Surface-enhanced Raman spectroscopy measurement of cancerous cells with optical fiber sensor

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We develop optical fiber nanoprobe by spark fused taper and acid corrosion methods. By coupling with 3-aminopropyltrimethoxysilane, gold nanoparticles are solidified onto the surface of fiber optic and then the optical fiber sensor is prepared using surface-enhanced Raman spectroscopy (SERS) measurement of the cell solution. The SERS of the esophagus cancer cell solution is then measured by direct detection and fiber detection methods, and the relationship between SERS fiber detection and the length of optical fiber sensor is studied. This is helpful for the SERS measurement of tissues and organs using the optical fiber sensor.

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Surface-enhanced Raman spectroscopy (SERS) is a useful analysis method in analytical chemistry. It provides label-free molecular vibration spectrum information[1], and it has wide applications in many fields, such as biomedical[2], environmental science[3], pharmaceutical industry[4], etc.

Cell composed of proteins, nucleic acids, sugars, lipids, vitamins is a basic composition unit, which constitutes a complex life[5]. In the process of cell canceration, multiplication of malignant cells leads to the abnormal metabolism; e.g., increased synthesis and decomposition of proteins. Compared with normal cells, cancer cells are different in chemical composition, configuration and conformation of molecules. Raman spectroscopy provides highly detailed chemical information about a tissue sample and is an objective method for the diagnosis of diseases in tissues[6]. In stokes scattering process, a laser light elastically scatters by interacting with the molecules. Part of this energy is transferred to the molecular vibrational excitations in the sample. The health condition of an organ can be detected by bio-molecules contained in the cells. And, the unique composition of these bio-molecules results in a unique vibrational band, which represents the vibrational motions of these bio-molecules. Therefore, changes of the proteins caused by canceration can be observed with the help of SERS by comparing normal cells with cancerous cells.

In recent years, the development of optical fiber detection technology has greatly promoted the development of biomedical research, especially the improvement of biological detection means[7,8]. With the help of optical fiber sensor in near-field optical microscopy and nanoprobe preparation technology, the fiber nanosensors have been developed rapidly and have been widely used[9,10]. Raman spectra of the cells are obtained by combining the optical fiber sensor nanotechnology with Raman spectroscopy to study the differences between normal and cancerous cells in the molecular level. It is useful for the early diagnosis of the diseases and *in vivo* Raman detection[11,12].

In this paper, the SERS of a single esophageal cancer cell was obtained by directly focusing on the cell. The fiber detecting method and the direct detecting method of the SERS of esophageal cancer cell suspension were studied, and the effects of the optical fiber length on the SERS measurement were also studied.

Firstly, the gold colloids were prepared with strong SERS enhancement effects by using the microwave heating method, and they were used as active substrates of surface-enhanced Raman scattering. Secondly, micro-scale optical cone was drawn out by using spark fused taper method; and then by using HF acid corrosion, nano-scale fiber optic cone was prepared. Thirdly, the gold nanoparticles were solidified onto the fiber optic cone's surface by using 3-aminopropyltri-methoxysilane (APTMS) as a coupling agent, and the high-sensitivity surface-enhanced Raman scattering sensor was prepared successfully.

Esophageal cancer cells were seeded in high-glucose Dulbecco's modified Eagle medium (DMEM) supplemented with 10% fetal calf serum, 100 units/mL penicillin, and 100 mg/mL streptomycin in a 5% CO_2 incubator at 37 °C. After approximately 24 h in exponential growth conditions, cells were washed with phosphate buffered saline (PBS) three times and digested, and suspensions were transferred to 1.5 mL centrifuge tubes. Then, the suspensions were centrifuged at 1000 rpm for 5 min. The cell cluster at the bottom of the tubes was re-suspended in PBS, and centrifuged again at 1000 rpm for 5 min. By repeating more than three

times, the esophageal cancer cell suspension sample was prepared.

In order to measure the SERS of the esophageal cancer cell suspension, the objective lens of the microscope on the core of the optical fiber was focused, and the nanoprobe was placed in the centrifuge tube. The fiber used in this experiment was a multimode fiber with a cladding of 125 μm and core of 50 μm. The SERS spectra of the fiber end were detected with Renishaw microscopic confocal Raman spectrometer under 785-nm laser excitation. The output laser power was about 10 mW and the SERS spectra were measured in a collection time of 10 seconds. Raman signals were collected in the spectral range from 200 to 1800 cm^{-1}. The experimental setup is shown in Fig. 1.

