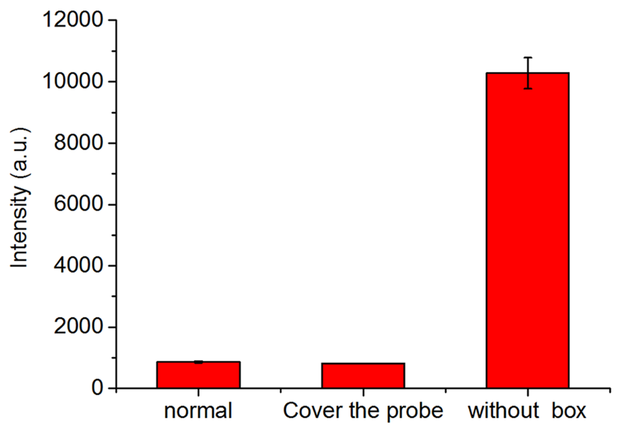


**Figure S1** Relevant results of the noise analysis. Three groups of investigations were conducted. The experimental conditions were exactly the same throughout all experiments in this study, labeled as the "normal group" in the figure. The endoscope probe was covered so that no light was able to enter through the probe, which is labeled as the "cover the probe" group in the figure. In the first 2 groups, it was necessary for the light in the data acquisition room to be left off and the endoscope probe to be kept inside the light-tight box during the experimental data acquisition. In the third group, the light-tight box was not used, and the entire CLE system was exposed in the data acquisition room. The light in the data acquisition room was also left off during the experimental data acquisition. The noise level of the first 2 groups was similar and far less than that of the third group. We concluded that the light-tight box played a significant role in isolating ambient light noise. Within real-world clinical application, the human body is substituted for the role of the light-tight box. Thus, such an experimental configuration is similar to the reality of clinical applications. The relevant results showed that the effect of ambient noise in this kind of experimental setup is negligible. CLE, Cerenkov luminescence endoscope.

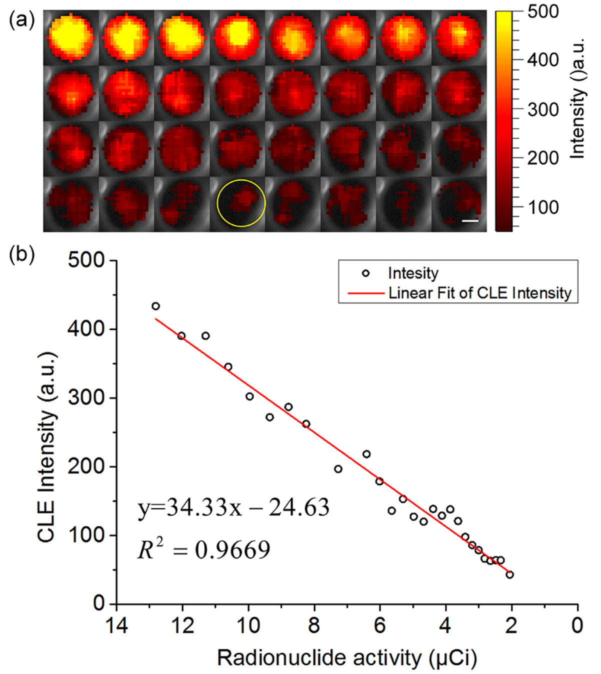


**Figure S2** Detection capability of the proposed CLE system for $^{18}$F-FDG. (A) Sequential images over the decay of radionuclide of $^{18}$F acquired by the CLE system at the image integration time of 300 s. The radionuclide decays from 12.81 to 1.41 μCi from the upper left to lower right. Scale bar: 2 mm. (B) CLE intensity as a function of the radionuclide activity of $^{18}$F and corresponding linear fitting results. (A) The minimum resolvable activity of the developed CLE system for $^{18}$F is 1.82 μCi. The corresponding theoretical minimum detectable activity is 0.72 μCi. These results revealed that the developed CLE system also had a submicrocurie detection sensitivity for radionuclide of $^{18}$F. CLE, Cerenkov luminescence endoscope.

