Electronic Supplementary Material (ESI) for Nanoscale.
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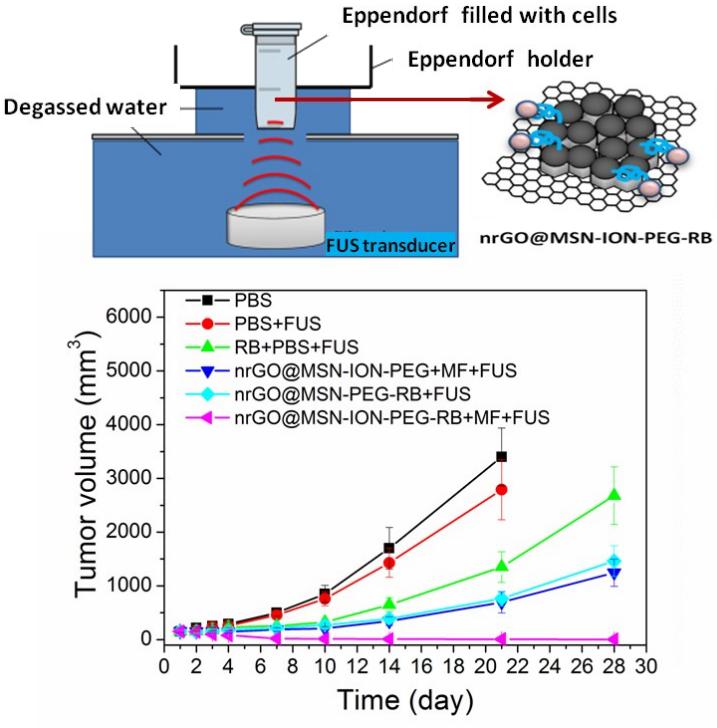
Table of content entry

A newly developed theranostic agent, nrGO@MSN-ION-PEG-RB was fabricated by nanosize reduced graphene oxide/porous silica nanosheets capped with RB-conjugated iron oxide nanoparticles. The nrGO@MSN-ION-PEG-RB demonstrates combination effect of sonodynamic therapy/sonication-induced hyperthermia and magnetic targeting for treating cancer cells.



Supporting information

A theranostic nrGO@MSN-ION nanocarrier with combination effect of sonodynamic therapy and ultrasound hyperthermia for treating tumor

Note-1. Acronyms list:

The acronyms list was added in the revised manuscript.
low-power FUS (LFUS)
Photodynamic therapy (PDT)
sonodynamic therapy (SDT)
photothermal (PTT)
reactive oxygen species (ROS)
photosensitizer (PS)
sonication-induced hyperthermia (SHT)
magnetic field (MF)
mesoporous silica (MSN)
reduced graphene oxide nanosheet (nrGO)
nanosize reduced graphene oxide/mesoporous silica nanocomposites (nrGO@MSN)
iron-oxide nanoparticles (IONs)
Fe_3O_4 /nrGO/mesoporous silica nanosheets(nrGO@MSN-ION)
Rose Bengal (RB)
Polyethylene glycol (*PEG*)
mesoporous silica grown on reduced graphene oxide nanosheet capped with Rose Bengal-PEG-conjugated iron-oxide nanoparticles (nrGO@MSN-ION-PEG-RB)

Note-2. Character of graphene oxide (GO) and reduced graphene oxide (nrGO)

Atomic force microscope (AFM) image:

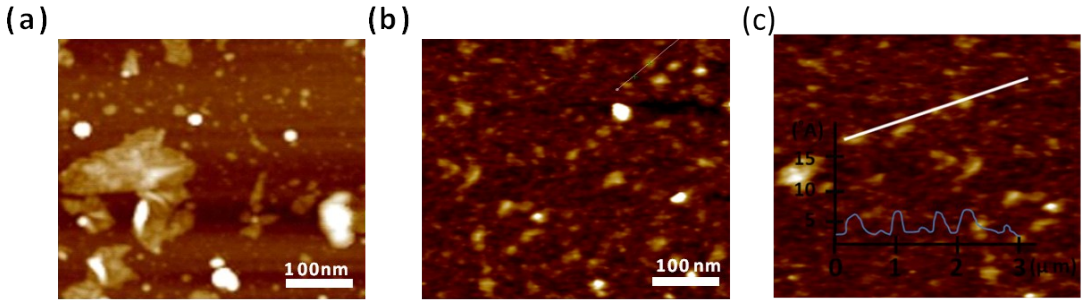


Figure S1. Atomic force microscope (AFM) image of (a) rGO and (b) nrGO (c) size measurement of nrGO.

