Supporting Information

Title: A matrix metalloproteinase-activated magnetic resonance imaging and Photoacoustic imaging contrast agent with improved turn-on relaxivity response and anion compatibility

Tingwei Meng[1,3#], Bo Fan[2#], Qian Li[2], Xiaoyang Peng[1], Jun Xu[4*]， Ruiping Zhang [3*]

1 School of Basic Medical Sciences, Department of Biochemistry and Molecular Biology, Shanxi Medical University, Taiyuan 030001, Shanxi, People's Republic of China

2 Department of Pharmacy, School of Pharmacy, Shanxi Medical University, Taiyuan 030001, Shanxi, People's Republic of China

3 Imaging Department of the Affiliated Bethune Hospital of Shanxi Medical University, Taiyuan 030001, People's Republic of China

4 First Hospital of Shanxi Medical University, Taiyuan 030001, People's Republic of China

# These authors contributed equally to this work

* Correspondence: Ruiping Zhang, jun Xu

Imaging Department of the Affiliated Bethune Hospital , Shanxi Medical University,

Email zrp_7142@163.com

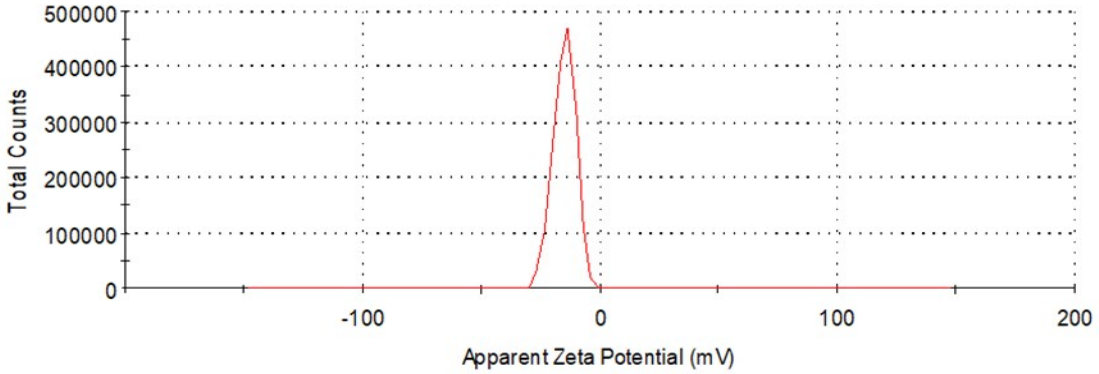


Fig.S1 Zeta potential of PEG-PepMMP2-MNP-Gd.

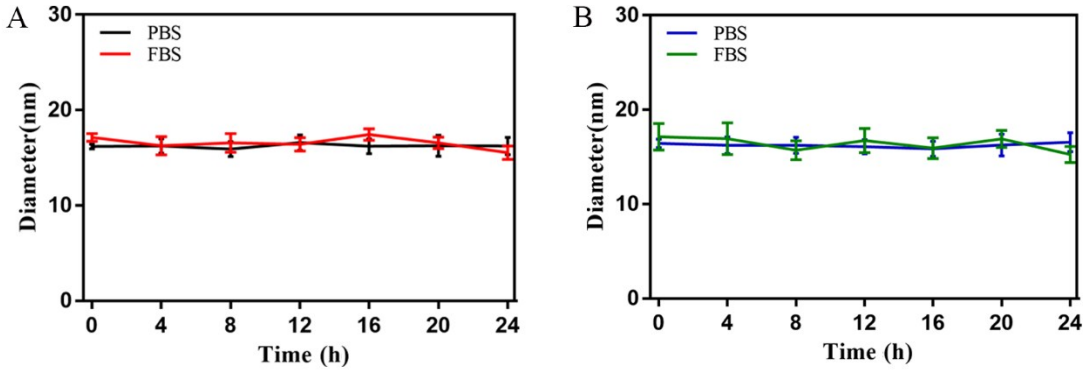


Fig.S2 Stability study of PEG-PepMMP2-MNP-Gd (A) and PEG-MNP-Gd (B) in PBS and FBS over 24 hours

