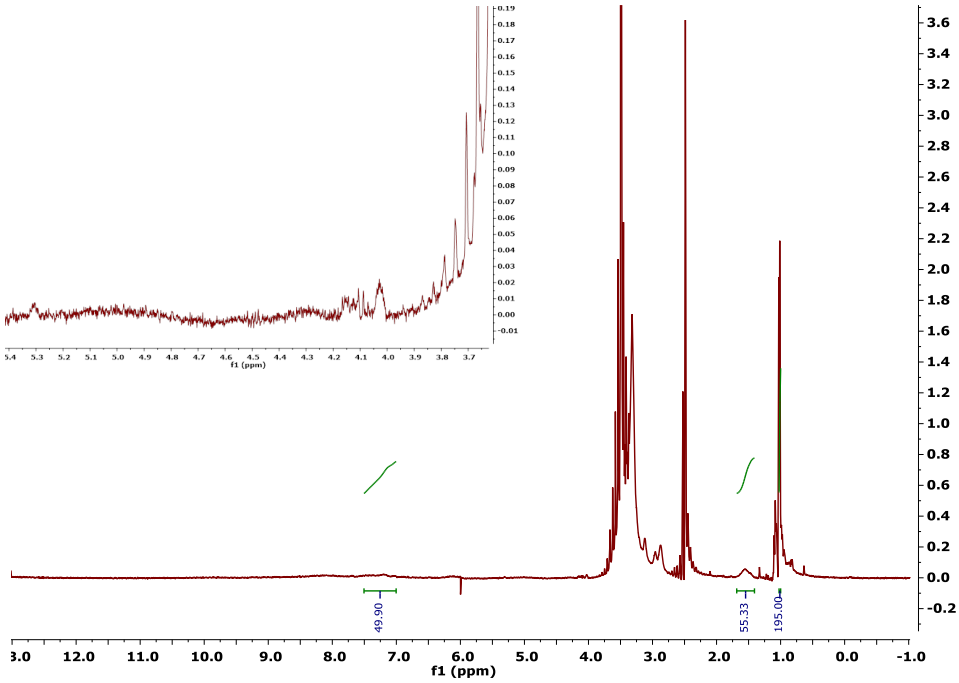


Figure S6. 400 MHz ^{1}H NMR of DOTA-HPβCD/SBEβCD F127 in DMSO-D_6, 25 °C.

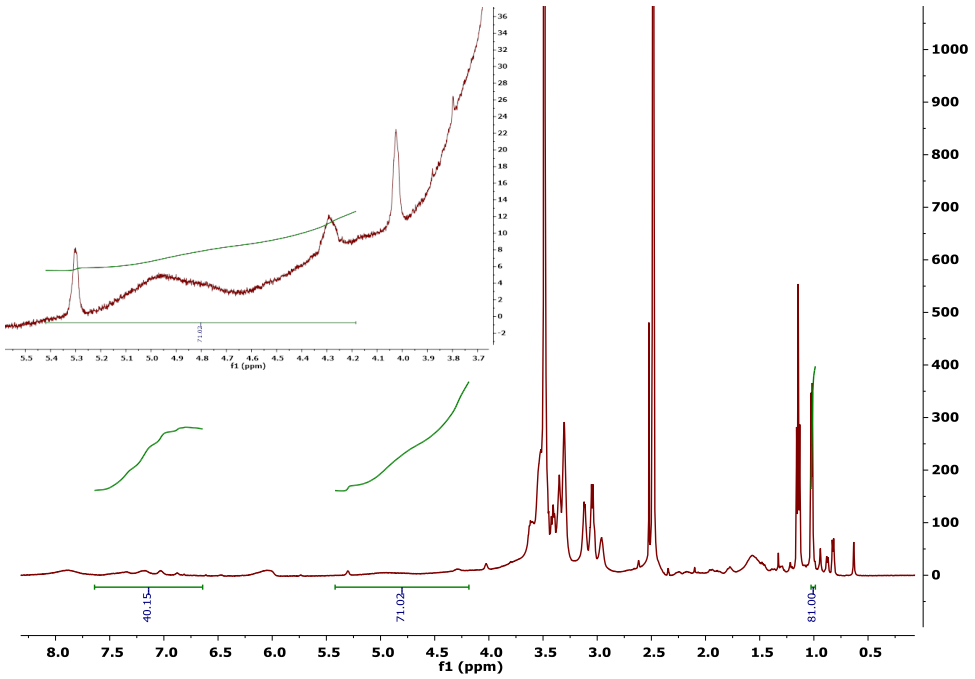


Figure S7. 500 MHz ^{1}H NMR of DOTA-HPβCD/SBEβCD F68 in DMSO-D_6, 25 °C.

