Supporting information

Raman-Guided Bronchoscopy: Feasibility and Detection Depth Studies Using Ex Vivo Lung Tissues and SERS Nanoparticle Tags

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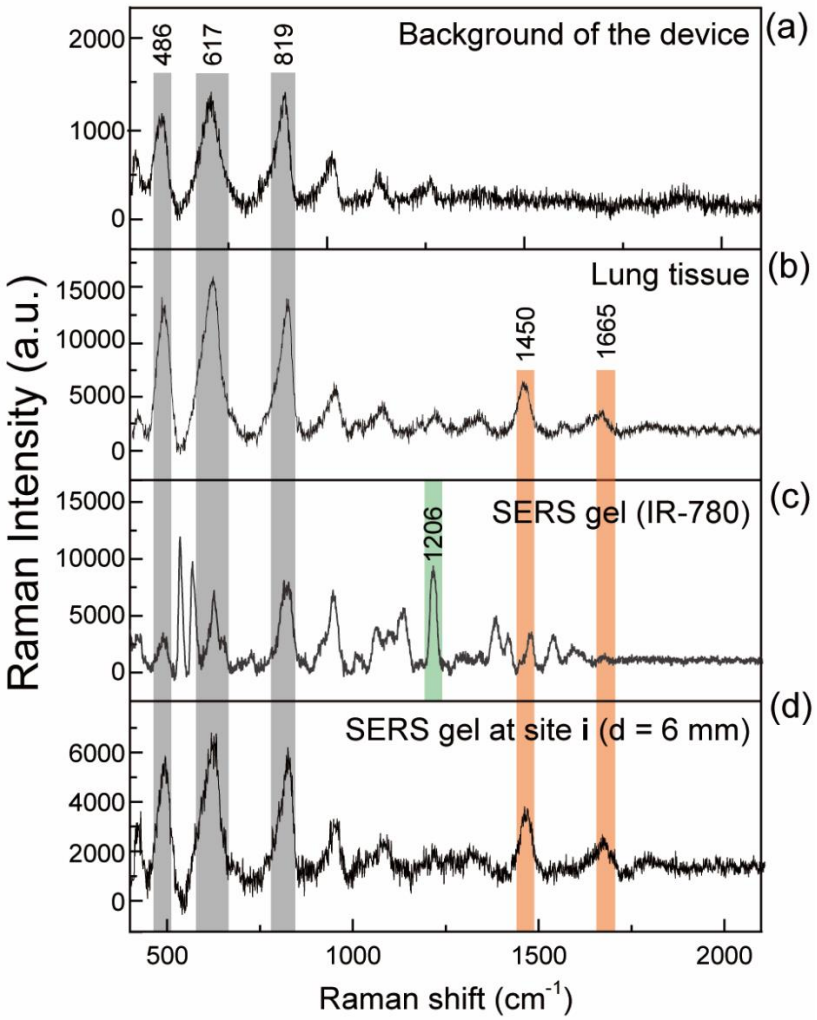

Figure S1. The Raman spectra of (a) device background (collected without any samples), (b) lung tissues, (c) a SERS gel containing IR-780 as the Raman reporter, and (d) the SERS gel embedded at site **i** of the lung tissue, with tissue thickness of 6 mm. All spectra were measured by the endoscopic probe, and the baselines of raw spectra were substracted. Peaks at 486, 617, 819 cm^{-1} observed in background spectrum are assumed to be caused by the optics fiber materials. Peaks at 1450 and 1665 cm^{-1} are assigned to lung tissues, corresponding to the CH_2 deformation peak and amine I band [1-2]. The SERS gels exhibited a strong bands at 1206 cm^{-1}, corresponding to C-H in-plane deformation of IR-780 [3]; this peak is not overlapped with the fiber or tissue background. When SERS gel was embedded in lung tissues with a distance of 6 mm, the collected signal was close to that of the pure lung tissue in (b).

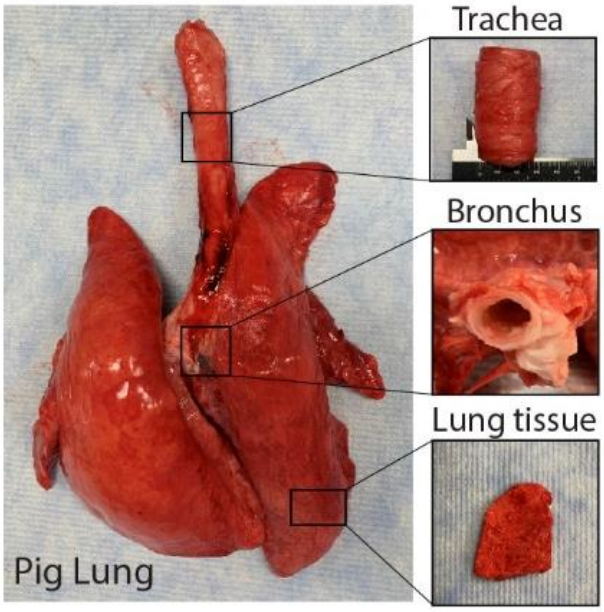

Figure S2. Photographs of a pig lung. The inner diameter and wall thickness of trachea is 20.7 and 3.4 mm; And that of bronchus is 12.18 and 1.7 mm, respectively.