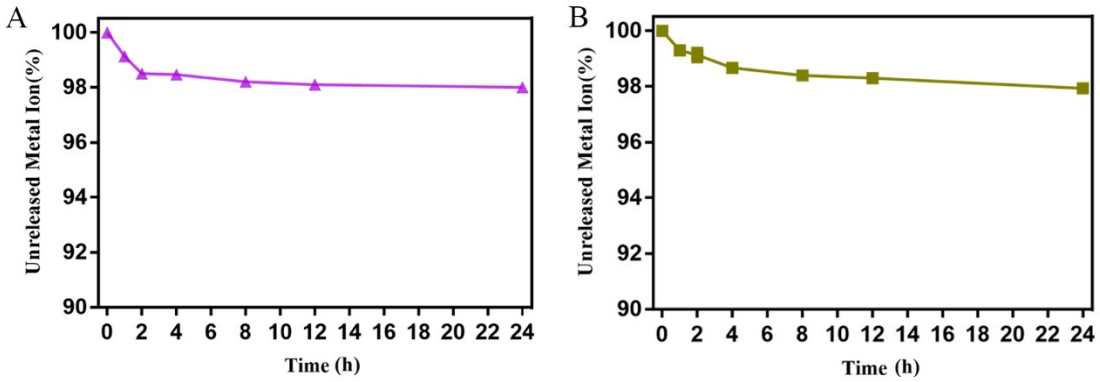


Fig.S3 Stability of PEG-PepMMP2-MNP-Gd (A) and PEG-MNP-Gd (B) with Gd^{3+} ions in PBS (pH = 7.4).

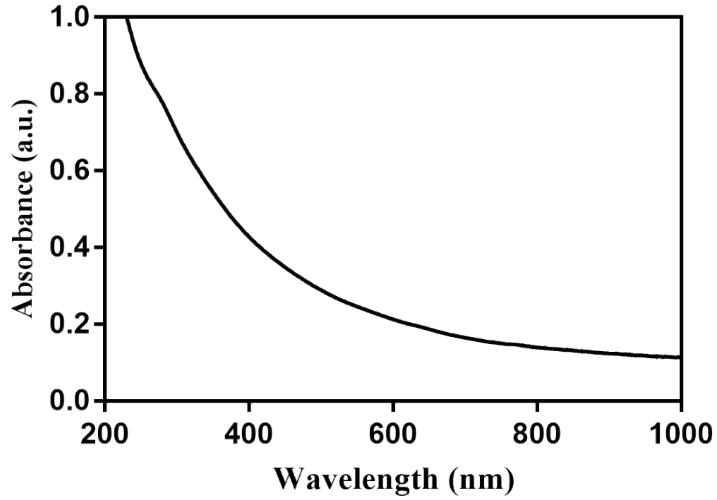


Fig.S4 UV-vis-NIR spectrum of PEG-PepMMP2-MNP-Gd. The nanoprobe exhibited a broad absorbance ranging from UV to NIR wavelengths for its potential application of PAI.

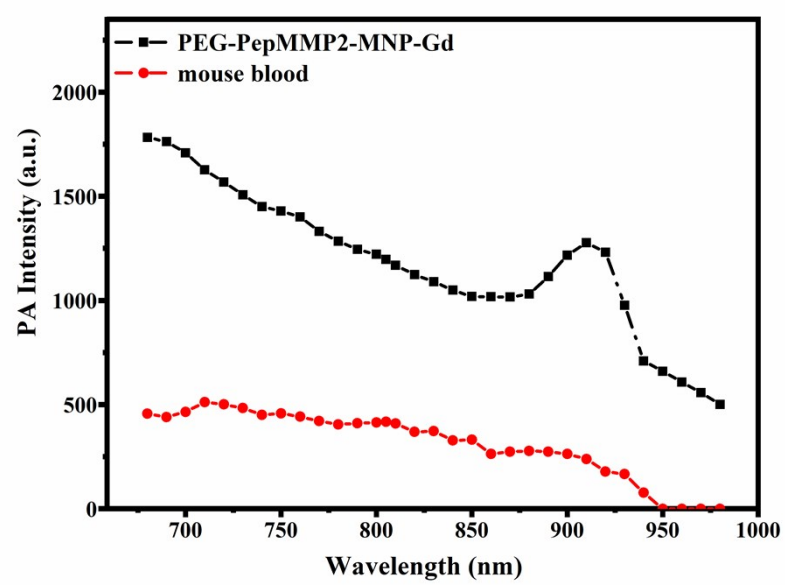


Fig.S5 The PA spectra of PEG-PepMMP2-MNP-Gd (800 μg/mL) and the mouse blood.