The optical fiber was about 6-cm long for the fiber detection SERS, as shown in Fig. 2. Figures 2(a) and (b) indicate the SERS of the suspension without esophageal cancer cells [Fig. 2(a)] and with esophageal cancer cells [Fig. 2(b)], respectively. Many characteristic peaks of esophageal cancer cells represent in Fig. 2.

Five optical fiber nanoprobes of 6 cm long were prepared under the same experiment condition (785-nm laser excitation, the output laser power 10 mW and 10 sec of collection time); the fiber detection SERS of esophageal cancer cells was measured with five probes. The spectra are shown in Fig. 2(b).

Before the fiber detection, the SERS of a single esophageal cancer cell was measured using direct detection method. The spectrum is shown in Fig. 3(b). The SERS

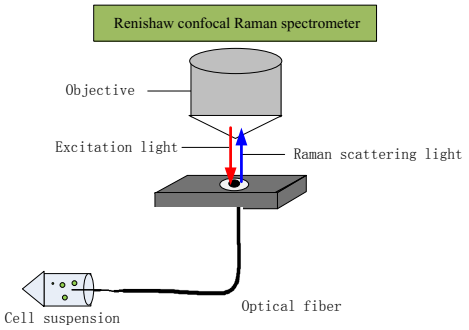

Fig. 1. Experimental setup for the fiber detection SERS of cancerous cells.

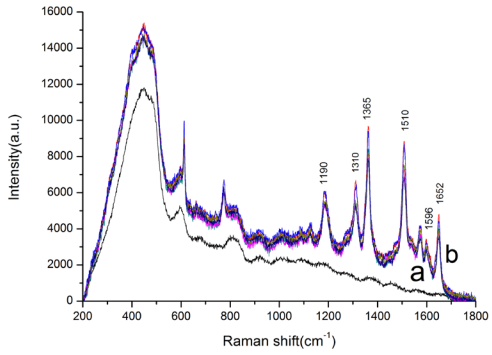

Fig. 2. The fiber detecting SERS of esophageal cancer cells with different optical fiber probes of 6-cm long.

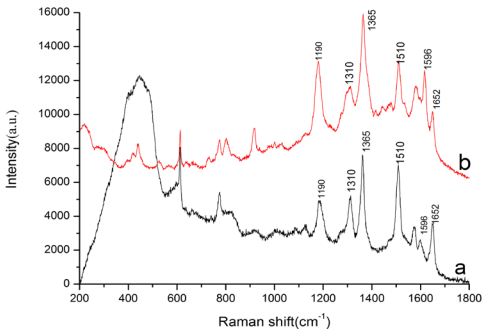

Fig. 3. The SERS comparison of esophageal cancer cells with (a) fiber detection and (b) direct detection.

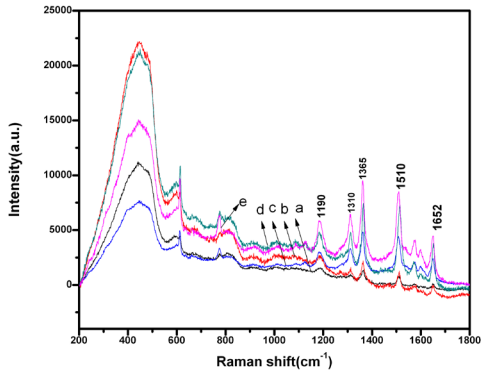

Fig. 4. The fiber detection SERS of esophageal cancer cells with optical fiber probes of different lengths of (a) 18 cm, (b) 15 cm, (c) 12 cm, (d) 9 cm and (e) 6 cm.

of direct detection [Fig. 3(b)] and the SERS of fiber detection [Fig. 3(a)] have many similar Raman peaks, although some peaks disappeared. This may be due to the attenuation of the transmission in optical fiber.

The optical fiber probes of 9-, 12-, 15- and 18-cm long were prepared, and they were used for the SERS fiber detection of the esophageal cancer cells. The results are shown in Fig. 4. The spectra from Figs. 4(a) to (e) represent the fiber detection SERS of esophageal cancer cells with optical fiber probes of 18-, 15-, 12-, 9- and 6-cm length, respectively.

From Fig. 4 it is understood that the length of optical fiber probe could affect the intensity of Raman spectra of esophageal cancer cells with fiber detection, and it may be due to increase in Raman intensity of the optical fiber.

The fiber detection SERS of the esophageal cancer cells is measured using the optical fiber sensor. The intensity of the Raman spectra is affected by the length of the optical fiber sensors, and the SERS measurement with the optical fiber is significant for the detection of *in vivo* Raman spectra of tissues or organs in the future.

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