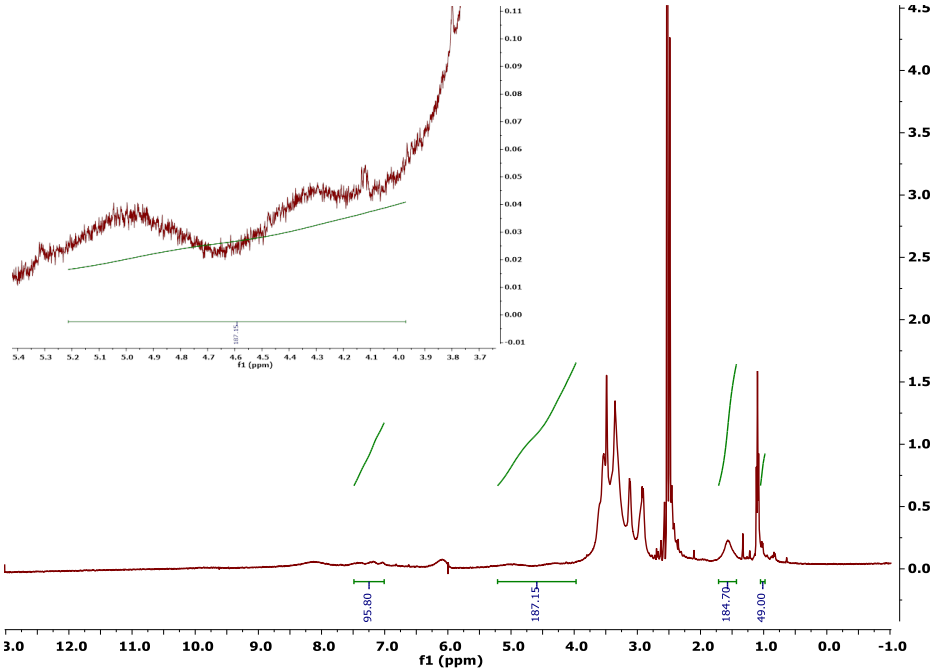


Figure S8. 400 MHz ^{1}H NMR of DOTA-HPβCD/SBEβCD L35 in DMSO-D_6, 25 °C.

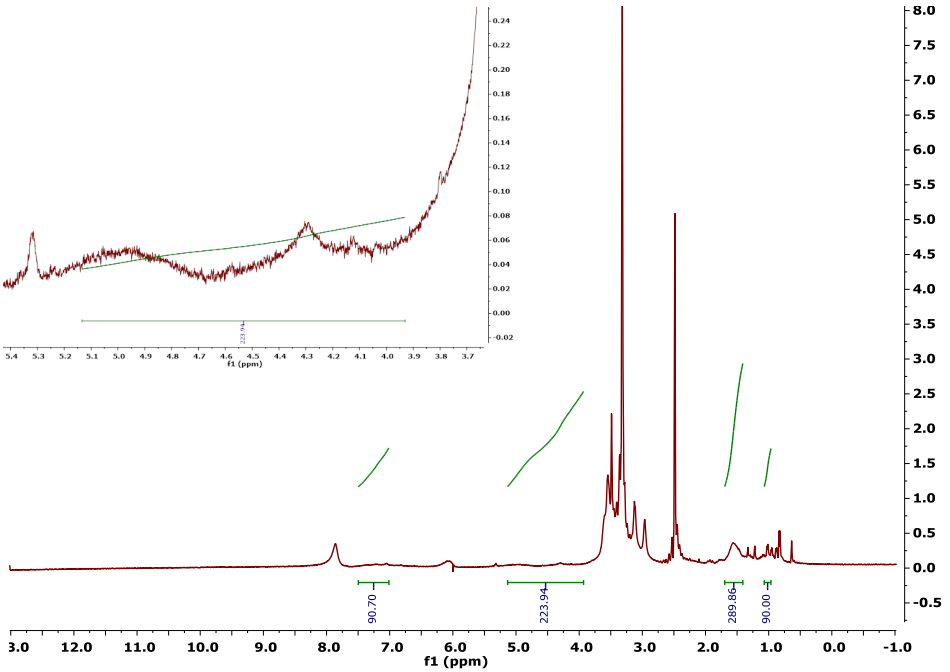


Figure S9. 400 MHz ^{1}H NMR of DOTA-HPβCD/SBEβCD L64 in DMSO-D_6, 25 °C.

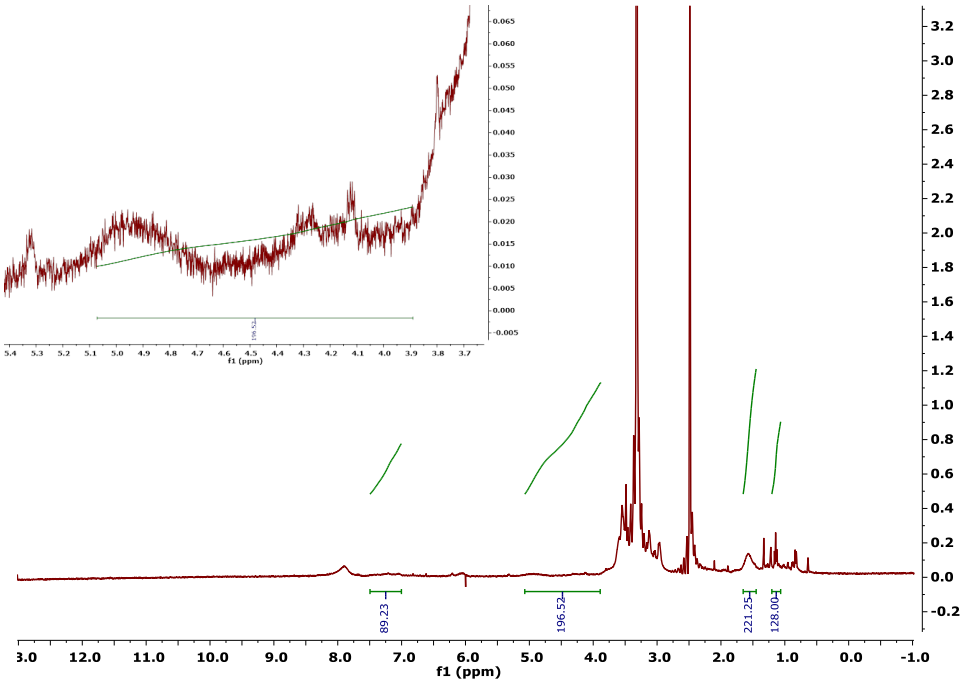


Figure S10. 400 MHz ^{1}H NMR of DOTA-HPβCD/SBEβCD L81 in DMSO-D_6, 25 °C.

