

Supplementary Material for

Ultrasmall Gd@Cdots as a Radiosensitizing Agent for Non-Small Cell Lung Cancer

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Abbreviation list

ALT	Alanine Aminotransferase
ATP	Adenosine Triphosphate
BUN	Urea Nitrogen
DLS	Dynamic Light Scattering
DMEM	Dulbecco's Modified Eagle's Medium
EDS	Energy Dispersive Spectroscopy
ESI	Electrospray Ionization
FBS	Fetal Bovine Serum
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
LDI	Laser Desorption Ionization
MRI	Magnetic Resonance Imaging
MTT	3-(4,5-Dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide
NPs	Nanoparticles
PBS	Phosphate-Buffered Saline
REF	Radiation Enhancement Factor
ROS	Reactive Oxygen Species
RPMI 1640	Roswell Park Memorial Institute Medium 1640
RT	Radiation
SEM	Scanning Electron Microscopy
SOD	Superoxide Dismutase
SOSG	Singlet Oxygen Sensor Green
STEM	Scanning Transmission Electron Microscopy
TA	Terephthalic Acid
TEM	Transmission Electron Microscopy

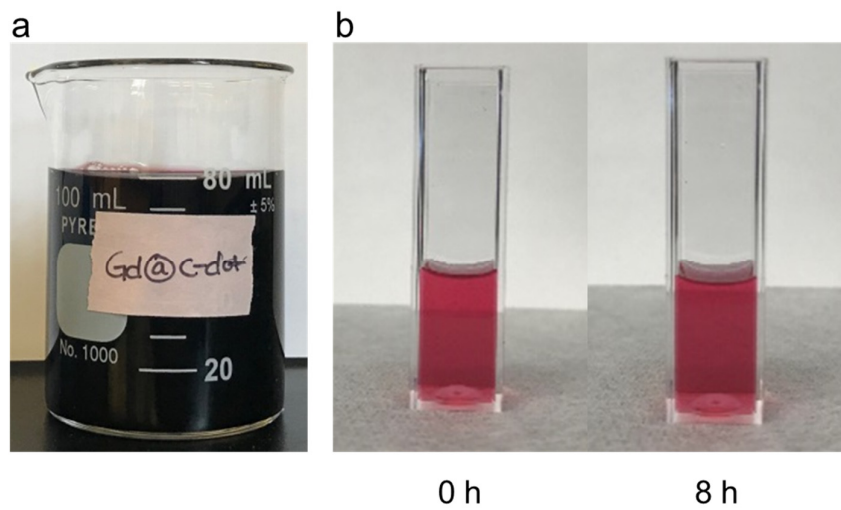


Figure S1. a) As-synthesized Gd@Cdots dispersed in water. b) Gd@Cdots solution in PBS at 0 h and 8 h. No precipitation was observed over incubation.

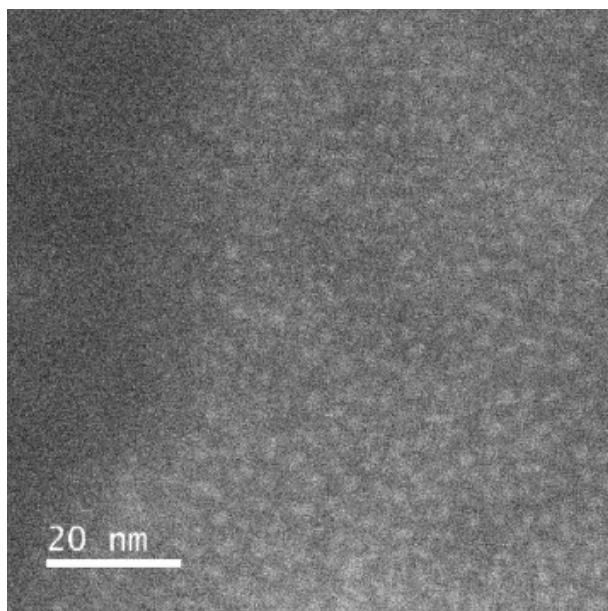


Figure S2. STEM image of Gd@Cdots.

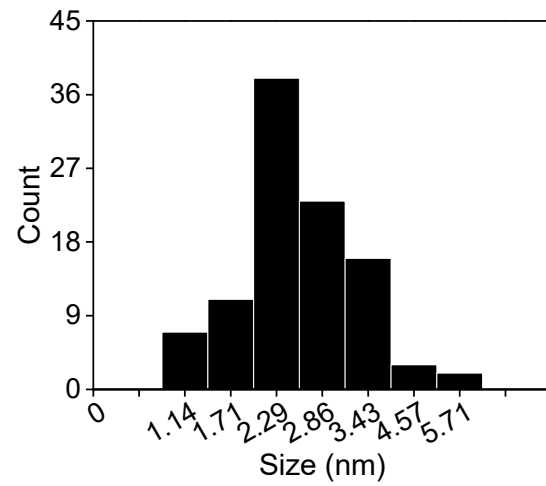


Figure S3. Statistics on size the distribution of Gd@Cdots, based on TEM results.

