RAMAN SPECTROSCOPY **OF SERUM** FOR CANCER DETECTION

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Abstract-**Laser induced auto- fluorescence and Raman spectra of serum from cancerous and normal people are measured and analyzed. Three Raman peaks were consistently observed from normal blood serum emission using 488.0nm and 514.5nm excitation of an Ar-ion laser, whereas no peak or only slight Raman peaks were detected from tumorous cases. The content of (- carotene) in the serum from normal is higher than that from the cancerous one ,this result agrees with other reports**.

***Key words*: laser, Fluorescence, Raman spectrum, blood serum, carcinoma, - carotene**

I. INTREDUCTION

Laser induced fluorescence spectroscopy and Raman spectroscopy are two kinds of optical tools to be used to probe the molecular structure and contents. It is well known that big biological molecules chromophores such as protein, flavins, riboflavin and porphyrins can display well-defined visible fluorescence spectroscopy with Raman spectroscopes are very sensitive to the microenvironment of pH, redox potential, bonding sites, polarity, ion concentration et [1], one can revdal the difference in the physical and chemical properties between the health and abnormal blood serum.

Resonance Raman scattering can enhance strongly certain vibration modes of chromophores because it involves transitions with the electronic absorption band of the chromophores when the induced laser wavelength approach the electronic absorption band.

In the late 1950's and early 1960's, fluorescence spectrum technology was widely used in the majority of the molecular system of tissues. In the early 1980's, laser induced fluorescence spectrum form normal and malignant tissues was measured and analyzed by R.R.Alfanl et al [2][3], and the difference of the spectroscopes form the two kinds of tissues was also used to diagnose the cancerous tissues, which normal tissue exhibited Raman spectra on fluorescence spectrum.

Because the difference between malignant cancer tissues and normal tissues, when the metabolic end product of cancer cells go into blood by circulation, the components and contents of the biological molecules and their local environment will be changed.

In this paper, the blood serum fluorescence spectroscopy from normal men and malignant patients is studied and analyzed .The results obtained by the laser induced native fluorescence and Raman spectroscopy reveal instrinsic difference between normal serum and cancerous serum. This new method may be a promising technology for diagnosing cancer from serum spectra.

II. METHODS AND MATERIALS

The experimental arrangement used to measure the fluorescence and Raman spectra from normal serum samples and malignant serum samples is shown in Fig.1. Anargon ion laser beam at 514.5nm was focused into the serum sample. The fluorescence signal from the serum was collected and focused into the entrance slit of a double 0.5-m grating scanning spectrometer (HRD-1) blazed at 500nm. A photo multiplier tube (PM; R456 Japan) located at the exit slit of the spectrometer measured the intensity at different wavelengths in scanning. The output signal of PMT was sent to lock-in amplifier (U.S Model 391) and an X-Y recorder combination to display the stable spectrum when measuring. The spectra were not calibrated for spectral response of the system. The laser power was about 100mW and laser was chopped at 700Hz. The spectral resolution was about 2nm.

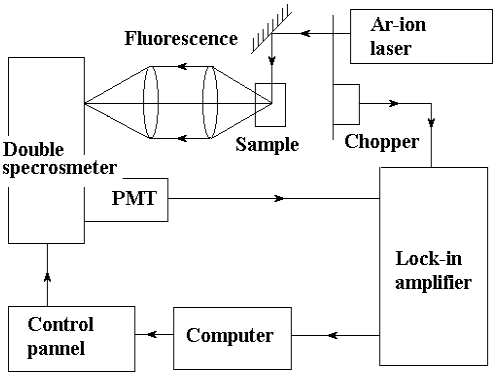

Fig. 1 Instrument

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Abstract

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The Hospital of DUT and The Hospital of Dalian Railway.422 normal serum specimens and 138 lung cancer serum specimens supported the experimental serum specimens and 330 other kinds of cancerous serum specimens have been measured.