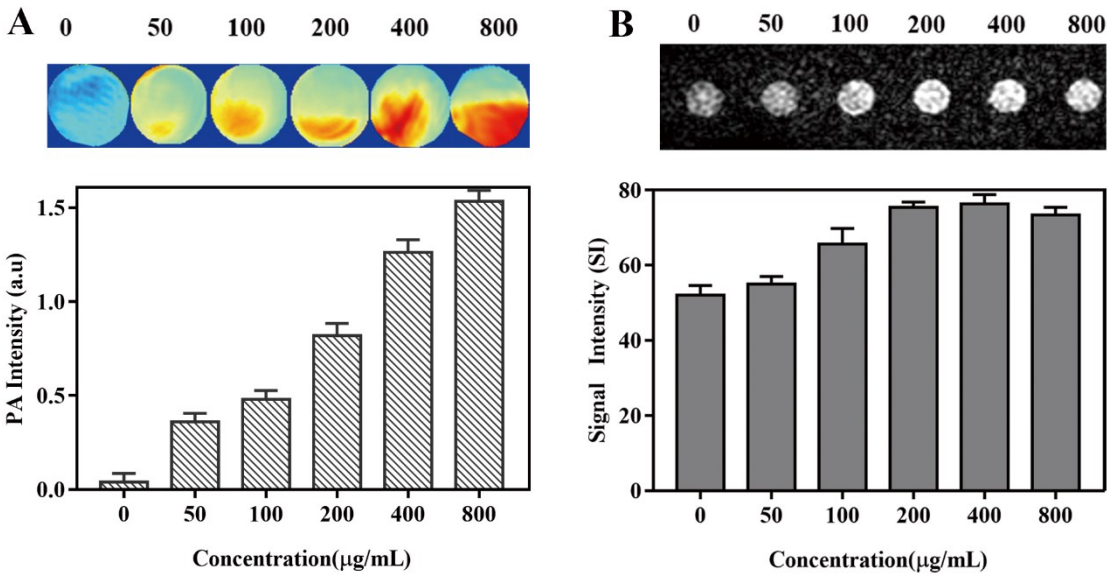


Fig.S6 (A) PA images and the quantitative data of 4T1 cells incubation with PEG-PepMMP2-MNP-Gd at various concentrations (0, 50, 100, 200, 400，and 800 μg/mL). (B) T1-weighted images and MR signal intensity changes of 4T1 cells incubation with PEG-PepMMP2-MNP-Gd at various concentrations (0, 50, 100, 200, 400，and 800 μg/mL).

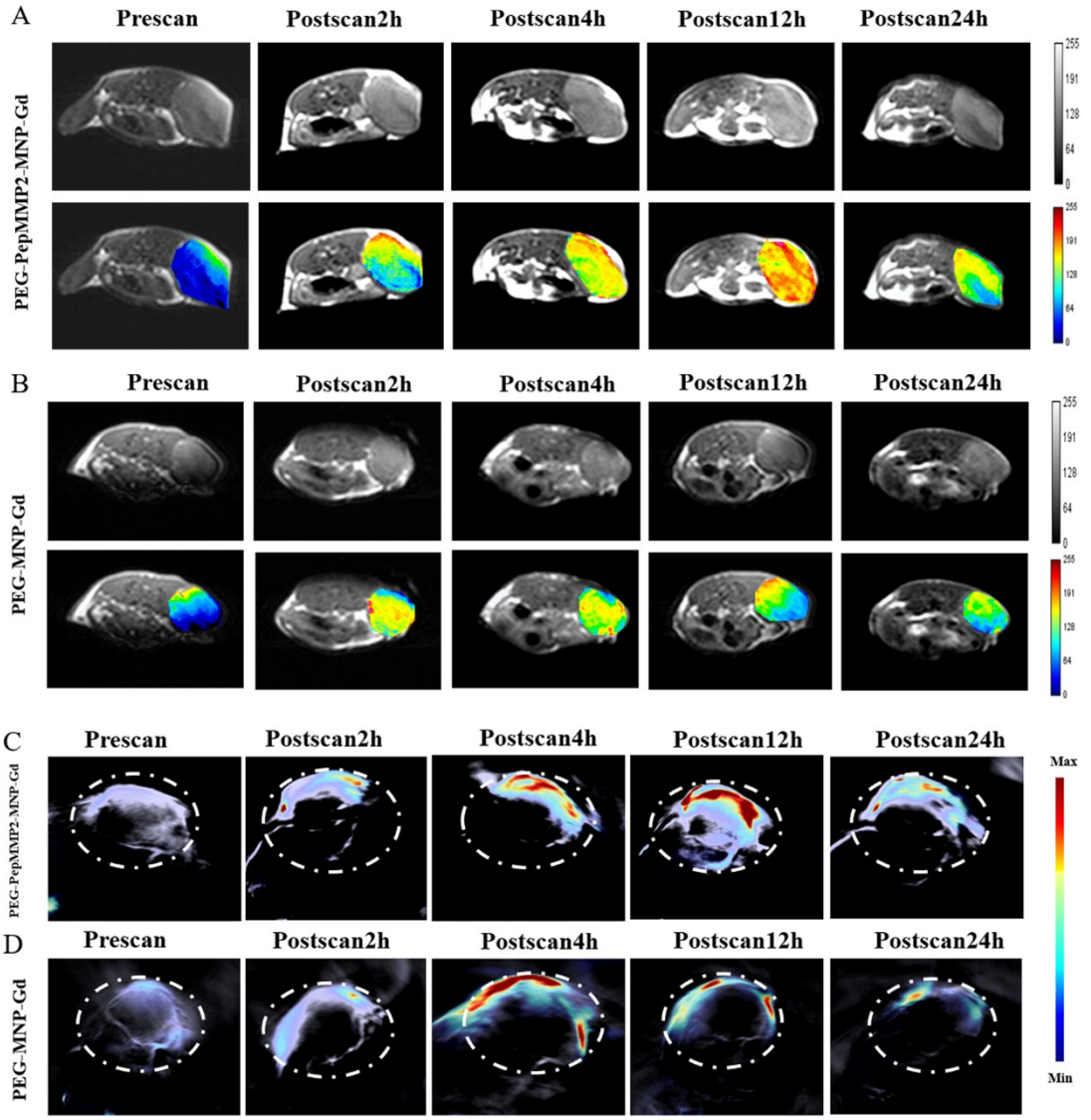
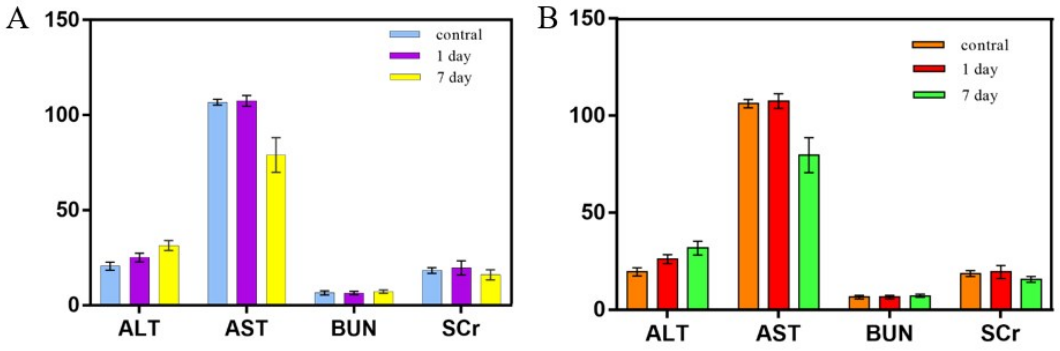