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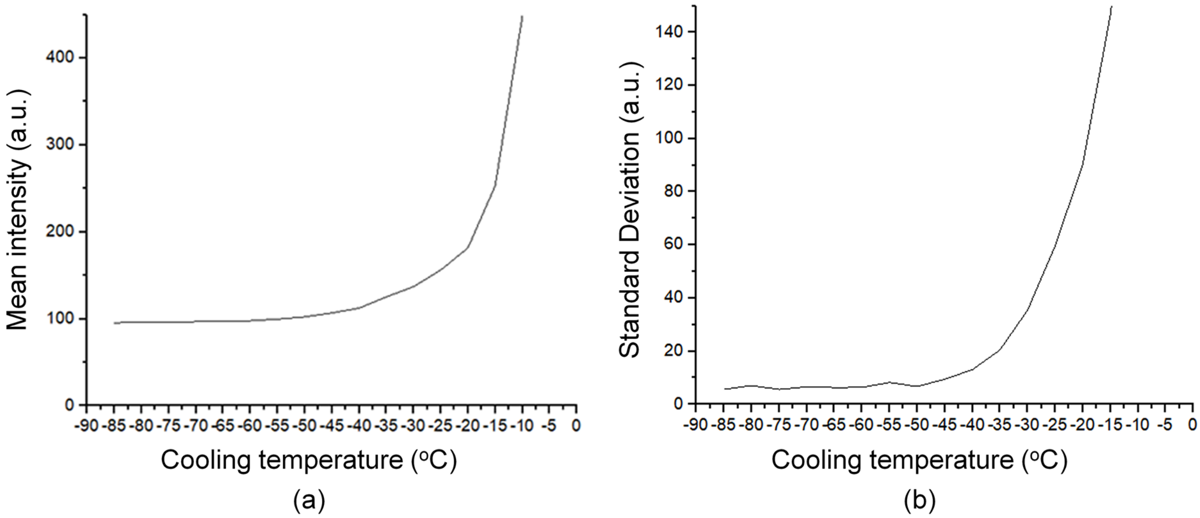


**Figure S3** Effect of the cooling temperature of the EMCCD on the signal collection efficiency. (A,B) show the change of the mean value and standard deviation of EMCCD signal intensity with its cooling temperature. We found that when the cooling temperature of EMCCD was lower than −50 ℃, the mean value and standard deviation of the detected signal tended to be flat. EMCCD, electron multiplying charge-coupled device.

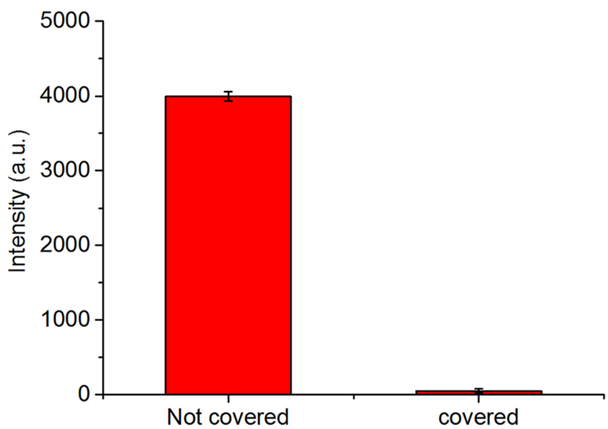


**Figure S4** Effects of scintillation effects arising from the interaction of high-energy radioactive particles with optical fibers. In the experiment, we used a piece of black cardboard to cover the radioactive source, which blocked the emission of CL light while still allowing high-energy gamma rays to pass through. We acquired 2 images using the proposed CLE system. One was acquired without the black cardboard covering the radioactive source, labeled as “Not covered” in the figure. The second image was collected with the radioactive source covered with black cardboard, labeled as “covered” in the figure. We found that the intensity of the image signal collected by the CLE system was much lower than that of the image signal without the black cardboard covering. This indicated that the scintillation effect produced by the interaction between high-energy gamma rays and optical fiber was very small. We can thus conclude that the influence of the scintillation effect on image acquisition was negligible under the experimental conditions of this study. CLE, Cerenkov luminescence endoscope.

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