EPR effect / BSB hypothesis

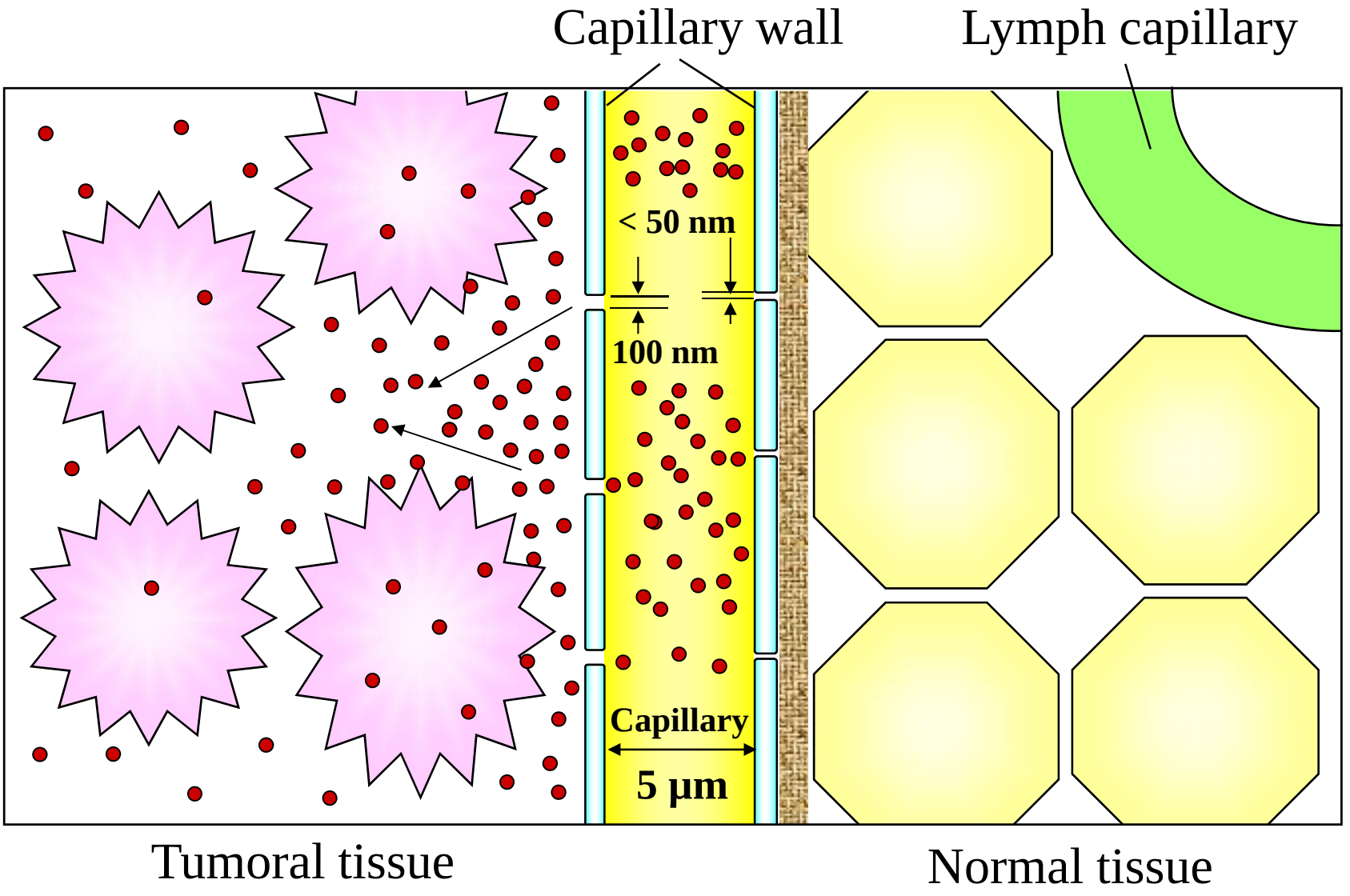
