NEAR-INFRARED RAMAN SPECTROSCOPY TOWARD CLINICAL LUNG CANCER DIAGNOSIS: RAMAN MEASUREMENT WITH FRESH HUMAN LUNG TISSUES

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Abstract: With fresh normal and cancerous lung tissues without any treatments, such as freezing and formalin-fixation, the near-infrared multichannel Raman spectroscopy clearly distinguishes normal and cancerous tissues as is the case of our previous reports using formalin-fixed lung tissues.

In the field of clinical cancer diagnosis, various medical imaging techniques such as computerized tomography, ultrasonography, magnetic resonance imaging, and positron emission tomography and so on, are utilized. With these medical diagnostic imaging systems, information of size, shape, and location of disease can be obtained. However, most diseases are caused by biochemical processes with molecular structural changes accompanied. Raman spectroscopy is sensitive to molecular composition and structure. By using Raman spectroscopy, more accurate diagnosis and elucidation of cancer mechanism will be able to be achieved. In order to apply Raman spectroscopy to human tissues, the problem of the background fluorescence must be solved. One effective means to diminish fluorescence is to use a near-infrared wavelength laser as the excitation source. From the comparison of the Raman spectra excited by two different near infrared lasers, we confirm that 1064 nm excitation gives much better signal-to-noise ratio than 785 nm (Fig. 1).

We have been developing deep near-infrared Raman spectroscopy using the 1064 nm line of the Nd:YAG laser [1]. A newly developed InP/InGaAsP multichannel detector has been used to achieve high sensitivity over the Raman shift range up to 1800 cm⁻¹ when excited by 1064 nm. For the feasibility study of 1064 nm excited multichannel Raman system for in-vivo lung cancer diagnosis, we used formalin fixed human lung tissues and obtained promising results [2,3]. Recently we studied fresh human lung tissues without any treatments, and found that 1064 nm excited Raman spectroscopy is capable of making clear distinction between cancerous and normal fresh lung tissues. By virtue of the results from fresh tissues, we can eliminate the worry about the effect of formalin fixation. Here, we show the results with fresh lung tissues in details.

For fresh lung tissues, the sampling for Raman measurement has been carried out at the hospital site from the dissected lung parts of 35 lung cancer patients right after surgery operation. Normal and cancerous tissues, blood, bronchi, lung blood vessel, and carbon matter were prepared as samples. From the Raman spectra of fresh normal and cancerous lung tissues, typical standard spectrum representing normal and cancerous tissues respectively could be extracted (Fig. 2). As shown in Fig. 2, a remarkable difference between the two spectra was found for the 1659 cm⁻¹ band of the amide I vibration. These standard spectra will be able to be used as criteria for distinguishing normal and cancer tissues. In addition, near-infrared Raman spectra of red blood cell and carbon matter existing in lung were also obtained. These spectra will be utilized for refining a crude spectrum into genuine lung spectrum by subtraction.

In conclusion, it was proved that normal and cancerous lung tissues can be distinguished by using our near-infrared multichannel Raman method. The results obtained with fresh tissues show the high applicability of near-infrared Raman system toward clinical lung cancer diagnosis.
Fig. 1. Near-infrared Raman spectra of the same fresh cancerous lung tissue. 
**Left**: 785 nm excitation (exposure time: 1 min, laser power: 46 mW, spectral slit width: 50 
•). **Right**: 1064 nm excitation (exposure time: 5 min, laser power: 38 mW, spectral slit 
width: 150 •).

Fig. 2. Typical standard near-infrared Raman spectra representing fresh normal and cancerous 
lung tissue respectively. These spectra were extracted from the Raman data obtained with 
fresh normal and cancerous lung tissues of 35 lung cancer patients.

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