Supporting Information

Nanoparticles Accumulate in the Female Reproductive System during Ovulation Affecting Cancer Treatment and Fertility

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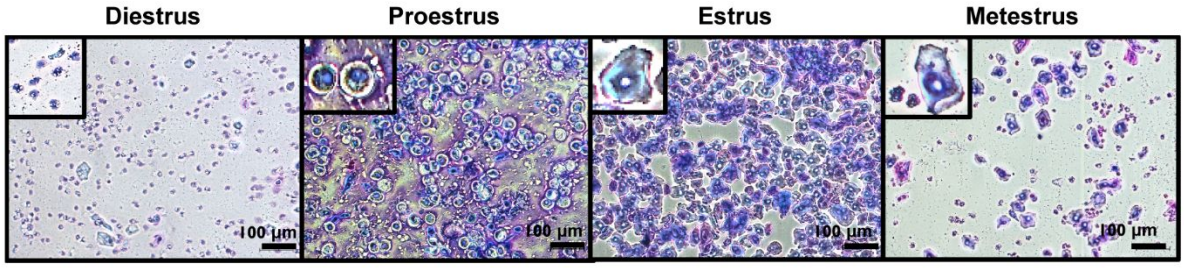


Figure S1. Cytology smears at different cycle stages of a healthy female C57BL/6 mouse. Enlarged imaged of each representative cell type is shown in the top left corner. Scale bar 100 µm.

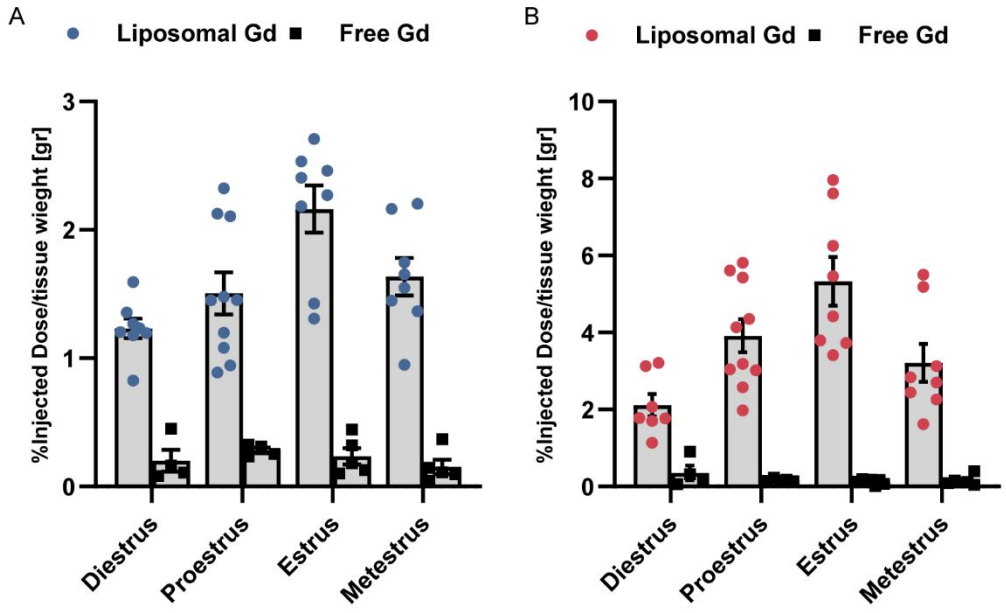


Figure S2. Free Gd vs. lipo-Gd accumulation in the ovaries (A) and the uterus (B).

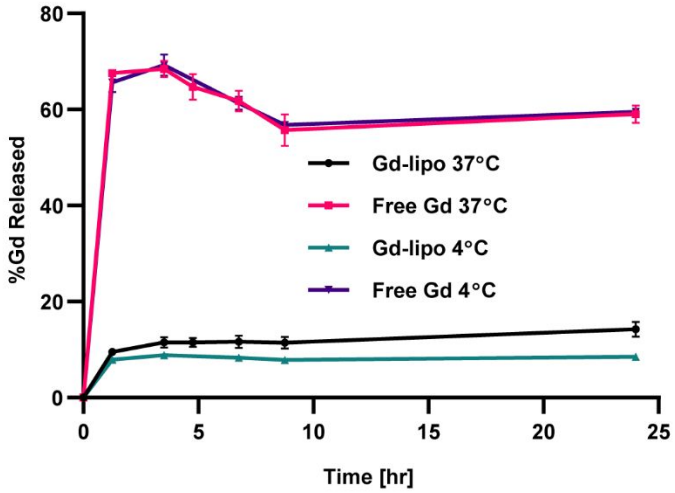


Figure S3. Release profile of Gd from liposomes at 37 and 4 degrees Celsius. Gd release from liposomes is 14.2% ± 1.5% at 37°C and 8.5% ± 0.4% at 4°C.

