Peer Review File

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Reviewer Comments

<u>Comment 1:</u> Please define "signature Raman spectra" mentioned in line 65. <u>Reply 1:</u> We have added to lines 30 and 65 clarifying this phrase to mean "Raman spectra unique to each material". <u>Changes in the text:</u> Lines 30 and 65; pages 2-3

<u>Comment 2:</u> In line 96 the word "make" should be changed to "makes". <u>Reply 2:</u> We have modified our text as advised to line 96. <u>Changes in the text:</u> Line 96; page 4

<u>Comment 3:</u> In line 102 "such as gold or silver" should be between commas. Change it to "metal, such as gold or silver, that..."

<u>Reply 3:</u> We have added commas to line 102.

Changes in text: Line 102; page 4

<u>Comment 4:</u> It is unclear what the sentence in lines 113-115 is trying to convey. <u>Reply 4:</u> Thank you for this comment. Chemical enhancement is an incompletely understood mechanism of surface-enhanced Raman spectroscopy with the predominant theory suggesting that new surface complexes between the analyte and substrate enhance the Raman signal. We have clarified this in lines 113-115. <u>Changes in text:</u> Line 104, 113-115; pages 4-5

<u>Comment 5:</u> Please define acronyms (e.g. EGRF, HER2, Ag). <u>Reply 5:</u> We have added definitions to these acronyms. <u>Changes in text:</u> Line 135, 243, 261; pages 5, 9

<u>Comment 6:</u> Please describe where the fiber optic probe is inserted in line 244. <u>Reply 6:</u> We have clarified in line 244 that the fiber optic probe is inserted directly into the esophagus.

Changes in text: Line 244; page 9

<u>Comment 7:</u> The purpose of the three asterisk in line 321 is unclear. <u>Reply 7:</u> We thank you for noting this, and have removed the three asterisks and the preceding sentence from the manuscript. <u>Changes in text:</u> Line 321; page 11

<u>Comment 8:</u> In Fig 1. The caption references Fig 1(a) and Fig 1(b). Please edit the figure to remove the (c) label and include labels for (a) and (b).

<u>Reply 8:</u> Thank you for noting this. We have reuploaded a corrected figure with labels for (a), (b) with (c) removed. In addition, we have reuploaded an updated permission from the Royal Society of Chemistry from which this figure is reproduced. <u>Changes in text:</u> Figure 1, figure permissions

Comment 9: Please increase the text size within Fig 2. To improve readability.

<u>Comment 10</u>: Please readjust the color or labelling for Fig 2(b) to more clearly display the SERS spectra of esophageal cancer urine; the red is difficult to differentiate with the green standard deviation region.

<u>Reply 9 and 10:</u> We have increased the text size and readjusted the colors as advised for Fig 2. <u>Changes in text:</u> Figure 2