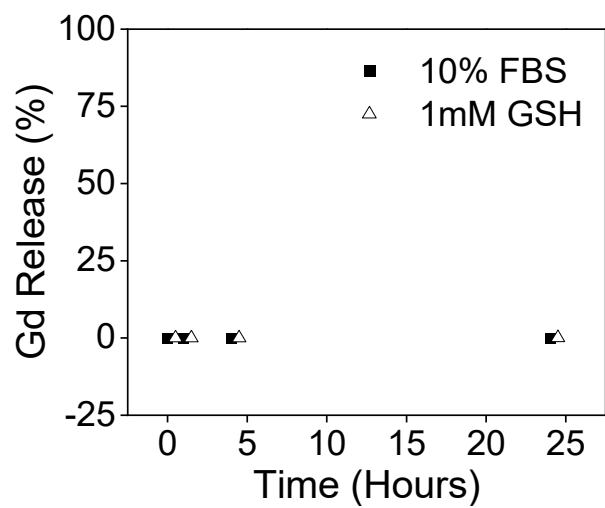


Figure S4. Gd release when Gd@Cdots were incubated in 10% fetal bovine serum (FBS) or solutions containing 1 mM glutathione (GSH). Gd was quantified by ICP-MS.

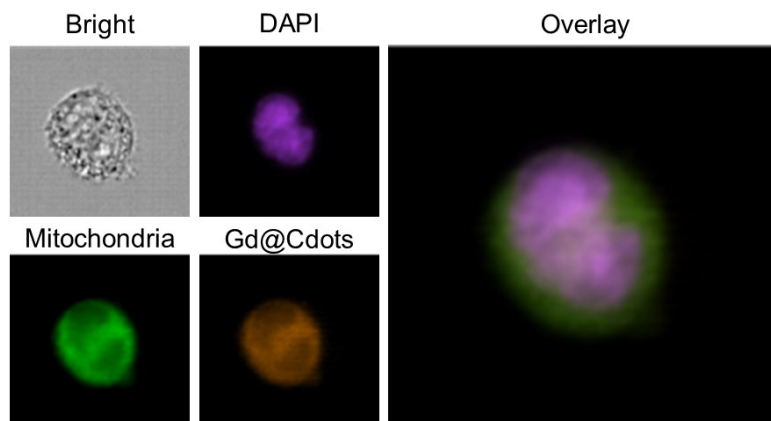
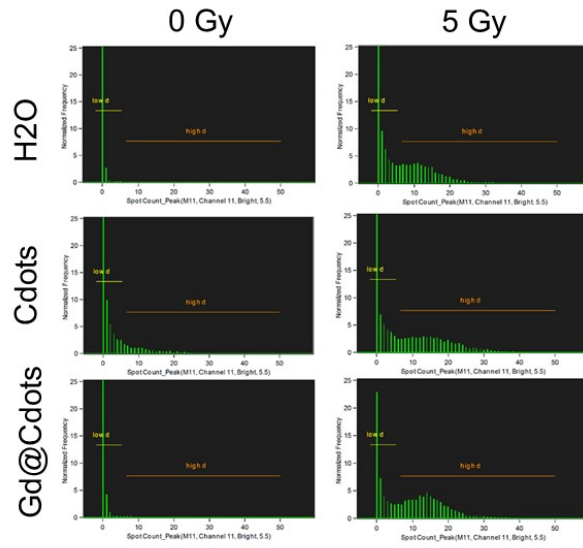
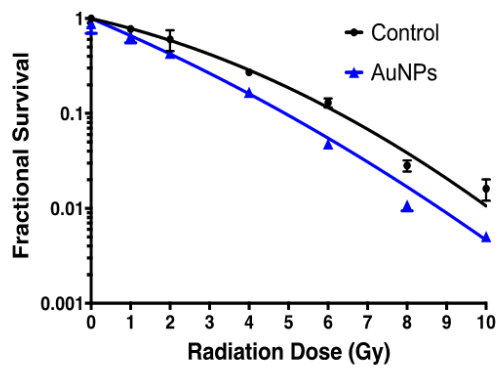


Figure S5. Gd@Cdots accumulation in mitochondria (stained with MitoTracker green). Images were acquired on an ImageStream X Mark II Imaging Flow Cytometer.



Population	%					
	Control	Cdots	Gd@Cdots	RT	Cdots +RT	Gd@Cdots +RT
DAIP positive rh2aX & cell & focused	100	100	100	100	100	100
low fluorescence & DAIP positive rh2aX & focused	99.7	87.6	99.6	56.1	48.6	42.4
high fluorescence & DAIP positive rh2aX & focused	0.29	10.7	0.39	40.6	48.9	55

Figure S6. Statistics for cell γ H2AX loci numbers, evaluated by ImageStream X Mark II Imaging Flow Cytometer.