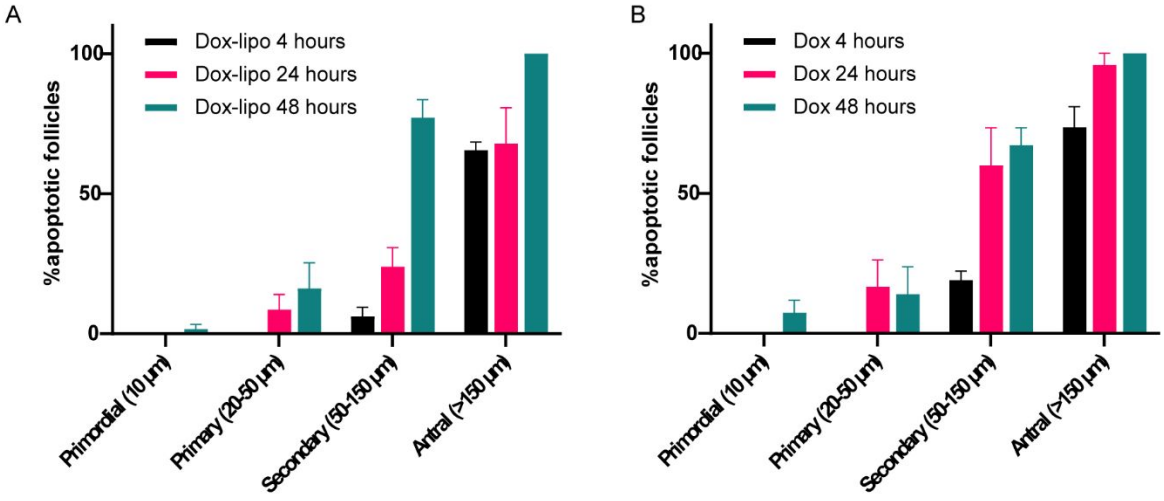
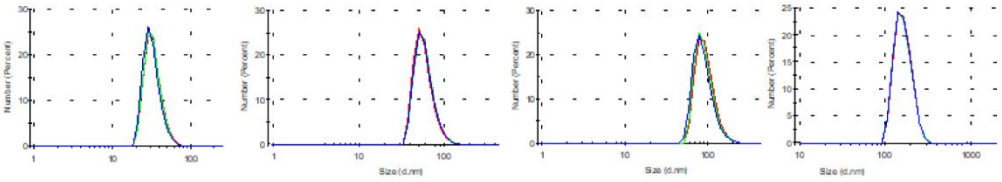


Figure S4. Percentage of apoptotic follicles categorized by their size 4, 24, and 48 hours after Dox-lipo i.v. administration (A). Percentage of apoptotic follicles categorized by their size 4, 24, and 48 hours after free-DOX i.v. administration (B).

A

Sample (Gold Nanoparticle)	GNP 20 nm	GNP 50 nm	GNP 100 nm	GNP 200 nm
Zeta Potential in H_2O (mV)	-37.2	-24.6	-25.4	-21.5
Size in H_2O (nm)	28.2	50.75	91.4	164.8
Size Distribution				

B

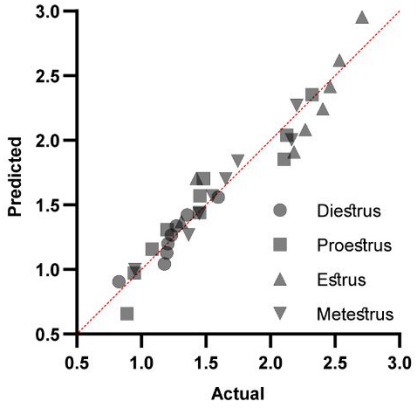
Sample (Liposomes)	Gd-Liposomes	DOX-Liposomes
Zeta Potential in H_2O (mV)	-31.9	-21.5
Size in H_2O (nm)	86.45	85.9

Figure S5. Size and Zeta measurements of gold nanoparticles (A) and liposomes (B).

