

SUPPORTING INFORMATION

Accurate *in vivo* tumor detection using plasmonic-enhanced shifted-excitation Raman difference spectroscopy (SERDS)

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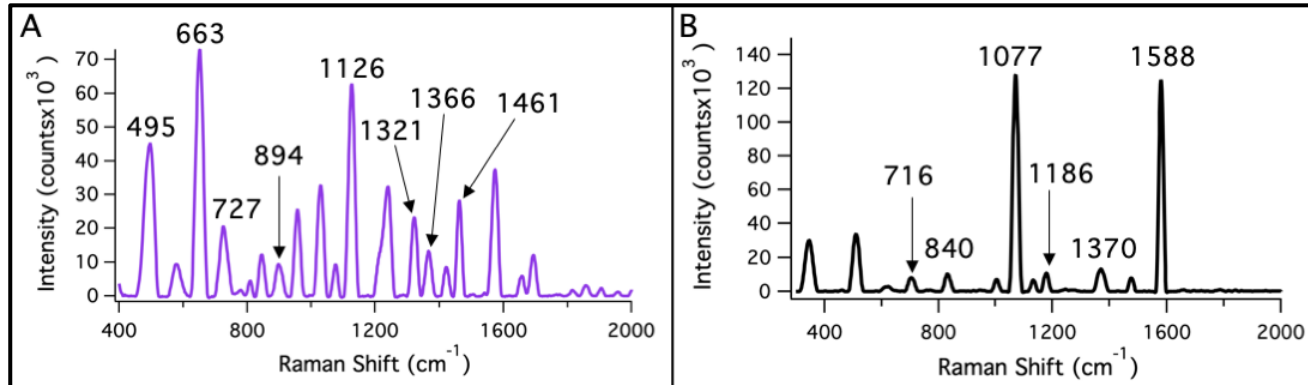


Figure S1. **A.** SERDS spectrum of the nanoprobes solution used in *in vivo* studies (SiO₂-coated-Ag-coated gold nanostars, Raman reporter = DTTC). **B.** SERDS spectrum of the nanoprobes solution used in lab tests (Ag-coated gold nanostars, Raman reporter = MBA).

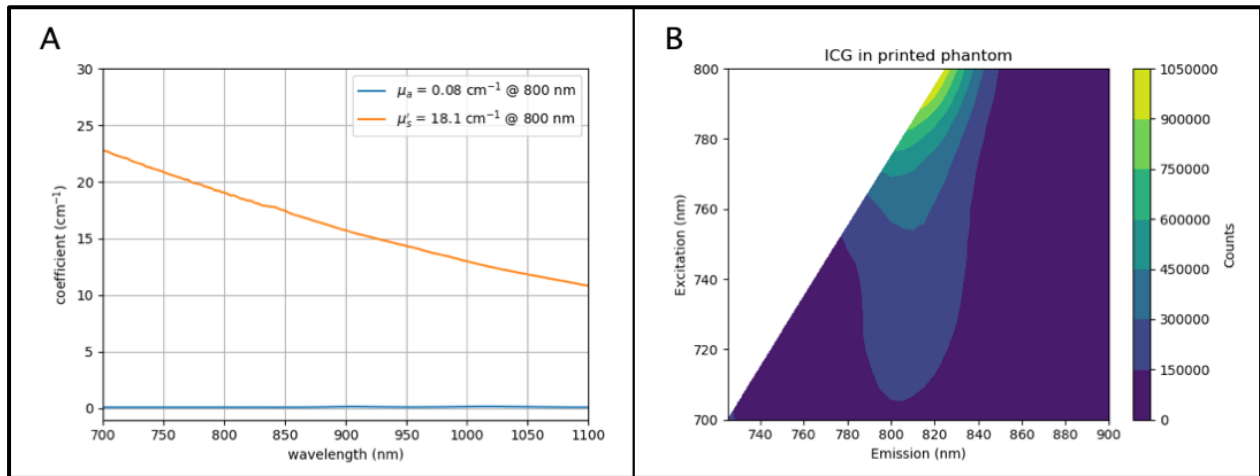


Figure S2. A. Scattering and absorption coefficient of the 3D-printed tissue phantoms used in the lab tests as a function of wavelength ($\mu_a @800 \text{ nm} = 0.08 \text{ cm}^{-1}$, $\mu_s @800 \text{ nm} = 18.1 \text{ cm}^{-1}$). **B.** Excitation-emission matrix for the fluorescence of ICG-3D-printed tissue phantom for excitation in the NIR.