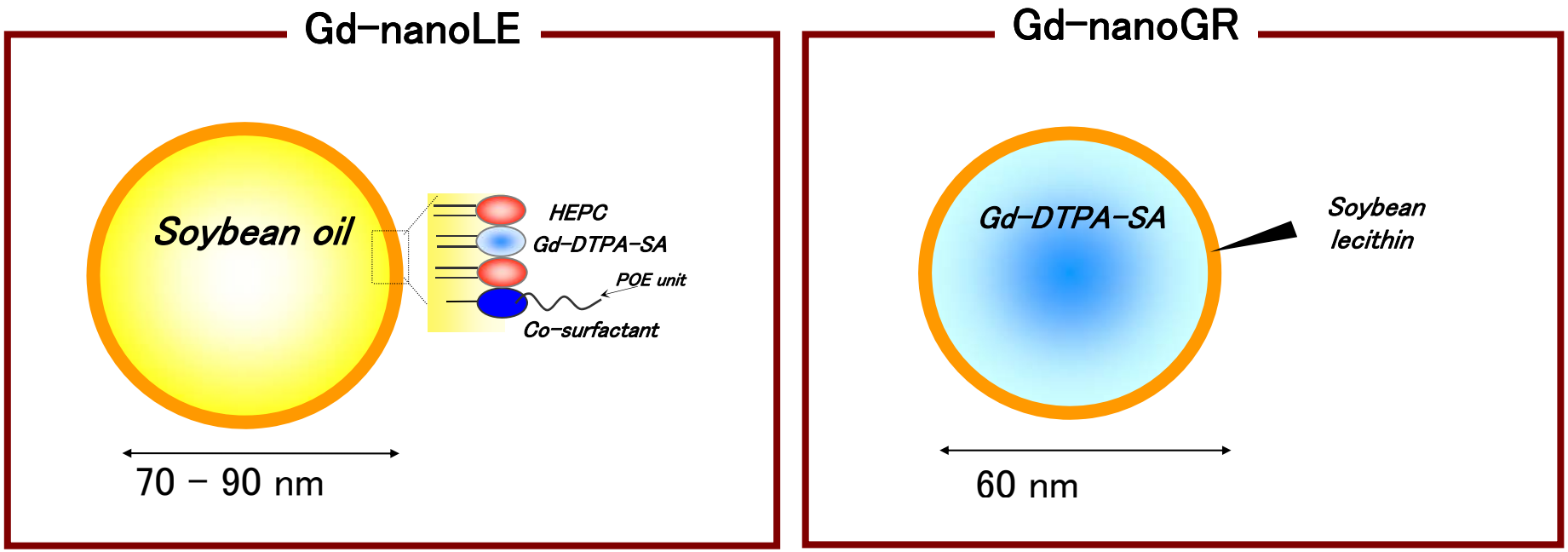