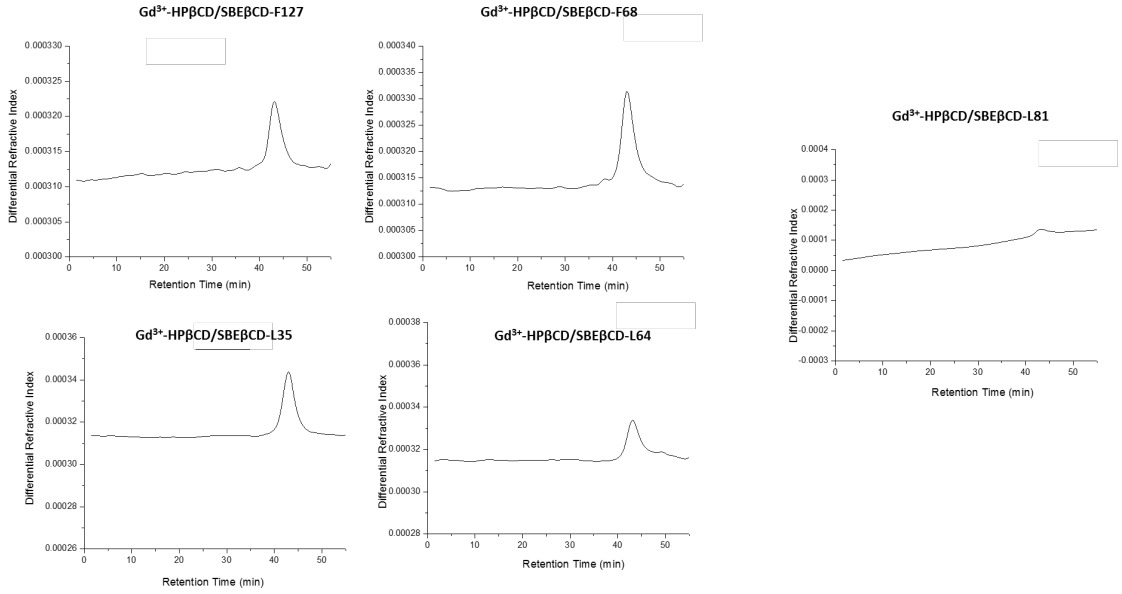
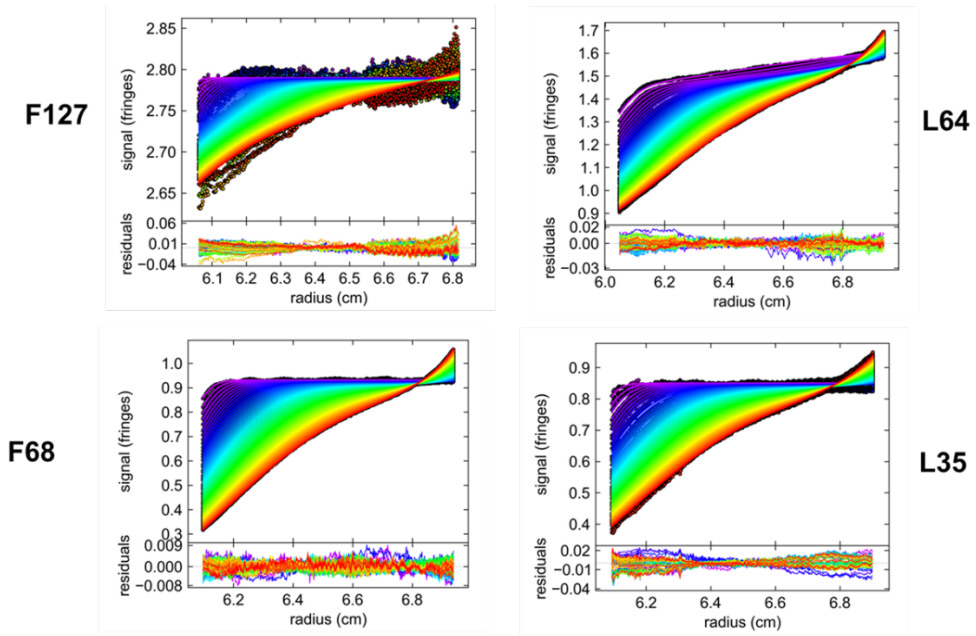


Figure S11. GPC-MALS/RI Chromatograms of Gd:DOTA-HPβCD/SBEβCD Pluronic-based Polyrotaxanes.



Sample	Calculated MW (kDa)
F127	33.3
L35	1.6, 29.1
L64	3.3, 15.7
F68	2.3, 11.8

Figure S12. Analytical Ultracentrifugation Analysis (AUC) Profiles of Gd:DOTA-HPβCD/SBEβCD Pluronic-based Polyrotaxanes.

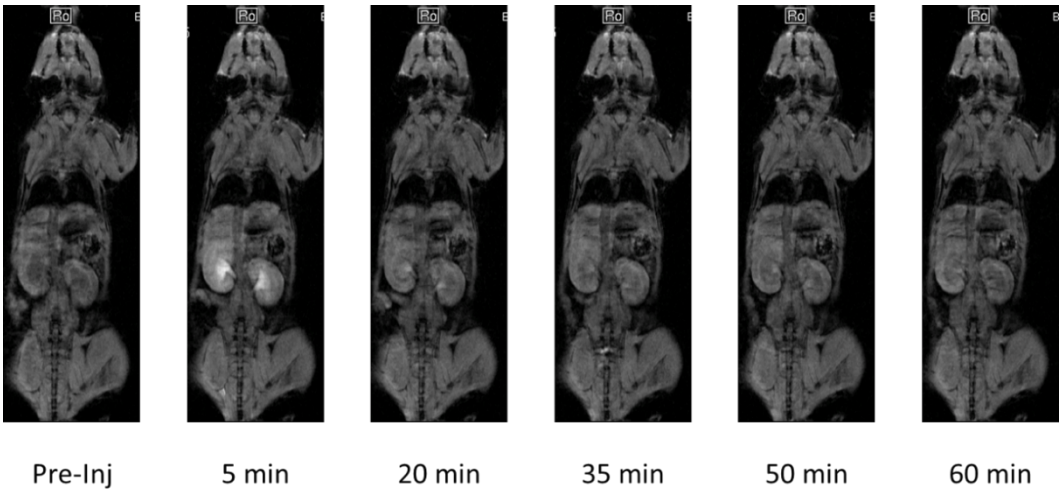


Figure S13. T_1-weighted MR images of DOTAREM® collected at 7T from Balb/c mice at 9 weeks of age.