For each sample, two spectra were measured: (1) The spectrum from 520nm to 560nm excited by 514.5nm (spectrum É); (2) The spectrum from 510nm to 530nm excited by 488.0nm after sample being radiated by laser (488.0 spectrum Ð) . What we recorded was relative intensity (absolute intensity divided

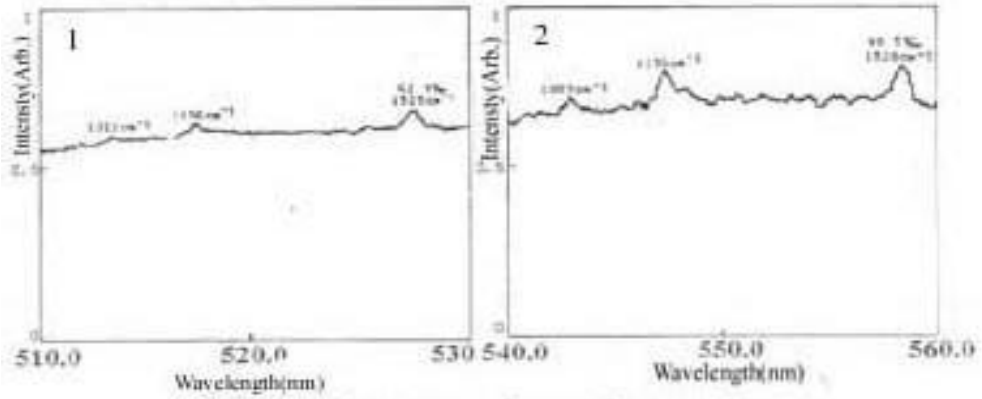


Fig.2 Typical spectrum of serum for normal case:
1 excite by 488.0nm; 2 excited by 514.5nm

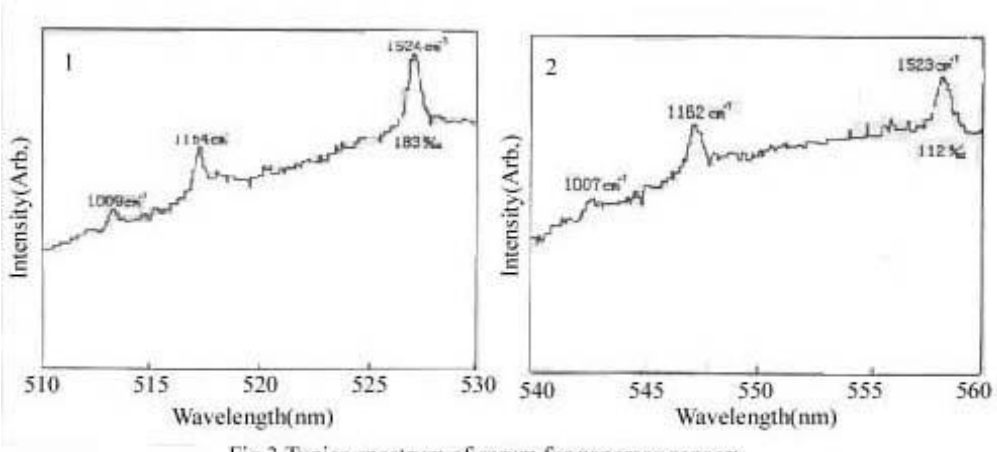


Fig.3 Typica spectrum of serum for pancreas cancer:
1 excited by 488.0nm; 2excited by 514.5nm