A

	Normality and Lognormality Tests Tabular results	A Diestrus	B Proestrus	C Estrus	D Metestrus
1	**Test for normal distribution**				
2	**Anderson-Darling test**				
3	A2*	0.5239	0.4533	0.6222	0.2378
4	P value	0.1230	0.2117	0.0667	0.6831
5	Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes
6	P value summary	ns	ns	ns	ns
7					
8	**D'Agostino & Pearson test**				
9	K2	2.657	1.555	1.997	0.01300
10	P value	0.2649	0.4596	0.3683	0.9935
11	Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes
12	P value summary	ns	ns	ns	ns
13					
14	**Shapiro-Wilk test**				
15	W	0.9016	0.8990	0.8418	0.9523
16	P value	0.2985	0.2135	0.0786	0.7344
17	Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes
18	P value summary	ns	ns	ns	ns
19					
20	**Kolmogorov-Smirnov test**				
21	KS distance	0.2752	0.2198	0.2659	0.1492
22	P value	0.0754	>0.1000	>0.1000	>0.1000
23	Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes
24	P value summary	ns	ns	ns	ns
25					
26	**Number of values**	8	10	8	8

B



C

	Normality and Lognormality Tests Tabular results	A Diestrus	B Proestrus	C Estrus	D Metestrus
1	**Test for normal distribution**				
2	**Anderson-Darling test**				
3	A2*	N too small	0.3682	0.3816	0.6106
4	P value		0.3546	0.3067	0.0719
5	Passed normality test (alpha=0.05)?		Yes	Yes	Yes
6	P value summary		ns	ns	ns
7					
8	**D'Agostino & Pearson test**				
9	K2	N too small	1.834	1.734	1.820
10	P value		0.3996	0.4201	0.4025
11	Passed normality test (alpha=0.05)?		Yes	Yes	Yes
12	P value summary		ns	ns	ns
13					
14	**Shapiro-Wilk test**				
15	W	0.8693	0.9201	0.8912	0.8516
16	P value	0.1831	0.3580	0.2399	0.0989
17	Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes
18	P value summary	ns	ns	ns	ns
19					
20	**Kolmogorov-Smirnov test**				
21	KS distance	0.2384	0.2030	0.1951	0.2743
22	P value	>0.1000	>0.1000	>0.1000	0.0776
23	Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes
24	P value summary	ns	ns	ns	ns
25					
26	**Number of values**	7	10	8	8

D

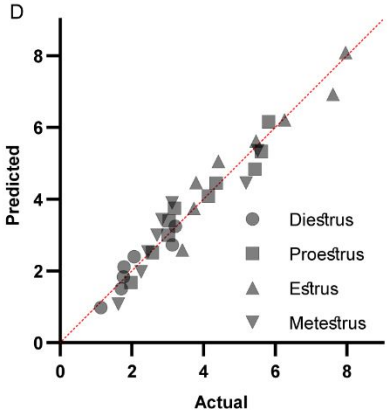
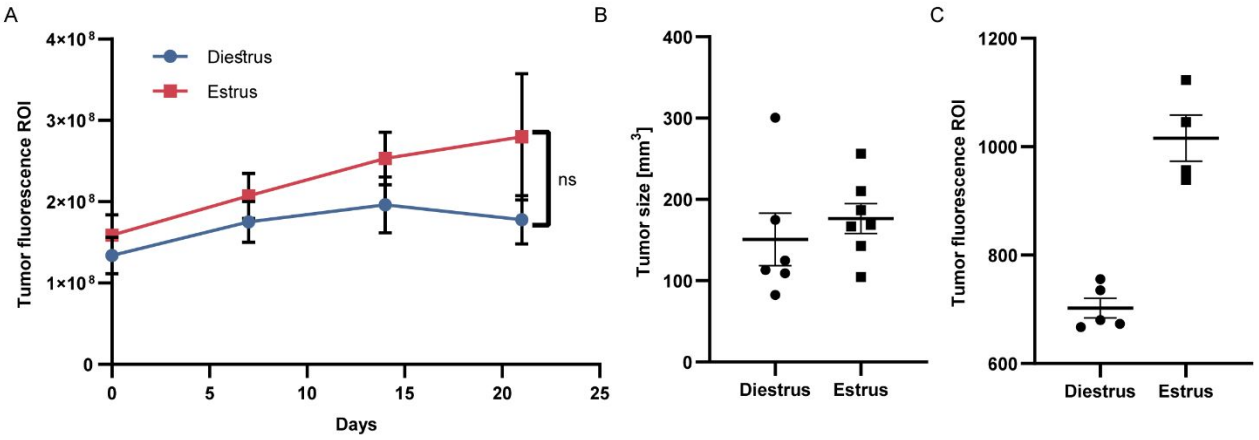


Figure S6. Normality test for Gd-lipo accumulation in the ovaries in figure 1f (A) QQ plot for normality results for the ovaries (B) Normality test for Gd-lipo accumulation in the uterus in figure 1g (C) QQ plot for normality results for the uterus (D).



41 **Figure S7**. Fluorescent quantification of the breast cancer tumor growth based on the IVIS imaging (A).
42 Tumor size distribution at treatment initiation for breast cancer (B) and ovarian cancer (C).

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