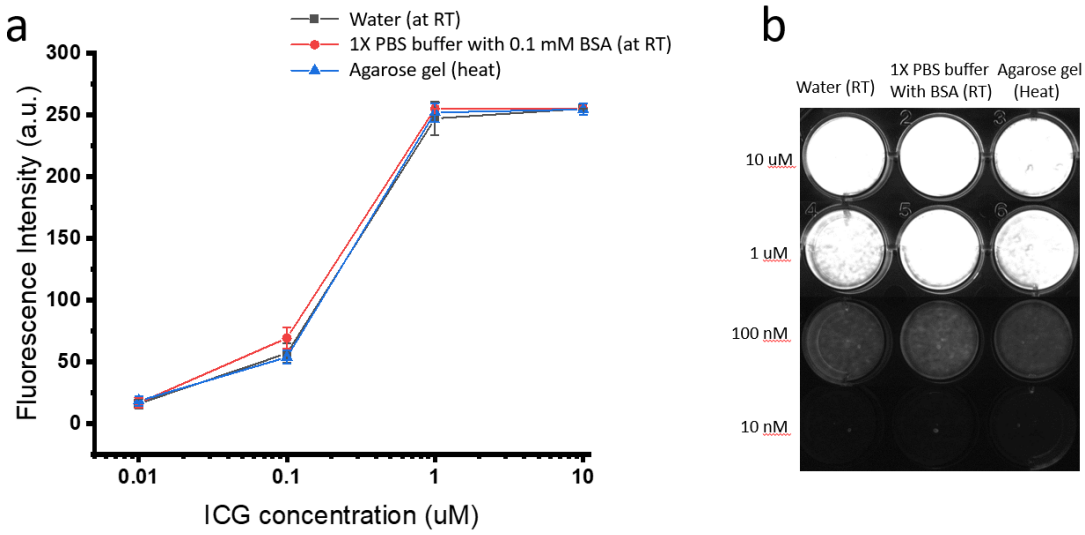

Figure S3. Comparison in the brightness of ICG in different media. (a) Quantative fluorescence intensities, and (b) Fluorescent images with different concentrations of ICG. The ICG power was first dissolved in DMSO solution with a high concentration, then diluted by water (black), 1x PBS buffer containing 0.1 mM bovine serum albumin (red), or heated agarose solution to form gels (blue). After forming gels, the brightness of ICG shows a very little decrease.

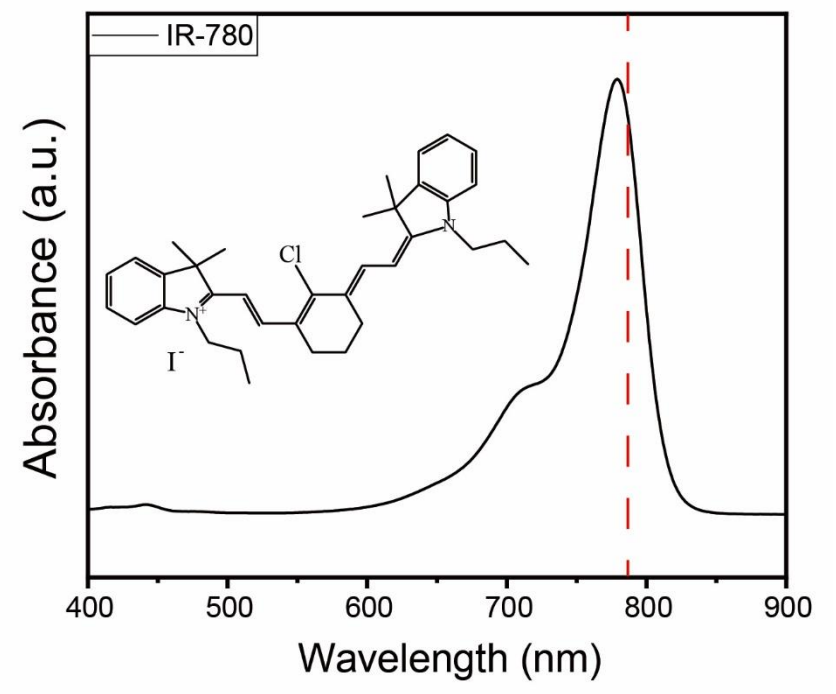

Figure S4. Molecular structure and absorption peak of IR-780. The molecules are dissolved in DMF. The red line indicated the laser wavelength (785 nm).