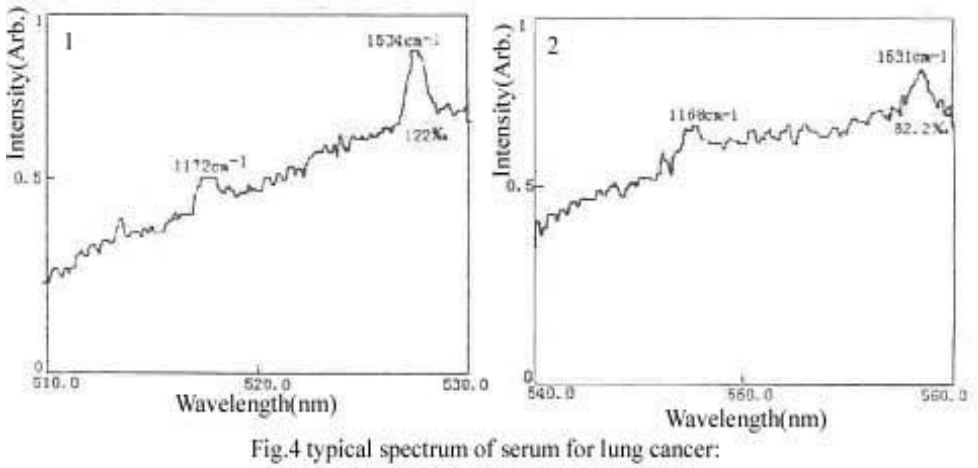
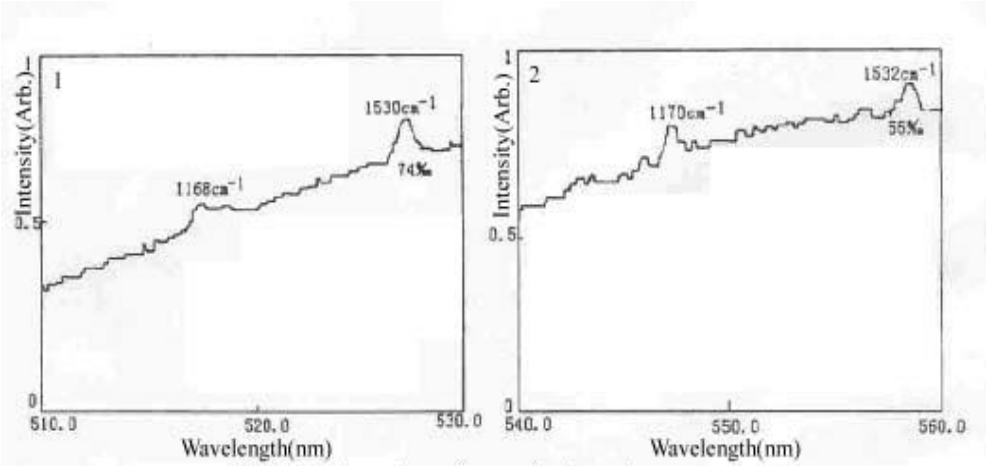


Fig.4 typical spectrum of serum for lung cancer:
1 excited by 488.0nm;2 excited by 514.5nm



Fir.5 Typical spectrum of serum for stomach cancer:
1 excited by 488.0nm; 2 excited by 514.5nm

by maximum intensity) in order to reduce such interference as the undulation of laser power.

III. Experimental Results

The typical auto- fluorescence and Raman spectrum obtained from the normal serum was displayed in Fig.2. The fluorescence peak is about 553nm. There are three stronger resonance Raman-shifted lines on the fluorescence spectral band, and the Raman line shifted by approximately 1518cm^{-1} is he strongest line, the line by 1006 $^{-1}$ the weakest. The relative intensities of the three Raman-shifted lines to the fluorescence signal are 1.94%, 8.28% and 8.96% respectively. Fig.3 shows spectrum from pancreas cancer serum. The main peak of fluorescence is at 552nm. 8 of 9 serum specimens have a smooth spectra from the esophagus cancer patients have the sane results as that of the pancreas cancer patients. Curve of 4 represents the typical fluorescence spectrum from the lung cancer serum, The fluorescence peak is at 552nm. Most spectroscopes from the lung cancer serums have no Raman-shifted lines or have the very weak resonance Raman signal. The relative intensity of the Raman line shifted by 1525 cm^{-1} to the fluorescence is about 1.72%.