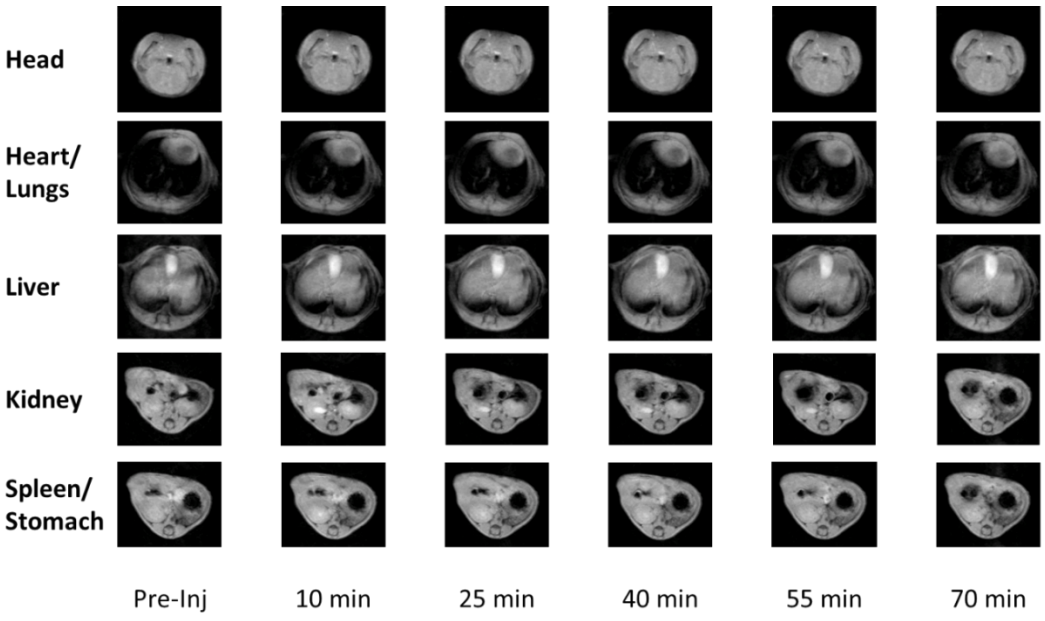


Figure S14. T_1-weighted cross-section MR images of DOTAREM® collected at 7T from Balb/c mice at 9 weeks of age. Slices were placed in diverse organs.

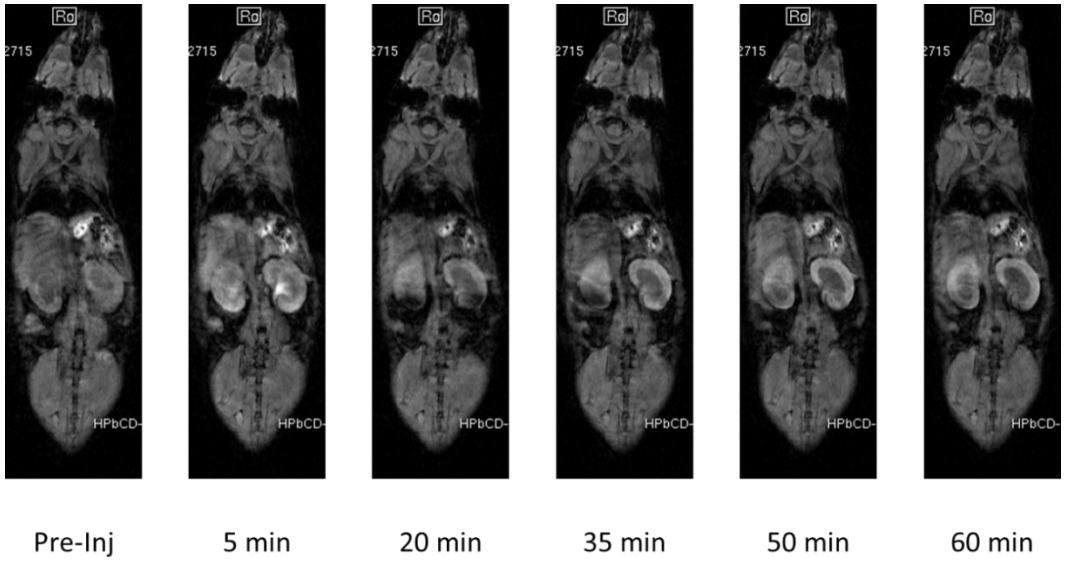


Figure S15. T_1-weighted MR images of Gd:DOTA-HPβCD/SBEβCD F127 collected at 7T from Balb/c mice at 9 weeks of age.