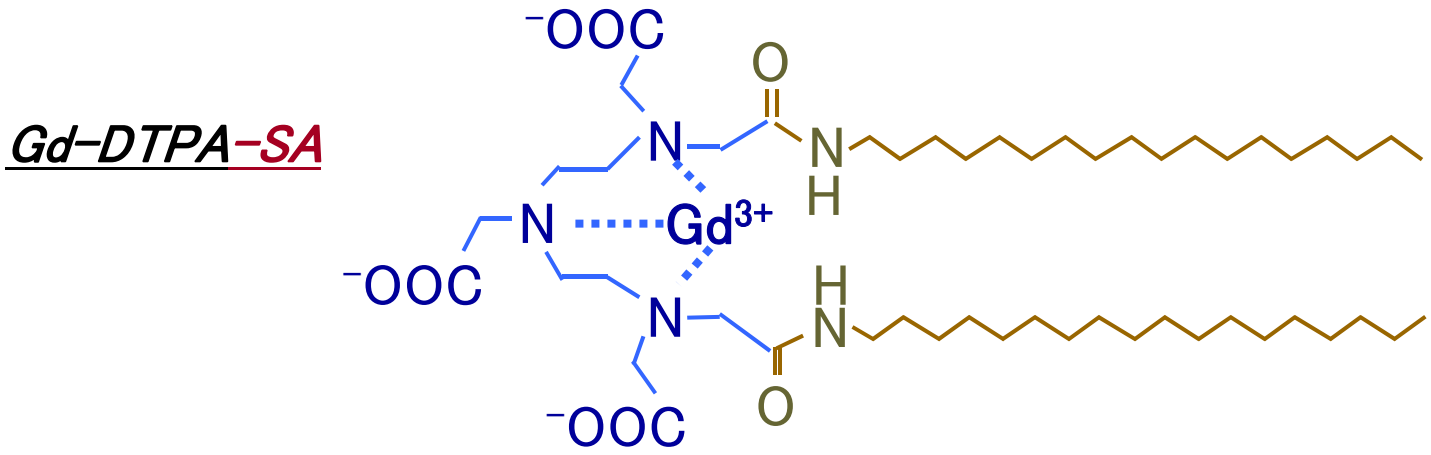
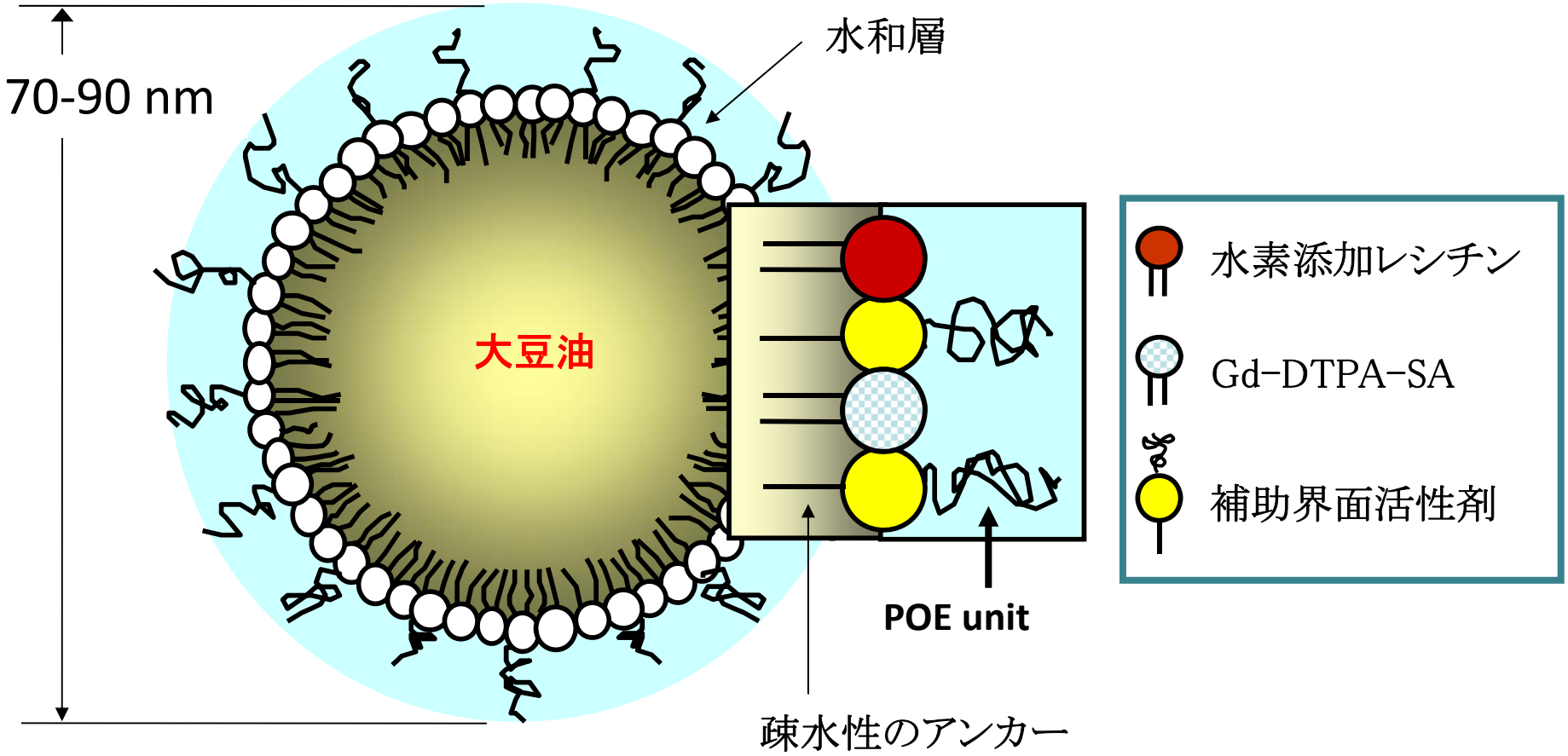