Raman spectrum of graphene oxide (GO) and reduced graphene oxide (nrGO):

Figure S2 showed the Raman spectrum of graphene oxide (GO) and reduced graphene oxide (nrGO) obtained at an excitation wavelength of 532 nm. Generally, the intensity of D peak (1350 cm^{-1}) in the Raman spectra of GO is comparable to the G peak (1600 cm^{-1}). In contrast, D/G ratio would increase when GO was transferred to nrGO by thermal reduction. [Ref. 1] Thus, we can confirm that in this experiment, the nrGO used to synthesize nrGO@MSN is reduced graphene oxide but not graphene oxide.

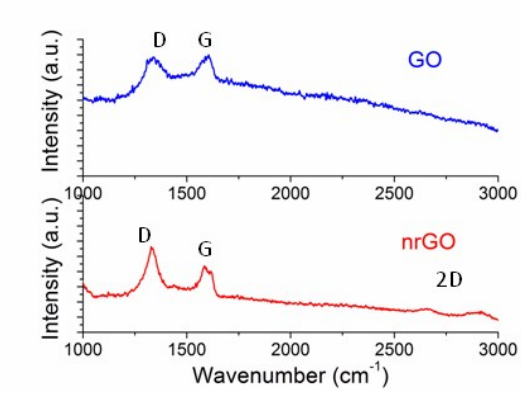


Figure S2. Raman spectrum of graphene oxide (GO) and reduced graphene oxide (nrGO)

FTIR spectra of nrGO@MSN, DMSA-Fe_3O_4 and nrGO@MSN-ION (Figure S3):

For the DMSA-Fe_3O_4, the typical Fe–O stretch is at 601 cm^{-1}, and the peak at 2374 cm^{-1} is assigned to S–H stretching. In addition, The C=O stretches at 1624 cm^{-1} is assigned to the stretching mode of carboxylate due to the interaction of the carboxylate anion with the Fe_3O_4 surface. For the nrGO@MSN-ION, Si–OH (1085 cm^{-1}) in the IR spectrum was identified as MSN due to the same as nrGO@MSN. The C=O stretching mode from the carboxylic acid was also detected, but its intensity was reduced because of amide bond formation. The finding indicates that both the N–H (1538 cm^{-1}) and C=O (1636 cm^{-1}) bonds were present because of the chemical reaction between the carboxylic acid group of DMSA-Fe_3O_4 and the amino group of MSN to form the amide linkage.

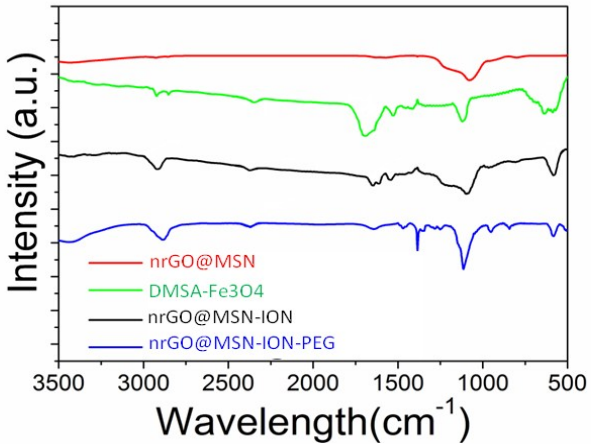


Figure S3. FTIR spectra of the nrGO@MSN, DMSA-Fe_3O_4, nrGO@MSN-ION and nrGO@MSN-ION-PEG.