Fig.S7 MR and PA imaging studies of PEG-PepMMP2-MNP-Gd after intratumoral adminstration. T1-weighted MR axial images of tumor-bearing mice before (Prescan) and at various time points (0 h, 2 h, 4 h, 12h, 24 h) after injection of PEG-PepMMP2-MNP-Gd (A) and PEG-MNP-Gd using 3.0 T clinical MRI equipment (B). PA images in the tumor region collected by MOST imaging system before (Prescan) and at various time points (0 h, 2 h, 4 h, 12h, 24 h) after intratumoral injection of PEG-PepMMP2-MNP-Gd (C) or PEG-MNP-Gd (D). The white circles point the tumor sites. In the image of pre injection, there were little intrinsic contrast between the tumors and surrounding tissue. After 2 hours, a remarkable brightened effect could be clearly detected in the local injection site of tumor in both groups. At 12 h after injection, the

MRI signals and PA signals of active nanoprobe reached a maximum. But in the inactive nanoprobe, the signal intensity diminished quickly within 24 h. The results indicated that the active nanoprobe had a longer residence time signal in tumor tissue as compared with inactive nanoprobe.



C

Mean±SE		WBC(10^9/L)	RBC(10^12/L)	HGB(g/L)	HCT(%)
Reference range		5.67~14.84	8.16~11.69	124.00~189.00	43.00~67.00
Control		6.94	7.11	138.00	43.60
PEG-PepMMP2-MNP-Gd	1d	6.36	9.58	144.00	47.30
	7d	6.45	8.85	142.00	44.40
PEG-MNP-Gd	1d	6.96	8.38	150.00	46.30
	7d	7.27	8.45	147.00	48.40
Mean±SE		MCV(fL)	MCH(pg)	MCHC(g/L)	PLT(10^6/L)
Reference range		50.80~64.10	13.00~17.60	239.00~331.00	476.00~1611.00
Control		55.00	16.00	292.00	540.00
PEG-PepMMP2-MNP-Gd	1d	59.40	15.00	304.00	540.00
	7d	54.70	17.00	318.00	525.00
PEG--MNP-Gd	1d	56.36	16.70	320.00	483.00
	7d	54.40	14.85	242.00	643.00

Fig.S8 Blood chemistry indexes (ALT, AST, BUN and SCr) of mice for the control, and 1 d and 7 d after treatment with PEG-PepMMP2-MNP-Gd (A) and PEG-MNP-Gd (B). (C) Complete blood panel indexes of mice after PEG-PepMMP2-MNP-Gd and PEG-MNP-Gd treatments.