Fig. Penetration of Particles from Capillaries to Tumor


Gd-nanoLE
Soybean oil
HEPC
Gd-DTPA-SA
POE unit
Co-surfactant
70 – 90 nm
Gd-nanoGR
Gd-DTPA-SA
Soybean lecithin
60 nm


Gd-DTPA-SA
⁻OOC
O
N
N
H
N
Gd3+
⁻OOC
N
H
N
O
⁻OOC



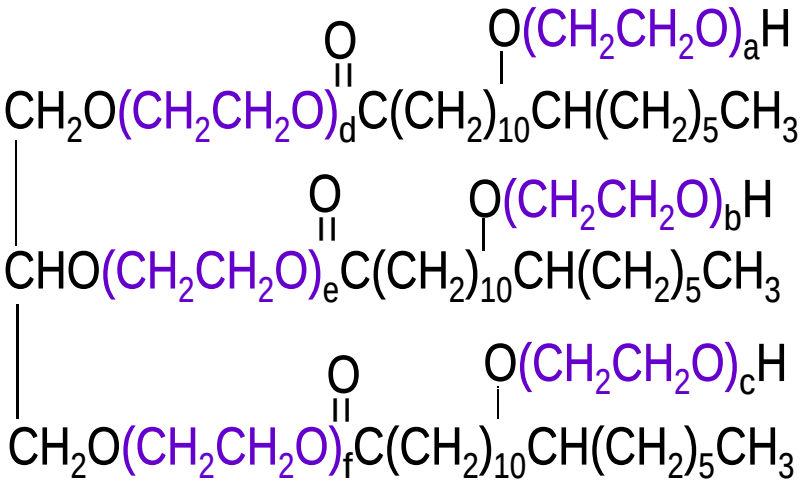
図．がん中性子捕捉療法用脂質ナノ粒子の構造

Tetsuya Watanabe, Hideki ichikawa Yoshinobu Fukumori. Tumor Accumulation of Gadolinium in Lipid-Nanoparticles intravenously Injected for Neutron-Capture Therapy of Cancer. Eur. J. Pharm. Biopharm, 54, 119-124 (2002).

Chemical Structure of Co-surfactants

HCO-60

(Polyoxyethylene 60 hydrogenated castor oil)



$(a + b + c + d + e + f \fallingdotseq 60)$

Myrj53

(Polyoxyethylene 50 stearate)

$H(OCH_2CH_2)_nOCOC_{18}H_{37}$ $(n \fallingdotseq 50)$

Brij700

(Polyoxyethylene 100 stearylether)

$H(OCH_2CH_2)_nOC_{18}H_{37}$ $(n \fallingdotseq 100)$

(CH_2CH_2O) –: Polyoxyethylene (POE) unit (hydrophilic)

In Vivo Experiments

Animal: Syrian (golden) hamster（female, b.w. 98±10 g, 6 weeks）

Tumor cell: $D_1$179（Green's melanoma ）

- $D_1$179 fragment (2×2×2 mm) was subcutaneously inoculated on the left nates of hamsters.
- The Gd-nanoLE was administrated at 10 days after inoculation, while the diameter of the tumor mass became about 10 mm.
- The Gd-nanoLE was i.v. injected into the hamsters at a dose of 1 mL per hamster (maximum tolerable volume).