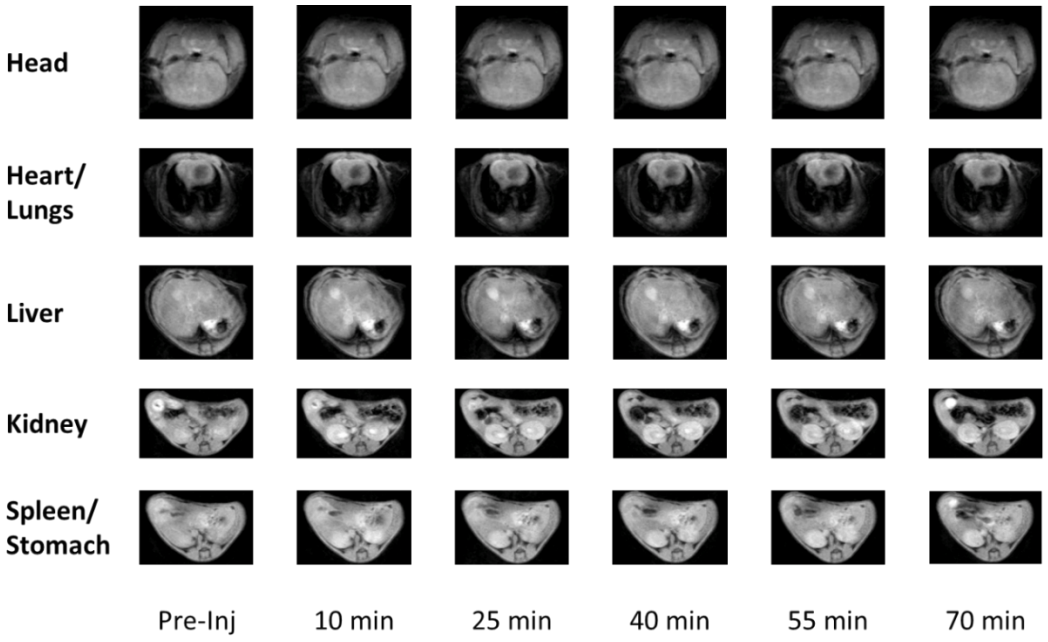


Figure S16. T_1-weighted cross-section MR images of Gd:DOTA-HPβCD/SBEβCD F127 collected at 7T from Balb/c mices at 9 weeks of age. Slices were placed in diverse organs.

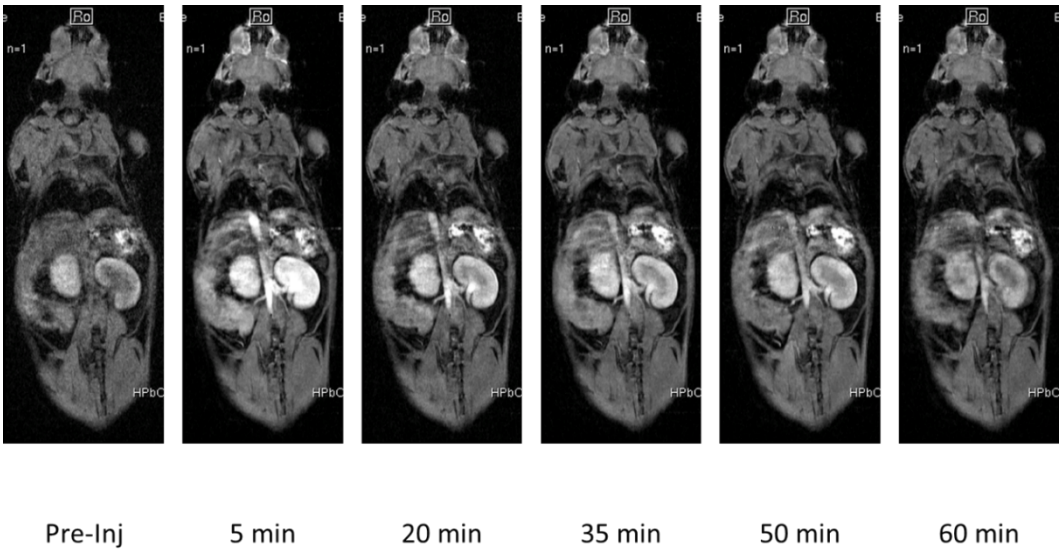


Figure S17. T_1-weighted MR images of Gd:DOTA-HPβCD/SBEβCD F68 collected at 7T from Balb/c mice at 9 weeks of age.

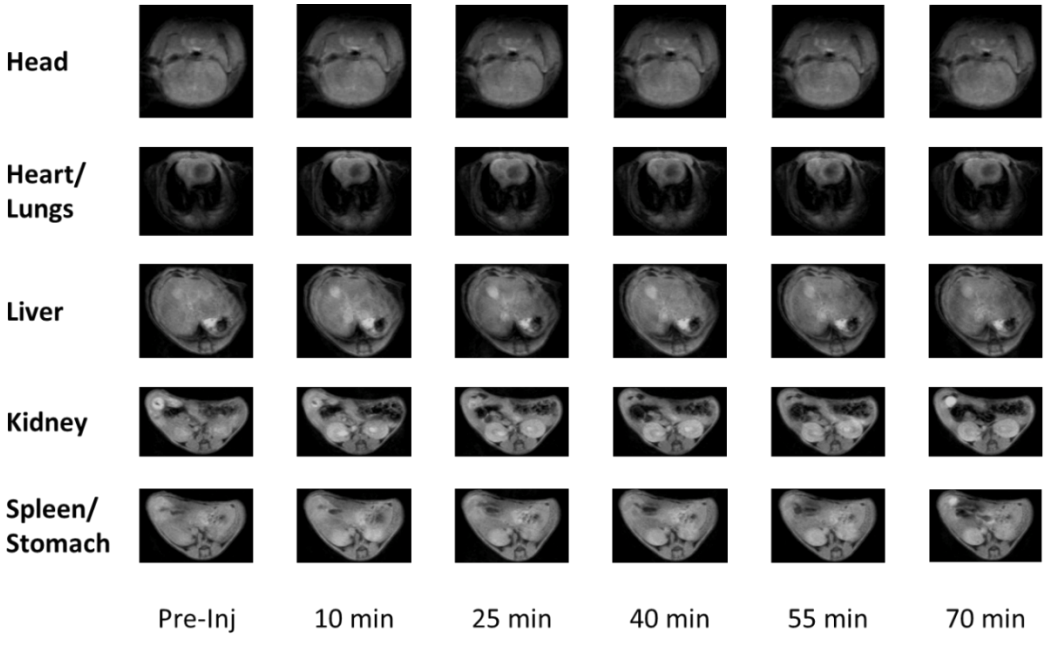


Figure S18. T_1-weighted cross-section MR images of Gd:DOTA-HPβCD/SBEβCD F68 collected at 7T from Balb/c mice at 9 weeks of age. Slices were placed in diverse organs.