Curve of Fig.6 shows the fluorescence spectrum of the stomach cancer serum with fluorescence peak at 554nm and weak Raman-shifted lines. The relative intensity of the Raman line shifted by 1518 cm^{-1} is about 3.02%.

IV. Discussion

The laser induced nature fluorescence and Raman spectra results indicate that the spectra from normal serums and from cancer patient serums are different. The main fluorescence peak excited at 514.5nm is from 549to 555nm. The normal serum spectra contour three strong resonance Raman-shifted lines, which are averagely shifted by 1010, 1160 and 1525 cm^{-1} respectively, while the fluorescence spectra from cancer serums contour no Raman-shifted lines or Raman-shifted lines weaker than the spectra from normal serum.

It was studied that the fluorescence spectra are partly from fiavin, cytochrome c and bilirubin, which is the metabolite of porphyrin ring in here proteins [3].

The resonance Raman-shifted lines can be assigned to -carotene. The part fundamental frequency, sum frequency and overtone Raman spectrum of - carotene in the CCl_4 solution are shown in Figure 6[4]. The three fundamental frequencies are shifted by 1005,1156 and 1523cm^{-1} ,and the Raman line shifted by 1523cm^{-1} is the strongest line. There is only one very weak polarized Raman-shifted line by 1539^{-1} over 800 cm^{-1} Raman-shifted spectrum range from the blank test of the liquid CCL_4 So it can be considered that liquid CCL_4 has no influence to the -carotene spectrum.

The experimental results show that the content of -carotene in blood serum from cancer patient is less than that from normal man. This conclusion is in agreement with the studies of Epidemiology and other experiments [5][6]. The survies of Eidemiology show the content of -carotene level in blood serum is much correlated with the danger degree of lung, uterus, stomach, and esophagus cancer. The higher is the contents of -carotene in blood serum, the lower is the danger of cancer[7]. The experiments of animal and cytology show that -carotene can inhbit the growth of cancer cells. Facts reveal that Vitamin A can not prevent cancer, although -carotene is the raw material of vitamin A.

V. Conclusion

In human blood serum, there are a great variety of fluorescence materials. And only a small part of them have been made certain of [6]. Furthermore, different wavelength

excitation often results in different emission. Other factors such as photochemical reaction, solution pH, temperature also has effect on it. Serum spectrum is combination of that fluorescence material emission. And another factor- absorption should also be taken into account.

In general, fluorescence emission is usually attributed to the transition of ð electron in conjugated molecule. Most fluorescence molecules have a carbon-atom-chain. The more the carbon atom number is, the bigger the value of fluorescence wavelength and the stronger the fluorescence emission are. Results of some studies indicate that porphyrin concentration occurs in cancerous serum [1][5]. Fluorescence ranging between 600nm and 640nm may be derived from the transition of ð electron in porphyrin in heme protein [7][8]. And riboflavin contributes to the fluorescence ranging between 510nm and 530nm[9]. In serum radiated by laser, many factors can influence its intensity distribution and spectral shape. The primary factor we supposed is photochemical reaction of some material accompanied with a serial of changes in serum.

Researches performed in epidemiology showed beta carotene has close relationship with the incidence of cancer [12]. The higher content of beta carotene in serum, the less incidence of cancer. Further studies discovered that beta carotene plays an important role in the process of anti-cancer [12][13].

In this paper, the differences of native fluorescence and Raman spectra from normal and malignant blood serums were displayed and analyzed. The normal serum fluorescence band contours strong resonance Raman lines, while cancerous serum fluorescence spectrum contours no Raman lines or relative veak Raman lines.

The intensities of the Raman scattering signals are correspondent to the contents of -carotene in blood serum. This result is agreement with the correlative studies. The further study of the changes of the resonance Raman signals may be one of main parameters to diagnose cancer.

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