Factors Affecting Biodistribution

1) Administration route
2) Particle size
3) Type of co-surfactant
4) Type of core component
5) Comparison with Gd-nanoLP
6) Formulation of surface layer

Effect of Cosurfactant

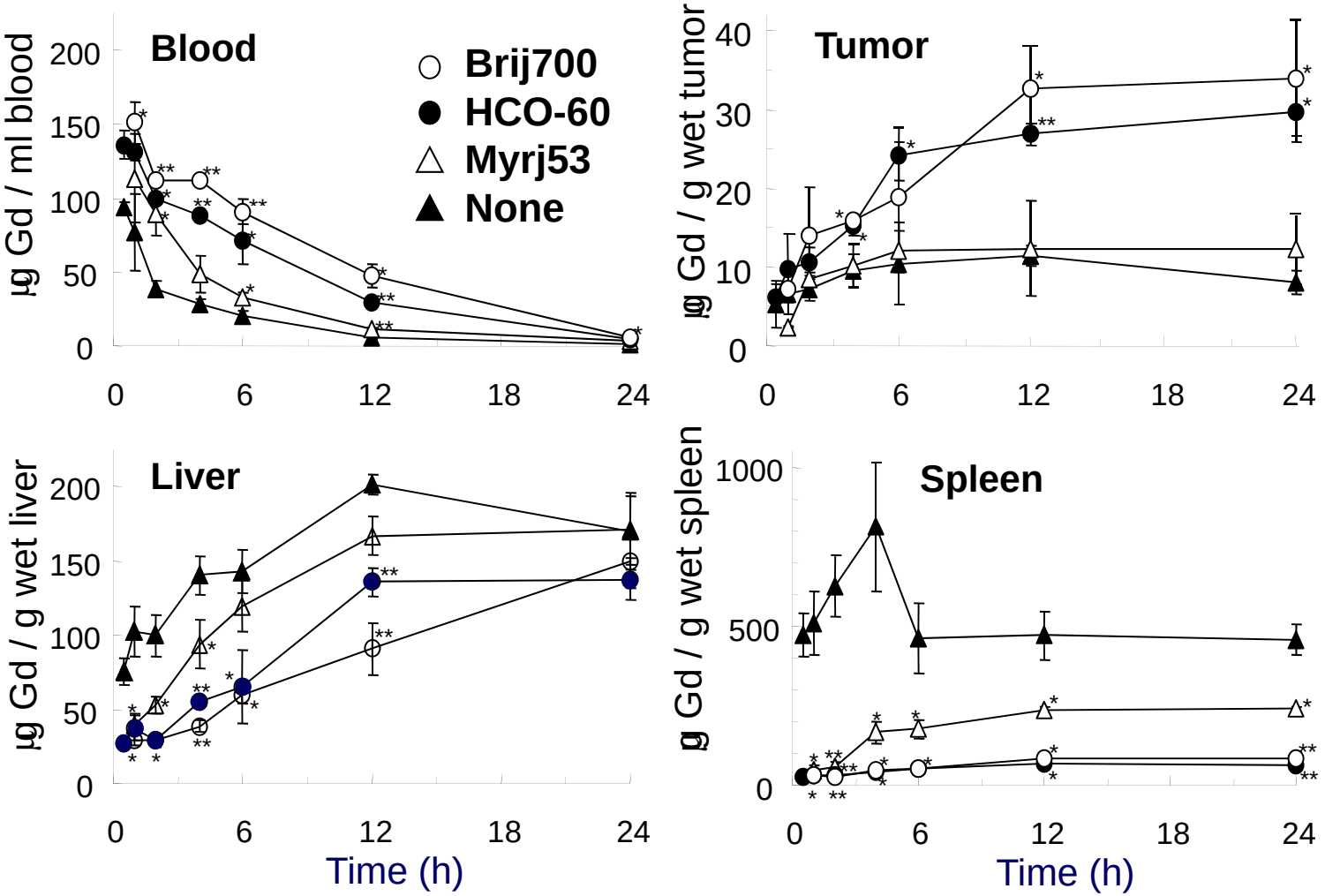


Figure 1. Effect of the type of co-surfactant on biodistribution after I.V. administration of standard-Gd-nanoLP at a dose of 1.5 mg Gd/ml/hamster. **(closed triangle) Gd-nanoLP-PL; (open triangle) Gd-nanoLP with Myrj53; (closed circle) Gd-nanoLP with HCO-60; (open circle) Gd-nanoLP with Brij700. Each value represents the mean ± S.D. (n=3). * p<0.05 and ** p<0.01, significantly different from the Gd concentration of Gd-nanoLP-PL.**