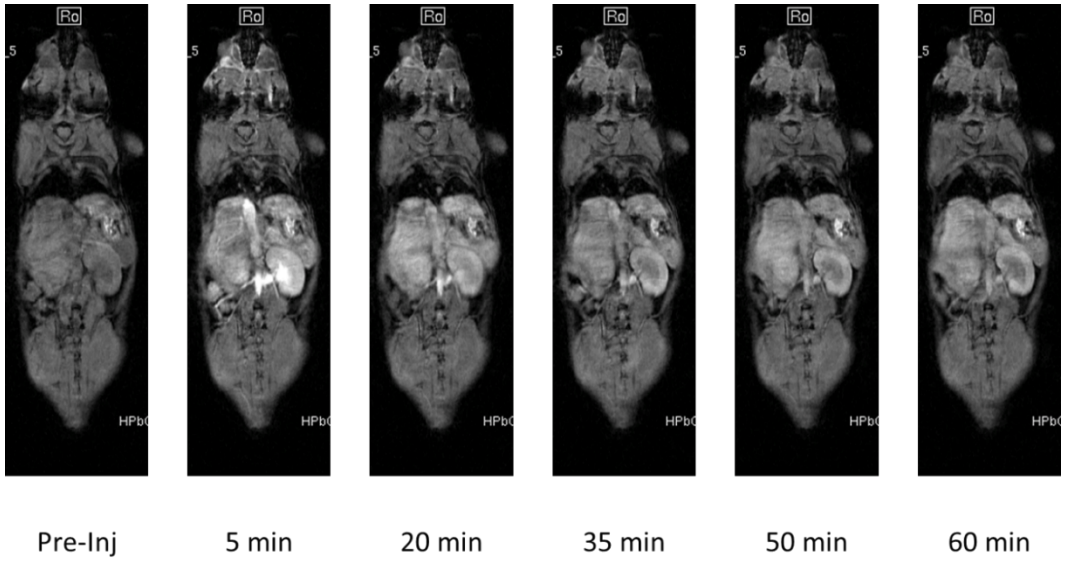


Figure S19. T_1-weighted MR images of Gd:DOTA-HPβCD/SBEβCD L35 collected at 7T from Balb/c mice at 9 weeks of age.

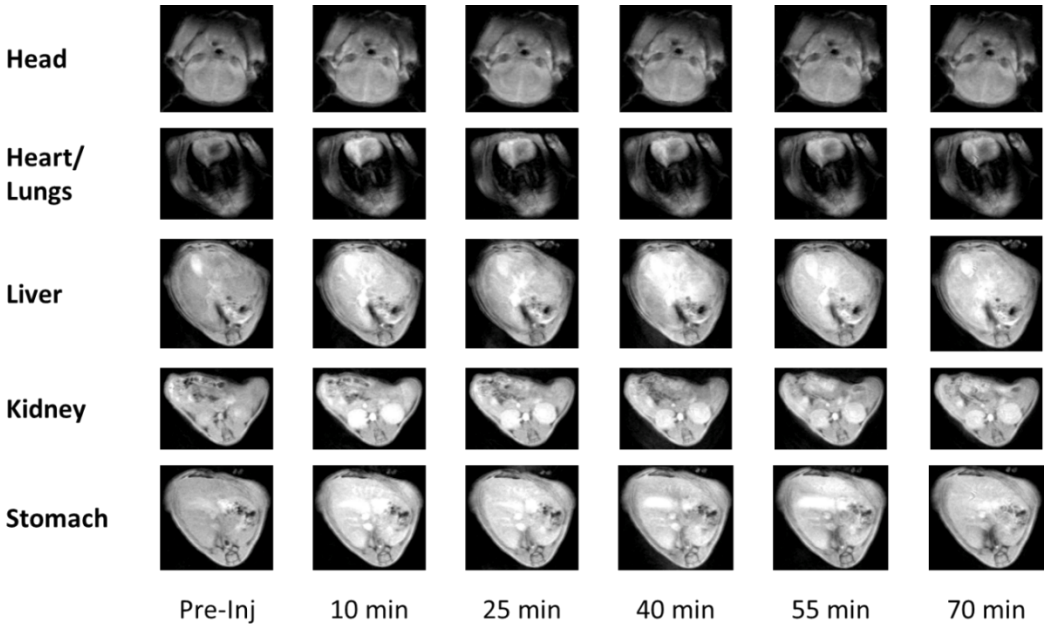


Figure S20. T_1-weighted cross-section MR images of Gd:DOTA-HPβCD/SBEβCD L35 collected at 7T from Balb/c mice at 9 weeks of age. Slices were placed in diverse organs.

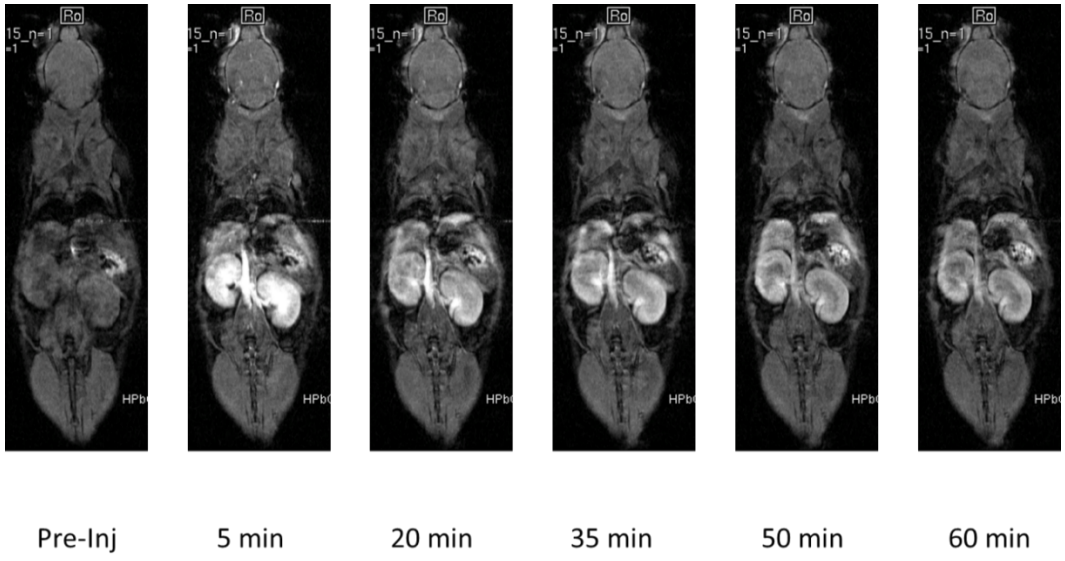


Figure S21. T_1-weighted MR images of Gd:DOTA-HPβCD/SBEβCD L81 collected at 7T from Balb/c mice at 9 weeks of age.