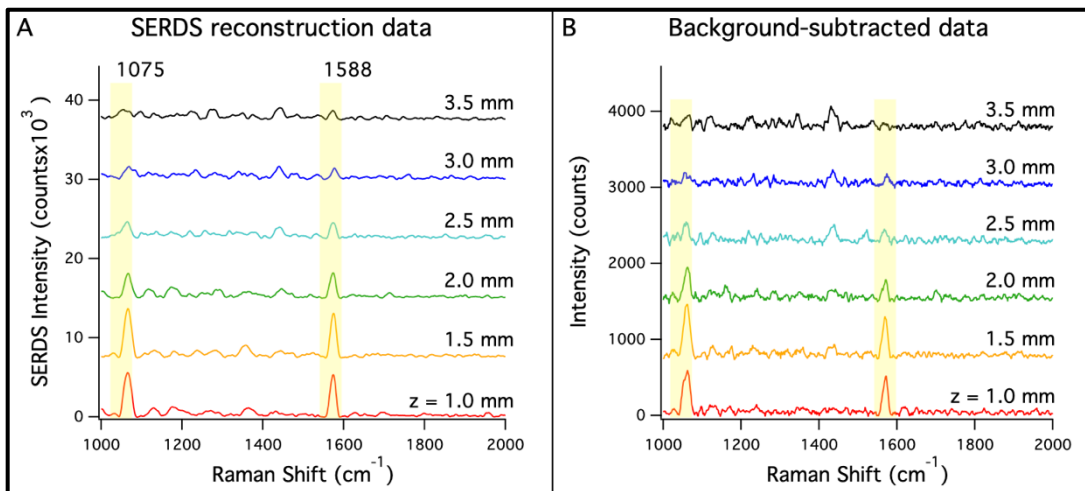


Figure S3. SERDS (A) and background subtracted (**B**) spectra measured on a tissue phantom with MBA-nanoprobes injected in channels at different depth. Each spectrum is labeled with the relative channel depth. The two main MBA bands are labeled and highlighted in the spectra.

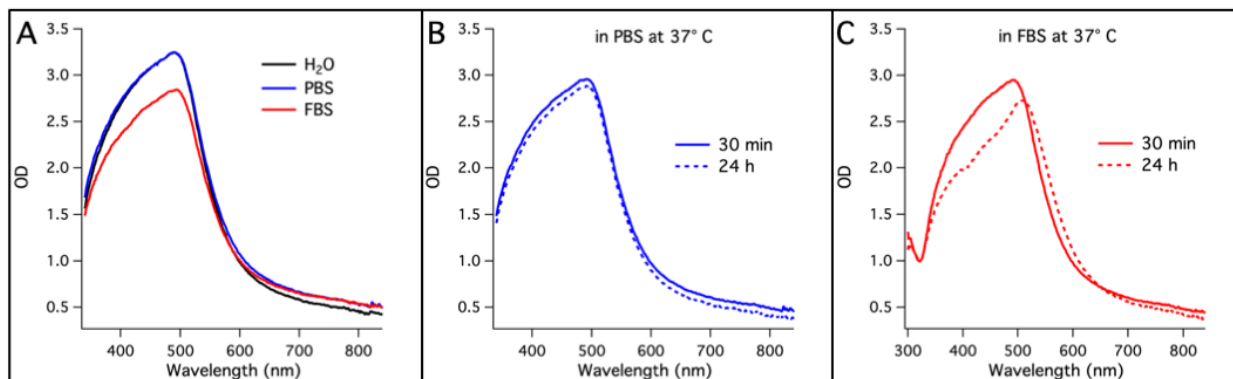


Figure S4. **A.** UV-Vis extinction spectra for the nanoprobe used in the *in vivo* studies in different media: water (H₂O), phosphate buffer saline (PBS), 90% fetal bovine serum (FBS). **B.** UV-Vis extinction spectra for the nanoprobe in PBS at different time points. **C.** UV-Vis extinction spectra for the nanoprobe in FBS at different time points.