Small angle X-ray diffraction pattern:

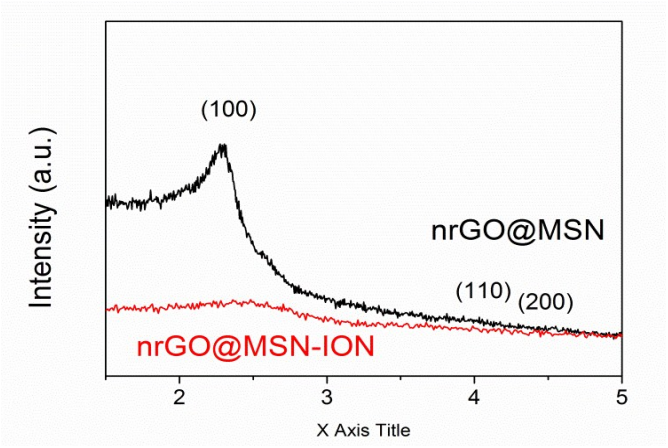


Figure S4. Small angle X-ray diffraction pattern of nrGO@MSN and nrGO@MSN-ION.

Nitrogen adsorption–desorption isotherms:

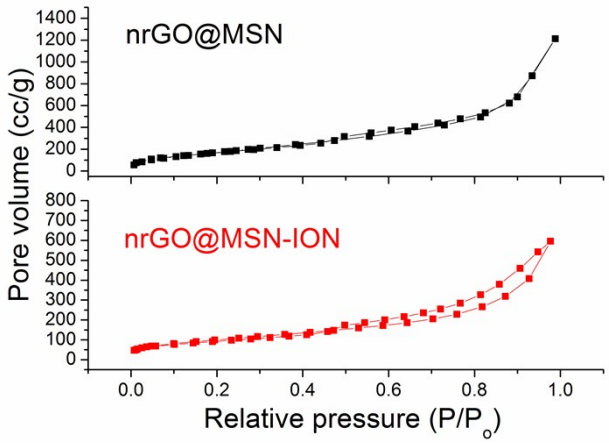


Figure S5. Nitrogen adsorption–desorption isotherms of nrGO@MSN and nrGO@MSN-ION

Field-dependent magnetization curves:

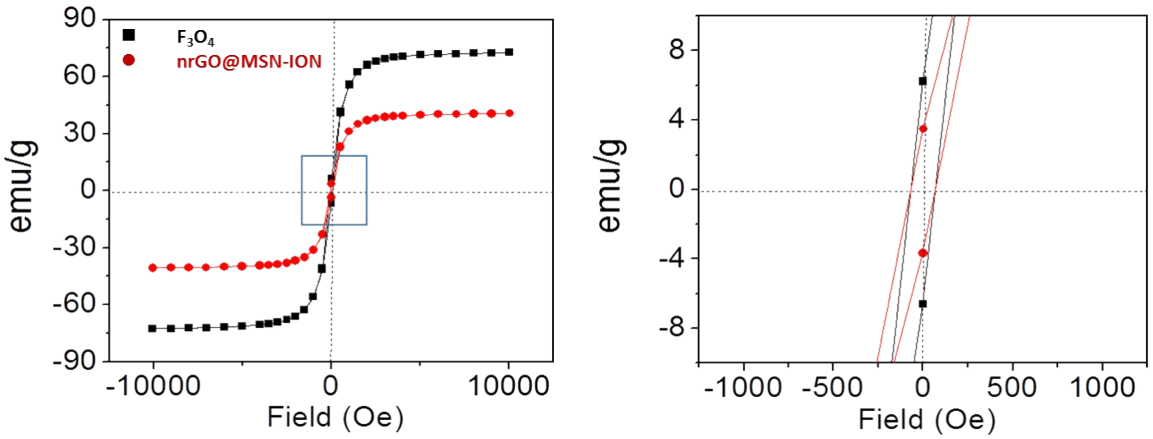


Figure S6. Field-dependent magnetization curves of as-synthesized Fe_3O_4 nanoparticles and nrGO@MSN-ION nanocomposite at room temperature.

Calibration curve of RB concentration:

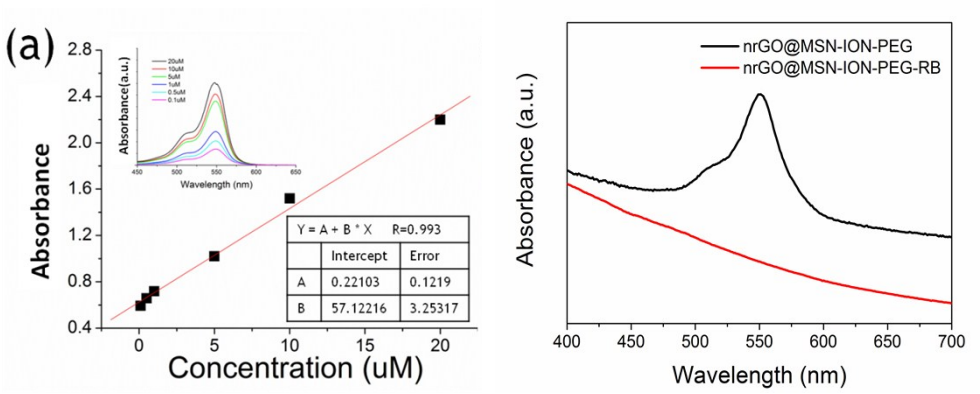


Figure S7. (a) Calibration curve of RB concentration with the inset showing UV-vis spectra of free RB solution with various concentrations. (b) UV-vis spectrum of nrGO@MSN-ION-PEG and nrGO@MSN-ION-PEG-RB solution.

Ultrasonic images:

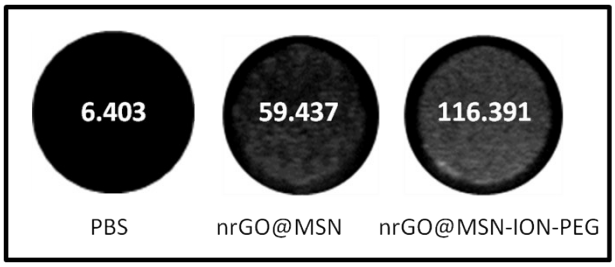


Figure S8. Typical US images with SonoVue bubble as compared with nrGO@MSN and nrGO@MSN-ION-PEG nanocomposites.

Table S1. Characteristics of nrGO@MSN and nrGO@MSN-ION nanocomposites

Structure Type	Particle Size (nm)[a]	SBJH(m^2/g)[b]	VBJH(cm^3/g)[b]	Pore Size (nm)[b]	Fe Conc.[c]
nrGO@MSN	**50-100nm**	**819.14**	**0.84**	**1.8**	**X**
nrGO@MSN-ION	**50-100nm**	**105.47**	**0.50**	**2.4**	**7.4%**

[a]From transmission electron microscopy (TEM); [b]Mesopore surface area (S_{BJH}) and mesopore volume (V_{BJH}) calculated by the BJH model from the BET absorption/desorption data. [c] Fe concentration of nanocomposites from ICP-Mass.

Note-3. Histological analysis

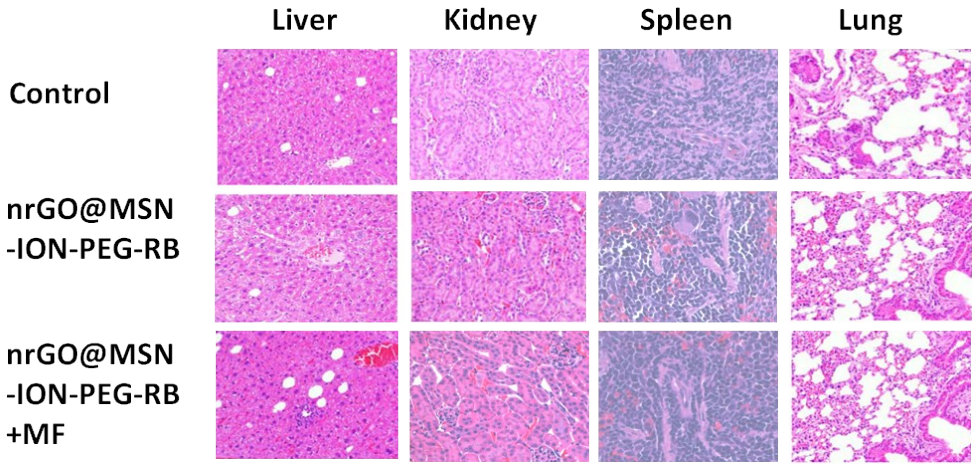


Figure S9. Histological analysis of liver, kidney, spleen, and lung collected from the nrGO@MSN-ION-PEG-RB-injected mice with and without application of magnetic field (MF) and control untreated mice.

Table S2. The accumulation ratio of various organs to tumor at 24 h post-treatment with and without magnetic field

	Lung/Tumor	Liver/Tumor	Spleen/Tumor	Kidney/Tumor
-MF	1.68	1.56	2.84	1.12
+MF	0.66	0.52	1.11	0.41