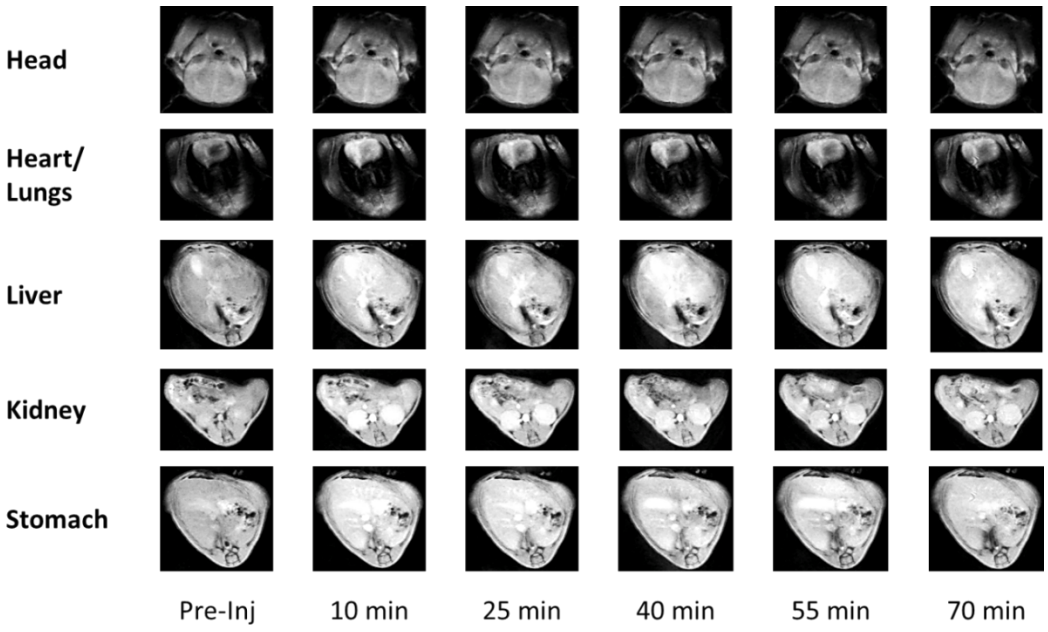


Figure S22. T_1-weighted cross-section MR images of Gd:DOTA-HPβCD/SBEβCD L81 collected at 7T from Balb/c mice at 9 weeks of age. Slices were placed in diverse organs.

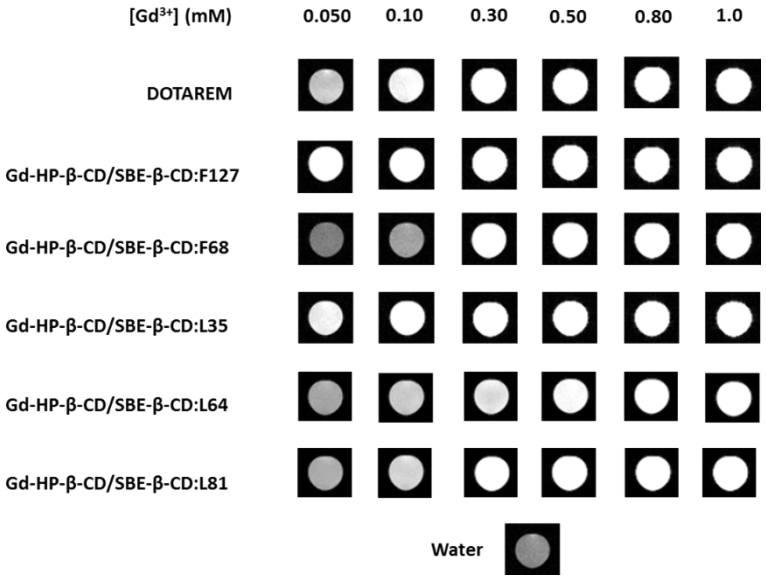


Figure S23. MR imaging of Gd:DOTA-HPβCD/SBEβCD Pluronic polyrotaxanes recorded at 25 °C, 7 T.

Table S1. *Hydrodynamic diameters and ζ potentials for Gd:DOTA-HPβCD/SBEβCD Pluronic polyrotaxanes.*

Gd:DOTA-HPβCD/SBEβCD PR	Size (nm)	PDI	ζ-Potential (mV)
F127	230	0.46	- 3.5
F68	138	0.49	- 13
L35	116	1.0	- 6.0
L64	120	0.40	- 9.4
L81	173	1.0	- 11

Table S2. *Summary of number and coverage of βCD in L81-based polyrotaxanes used in proteomics analysis of PR corona.*

Polyrotaxane	CD Feed Ratio	Total CD	SBEβCD	MW (NMR) (kD)
βCD	100	18	0	26
HPβCD	100	11	0	22
MeβCD	100	8	0	16
HPβCD/SBEβCD	50:50	19	8	58

Table S3. *Top 20 proteins identified in the PR corona as a function of βCD type in L81-based polyrotaxanes.*

βCD PR

Protein ID	Average % Corona
Serum albumin	16.53602536
Ig kappa chain C region	15.00432799
Complement C3	11.74536491
Ig gamma-1 chain C region	7.757086463
Apolipoprotein E	5.161341666
Apolipoprotein A-II	4.808387011
Apolipoprotein D	4.074641027
Apolipoprotein A-I	3.408645335
Ig lambda-1 chain C regions	3.358983503
Apolipoprotein B-100	2.938530875
Complement component C9	2.077125525
Ig gamma-2 chain C region	1.801673851
Transthyretin	1.609643609
Alpha-1-antitrypsin	1.401363144
Apolipoprotein C-I	1.370046556
Clusterin	1.286344099
Ig lambda-2 chain C regions	1.184513069
Haptoglobin	1.173103474
Serotransferrin	1.119652755
Complement C4-B	1.090155363