Group	a	b	SF4	REF4
Contro	0.218	0.024	0.285	1.759
AuNPs	0.403	0.013	0.162	

Figure S7. Clonogenic assay with Au nanoparticles (10 $\mu\text{g}/\text{mL}$) and linear-quadratic data fitting.

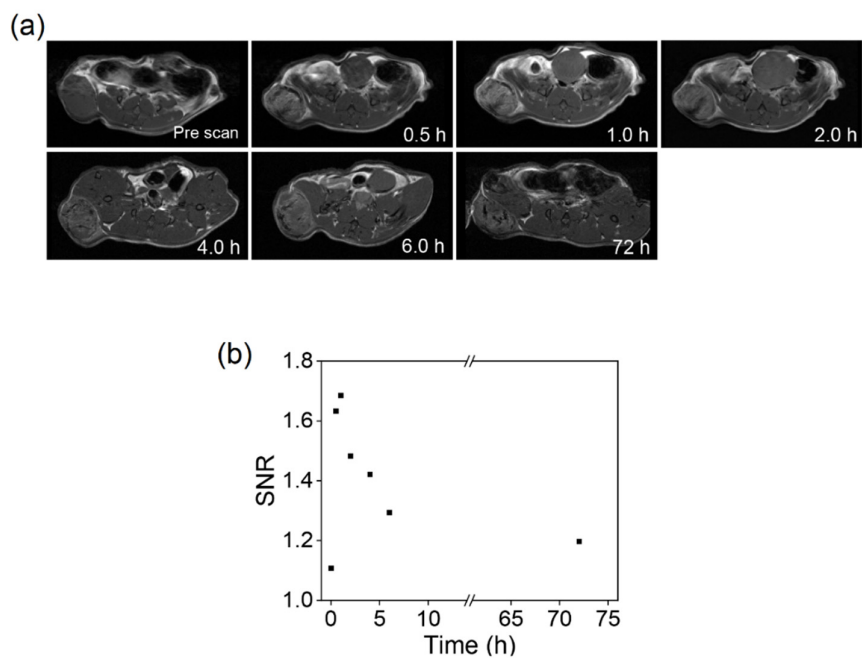


Figure S8. *In vivo* MRI scans. The studies were performed with H1299 tumor bearing nude mice ($n = 3$) on a Varian 7T magnet. When the tumor size reached 500 mm^3 , Gd@Cdots (0.1 mmol/kg based on Gd) were intravenously injected. Transverse and coronal T_1 -weighted MR images were obtained at 0.5, 1, 2, 4, 6, and 72 h using the following parameters: field-of-view (FOV) = $70 \times 70 \text{ mm}^2$, TR/TE = 500/12 ms, matrix size = 256×256 , slice = 4, thickness = 1 mm. The signal to background ratio was calculated using ImageJ software. a) T_1 -weighted MRI images, taken at different time points after Gd@Cdots injection (0.1 mmol Gd/kg). b) Signal-to-background ratios (SNRs), based on imaging results from a).

	Unit	Reference (95% interval)		Experiment			
				Control		Gd@Cdot	
		Low	High	Average	Std	Average	Std
RBC	x 10 ⁶ /ul	8.16	11.69	11.75	0.21	11.10	0.26
HGB	g/dl	12.40	18.90	18.50	0.14	17.30	0.61
HCT	%	43.50	67.00	54.60	1.84	52.67	2.06
MCV	fl	50.80	64.10	46.60	0.85	47.57	0.67
MCH	pg	13.00	17.60	15.75	0.07	15.63	0.47
MCHC	g/dl	23.90	33.10	33.85	0.78	32.40	1.27
RDW	%	16.90	23.50	13.75	0.35	14.10	0.17
Platelets	x10 ³ /ul	476.00	1661.0	229.50	94.05	538.67	250.23
MPV	fl	4.60	5.80	5.55	0.49	6.17	0.15
WBC	x10 ³ /ul	5.69	14.84	6.00	1.41	7.03	0.45
Neutrophils	x10 ³ /ul	0.74	3.01	1.27	0.11	1.38	0.41
Lymphocytes	x10 ³ /ul	3.60	11.56	4.03	1.24	5.18	0.56
Monocytes	x10 ³ /ul	3.75	14.33	0.10	0.06	0.23	0.07
Eosinophils	x10 ³ /ul	0.01	0.35	0.34	0.41	0.12	0.05
Basophils	x10 ³ /ul	0.00	0.16	0.27	0.18	0.12	0.04
BUN	mg/dL	7.00	31.00	24.39	4.19	21.17	3.71
ALT	unit/L	40.00	170.00	58.29	3.63	54.10	1.50

Table S1. Complete blood count (CBC) results as well as liver & kidney function tests.