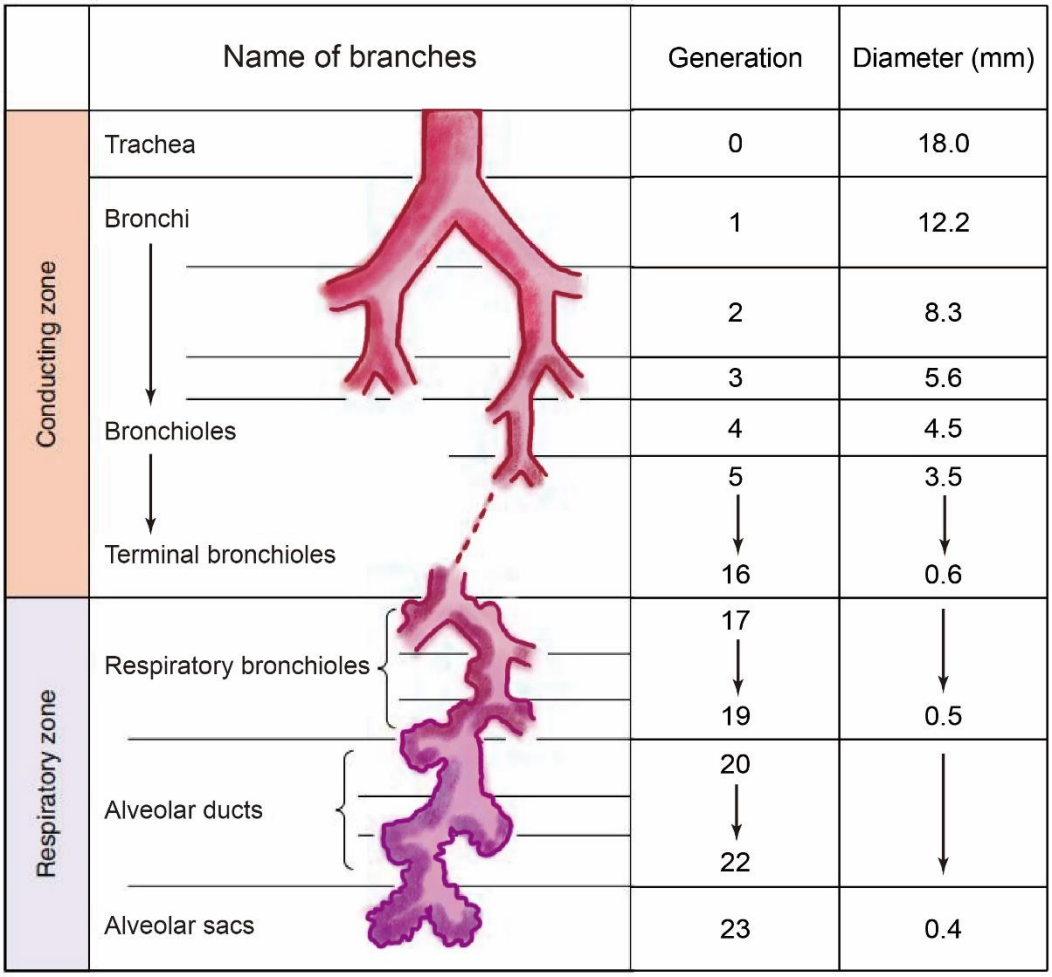

Figure S5. The scheme of lung airways, generations, and bronchus diameters. On average, a total of 21-25 generations are found between the trachea and the alveoli. Redrawn from ref [4].

Table S1. The fluorescence imaging depths in lung tissues with ICG gels of different concentrations as the imaging contrast.

ICG concentration	Detection depth in lung tissue	SNR at the detection depth
10 μM	3 mm	10.83 ± 3.16
1 μM	4 mm	6.15 ± 5.79
100 nM	3 mm	5.30 ± 3.40
10 nM	<1 mm	10.76 ± 2.11

References

[1] Rivas-Arancibia, S., et al., Structural Changes of Amyloid Beta in Hippocampus of Rats Exposed to Ozone: A Raman Spectroscopy Study. Front Mol Neurosci, 2017, 10, 137.

[2] G. Thomas, T.Q. Nguyen, I.J. Pence, et al. Evaluating feasibility of an automated 3-dimensional scanner using Raman spectroscopy for intraoperative breast margin assessment. Sci Rep 2017, 7, 13548.

[3] Varghese, H.T., et al., *IR, Raman and SERS studies of methyl salicylate.* Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2007. **66**(4): p. 959-963.

[4] Widmaier E P, Raff H, Strang K T. Vander's human physiology[M]. New York, NY: McGraw-Hill, 2006.