HPβCD PR

Protein ID	Average % Corona
Serum albumin	21.76828436
Ig kappa chain C region	19.04835025
Apolipoprotein A-II	10.81040494
Apolipoprotein A-I	7.919583224
Apolipoprotein E	7.066407588
Apolipoprotein C-II	4.992757233
Apolipoprotein C-III	3.944752799
Ig gamma-1 chain C region	3.311732771
Transthyretin	1.985551149
Complement C3	1.908027079
Alpha-1-antitrypsin	1.650830489
Serotransferrin	1.593952712
Haptoglobin	1.546604427
Ig alpha-1 chain C region	1.482215949
Clusterin	1.035208084
Ig lambda-1 chain C regions	0.931474445
Ig kappa chain V-III region	0.773907913
Apolipoprotein D	0.753715631
Ig gamma-2 chain C region	0.647140603
Ig lambda-2 chain C region	0.604695051

MeβCD PR

Protein ID	Average % Corona
Complement C3	17.35131077
Apolipoprotein E	16.92263363
Serum albumin	10.91695191
Apolipoprotein B-100	6.069452089
Ig gamma-1 chain C region	5.337392476
Ig kappa chain C region	5.311549879
Apolipoprotein A-II	5.010290265
Apolipoprotein D	3.573277261
Complement component C9	3.421953775
Apolipoprotein A-I	2.773780863
Complement C4-B	2.147698529
Serum paraoxonase/arylesterase 1	1.574657144
Apolipoprotein C-II	1.53214378
Apolipoprotein C-III	1.49304561
Apolipoprotein C-I	1.304540524
Clusterin	1.093414729
Apolipoprotein(a)	1.058981593
Transthyretin	0.965211466
Serum amyloid A-4 protein	0.928412544
Ig lambda-1 chain C regions	0.864075528

HPβCD/SBEβCD PR

Protein ID	Average % Corona
Complement C3	19.76495094
Apolipoprotein E	12.28036258
Serum albumin	9.427281564
Apolipoprotein A-II	6.865297508
Apolipoprotein C-II	6.692607783
Ig gamma-1 chain C region	5.92949059
Ig kappa chain C region	4.87297314
Apolipoprotein B-100	4.636129789
Complement component C9	3.846580792
Apolipoprotein D	3.114959404
Apolipoprotein A-I	2.537299079
Complement C4-B	2.083473432
Trypsin-3	2.050791718
Apolipoprotein C-III	1.876260875
StAR-related lipid transfer protein 13	1.437949237
Ig gamma-2 chain C region	1.169451568
Haptoglobin	0.937229713
Clusterin	0.91590978
Apolipoprotein(a)	0.856763959
Ig lambda-1 chain C regions	0.797377646

General Method for Heterogeneous Synthesis of Polyrotaxanes

The procedure described herein generally follows the methods reported by Mondjinou *et al.*,[1,2] that were roughly based on work reported by Liu *et al.*[3]

General Procedure for Preparation of TAEA-modified Pluronic core: The Pluronic precursor (10 g) was azeotropically dried four times from toluene and evaporated overnight on a high vacuum line. The dried Pluronic was suspended in dry acetonitrile (190 mL) before addition of carbonyl diimidazole (CDI, 21.3 g) with stirring for 5 h. Water was then added (8.1 mL) to quench unreacted CDI, followed by addition of tris(2-aminoethyl)amine (TAEA, 21.3 mL) and stirring at 20 °C overnight. Partial solvent removal by rotary evaporation to reduce the volume by approximately 66% was performed before adding water (75 mL) and dialyzing the mixture for 3 d against 30% ethanol in water using 2 kD MWCO dialysis membranes. The dialysate was then subjected to rotary evaporation to remove as much solvent as possible before azeotroping drying the product three times from toluene.

L81 HPβCD Polyrotaxane with Cholesterol Endcaps. TAEA-modified L81 Pluronic (2.44 g) was suspended in 146 mL hexanes and stirred overnight at 20 °C before adding 24.174 g HP-β-CD. The resulting suspension was bath sonicated for 1 h, probe sonicated for 30 min, and then stirred at 20 °C for 3 d. The solvent was removed by rotary evaporation, followed by addition of cholesteryl chloroformate (4.1824 g) and 1.3 mL of trimethylamine in 73.2 mL dry dichloromethane, with subsequent stirring of the mixture of 1 d at 20 °C under Ar. The mixture was then precipitated in cold diethyl ether and the suspension separated by centrifugation. The pellet was dissolved in DMSO and dialyzed against DMSO using 6-8 kD MWCO dialysis tubing, followed by dialysis for 4 d against deionized H_2O. The dialyzed product was lyophilized to give 352 mg of L81 HPβCD Polyrotaxane with Cholesterol Endcaps. The other members of the polyrotaxane were prepared using the appropriate TAEA-modified Pluronics and mixtures of HPβCD and SBEβCD instead of pure HPβCD.

1. Y. A. Mondjinou, L. McCauliff, A. Kulkarni, L. Paul, S.-H. Hyun, Z. Zhang, Z. Wu, M. Wirth, J. Storch, D. H. Thompson, *Biomacromolecules* **2013** *14*, 4189-4197.
2. Y. A. Mondjinou, S.-H. Hyun, M. Xiong, C. J. Collins, P. L. Thong, D. H. Thompson, *ACS Appl. Mat. Interfac.* **2015** *7*, 23831-23836.
3. R. T. Liu, T. Maeda, N. Kihara, A. Harada, T. Takata, *J. Polym. Sci. Part A Polym. Chem.* **2007** *45*, 1571-1574.