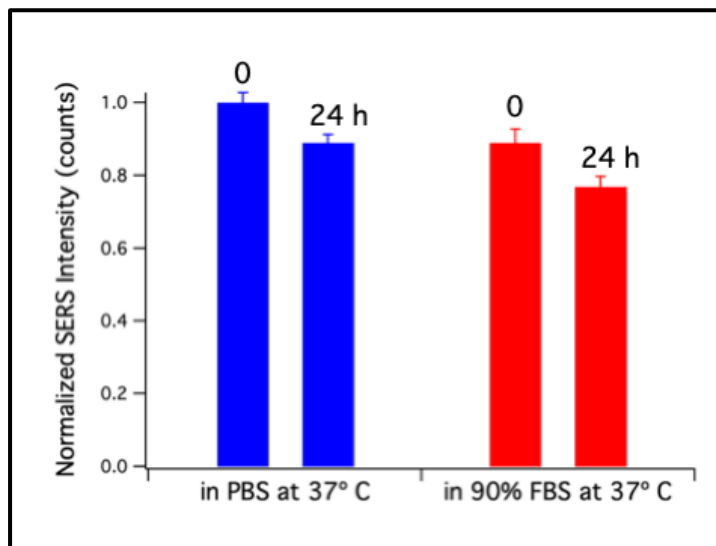


Figure S5. SERS intensities at 663 cm⁻¹ for the nanoprobe used in the *in vivo* studies in different media: phosphate buffer saline (PBS), 90% fetal bovine serum (FBS) at different time points.

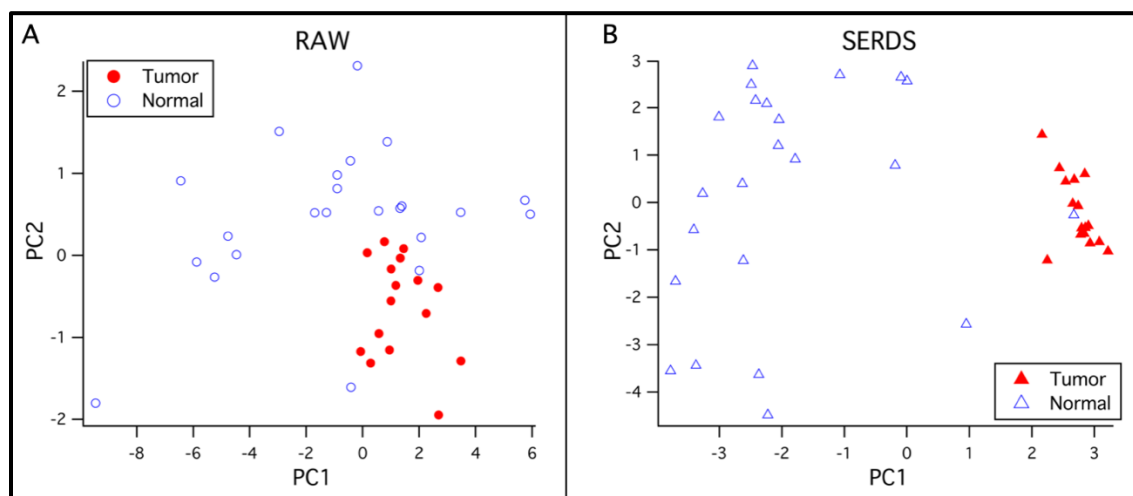


Figure S6. PCA analysis results for the *in vivo* measurements using the raw data set (A) and the SERDS reconstructed data (B). Reporter here are the PCA scores for the first two principal components for each set with data labeled based on the tissue type. Tumor data for control mice were excluded from this analysis.

Table S1. Tumor volume at the time of SERS-tag injection for the mice studied.

Mouse #	Tumor volume (mm ³)
1	102.1
2 (control)	30.1
3	20.3
4	32.7
5	73.3
6 (control)	55.5