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• *GASTRIC CANCER* •

Use of Fourier-transform infrared spectroscopy to rapidly diagnose gastric endoscopic biopsies

Qing-Bo Li, Xue-Jun Sun, Yi-Zhuang Xu, Li-Min Yang, Yuan-Fu Zhang, Shi-Fu Weng, Jing-Sen Shi, Jin-Guang Wu

Qing-Bo Li, Yi-Zhuang Xu, Li-Min Yang, Yuan-Fu Zhang, Shi-Fu Weng, Jin-Guang Wu, The State Key Laboratory of Rare Earth Materials Chemistry and Applications, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, China
Xue-Jun Sun, Jing-Sen Shi, Department of General Surgery, First Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China
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Correspondence to: Jin-Guang Wu, the State Key Laboratory of Rare Earth Materials Chemistry and Applications, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, China. wujg@pku.edu.cn
Telephone: +86-10-62757951 Fax: +86-10-62751708
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Abstract

AIM: To determine if Fourier-transform infrared (FT-IR) spectroscopy of endoscopic biopsies could accurately diagnose gastritis and malignancy.

METHODS: A total of 123 gastroscopic samples, including 11 cases of cancerous tissues, 63 cases of chronic atrophic gastritis tissues, 47 cases of chronic superficial gastritis tissues and 2 cases of normal tissues, were obtained from the First Hospital of Xi'an Jiaotong University, China. A modified attenuated total reflectance (ATR) accessory was linked to a WQD-500 FT-IR spectrometer for spectral measurement followed by submission of the samples for pathologic analysis. The spectral characteristics for different types of gastroscopic tissues were summarized and correlated with the corresponding pathologic results.

RESULTS: Distinct differences were observed in the FT-IR spectra of normal, atrophic gastritis, superficial gastritis and malignant gastric tissues. The sensitivity of FT-IR for detection of gastric cancer, chronic atrophic gastritis and superficial gastritis was 90.9%, 82.5%, 91.5%, and specificity was 97.3%, 91.7%, 89.5% respectively.

CONCLUSION: FT-IR spectroscopy can distinguish gastric inflammation from malignancy.

Key words: Fourier-transform infrared spectroscopy; Gastric endoscope; Gastric cancer; Chronic gastritis; Spectral analysis; Infrared detection

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INTRODUCTION

Fourier-transform infrared (FT-IR) spectroscopy can effectively provide chemical variation information of the structure and composition of biologic materials at molecular level[1]. Therefore, vibrational spectroscopy is becoming an increasingly powerful tool for the research on biochemistry of cancer[2-5]. Our research group has successfully used FT-IR spectroscopy to diagnose carcinomas, such as carcinoma of stomach, colon, esophagus, lung, salivary gland since 1995[6-9]. There are significant differences between the spectra of malignant and corresponding normal tissues[10-12]. In addition, FT-IR spectroscopy could detect molecular abnormalities which occur before the change in morphology seen under light microscope[13]. Therefore, FT-IR technology makes it possible to detect inflammatory and precancerous changes. Rapid, accurate and convenient detection of gastroscopic tissues can be performed using FT-IR spectroscopy if mid-infrared fiber optics technology and stomach endoscopy technology are combined, however the flexible mid-infrared optical fiber and mini probe are not yet available[14].

MATERIALS AND METHODS

Patients and materials

Informed consent was obtained from each patient prior to the study. A total of 123 fresh surgically resected gastric tissue specimens were obtained from the First Hospital of Xi'an Jiaotong University, China. There were 47 women and 76 men, aged between 18 and 80 years (mean 50.3 years). One endoscopic pinch biopsy, 1-3 mm in diameter, was obtained from each patient. The detected samples consisted of 11 cases of cancerous tissues, 63 cases of chronic atrophic gastritis tissues, 47 cases of chronic superficial gastritis tissues and 2 cases of normal tissues.

Spectral measurement

As the size of samples was too small to obtain an FT-IR spectrum with high quality, the modified ATR accessory linked to a WQD-500 FT-IR spectrometer was used. The FT-IR spectrometer was equipped with a liquid nitrogen cooled mercury cadmium telluride (MCT) detector.

The fresh tissue specimens were obtained in gastroscopy detection, and then immediately and non-invasively measured using the mobile FT-IR spectrometer near the operation room. The sample was put on ATR accessory to measure the spectrum. The background spectrum was collected. For the collection of each spectrum, 32 scans at a resolution of 4/cm, with a normal range from 4 000/cm to 800/cm were applied. It took about 1-2 min to non-invasively measure the spectrum. After measurement, the samples were stored in liquid nitrogen and sent for the pathologic examination of H&E staining as the reference in the spectral analysis.

RESULTS

The spectral differences among chronic superficial gastritis, atrophic gastritis and malignant gastric endoscopy samples were studied. For the sharper difference in the ratio of peak intensity, baseline corrections of the spectra were performed at first. Several typical spectra of malignant gastric tissues obtained by endoscopy are illustrated in Figure 1A. The spectral characteristics were similar to those of spectra of gastric tissues, which were obtained during surgical operation in our previous research[15]. The spectral features of malignant gastric tissues were in good agreement with the criteria established in our previous work[15]. For example, the broad -3 300/cm absorption band, assigned to N-H stretching vibration of protein and OH stretching vibration of water, was more intense in the malignant stomach samples because of the higher content of water in malignant tissues. C = O band near 1 741/cm was assigned to the fat in tissues, and C-H stretching vibration bands near 2 961, 2 927, and 2 853/cm were related to lipid and fat content and these bands usually disappeared in the spectra of malignant gastric tissues. -1 641/cm absorption peak belonged to amide I band of protein and H-O-H variable-angle vibration of water. In addition, amide II band of protein was located near 1 550/cm. The intensity of amide II band decreased in the spectra of malignant gastric tissues. Thus, the ratio of intensity of -1 641/cm band to -1 550/cm band was higher in the malignant gastric samples. The intensity of -1 400/cm peak was stronger than that of -1 460/cm peak in the spectra of cancerous samples. According to the statistical results, the relative intensity of $I_{1\,460}/I_{1\,400}$ was less than 1 for about 90% of malignant gastric samples. The intensity of absorption peak at about 1 308/cm increased. The peak position shifted to a low wave number. The peak position was lower than 1 310/cm for 72% of the malignant tissues. The intensity of -1 160/cm was often less than that of -1 120/cm in the spectra of stomach cancer samples.

The spectra of chronic atrophic gastritis were close to those of malignant gastric tissues (Figure 1B), and exhibited partial characteristic bands as those of malignant tissues. CH stretching vibrational band near 3 000-2 800/cm and C = O vibrational band about 1 740/cm were still weak in the spectra of atrophic gastritis samples. Compared with the spectra of malignant gastric tissues, the amide II band in the spectra of atrophic gastritis tissues was broader, and the relative intensity of amide II band to amide I band became higher. The decrease in the extent of the intensity of absorption peak near 1 460/cm was not significant, i.e., the intensity of band at about 1 460/cm became a little less than that at 1 400/cm in the spectra of atrophic gastritis samples. In the spectra of about 81% of atrophic gastritis samples, the relative intensity of $I_{1\,460}/I_{1\,400}$ was less than or equal to 1. Compared with the spectra of malignant tissues, the absorption peak near 1 310/cm was weaker in the spectra of atrophic gastritis samples. Similar to gastric cancerous tissues, the peak position of this band at about 1 310/cm often shifted to a low wave number, which was different from the situation of chronic superficial gastritis, indicating that

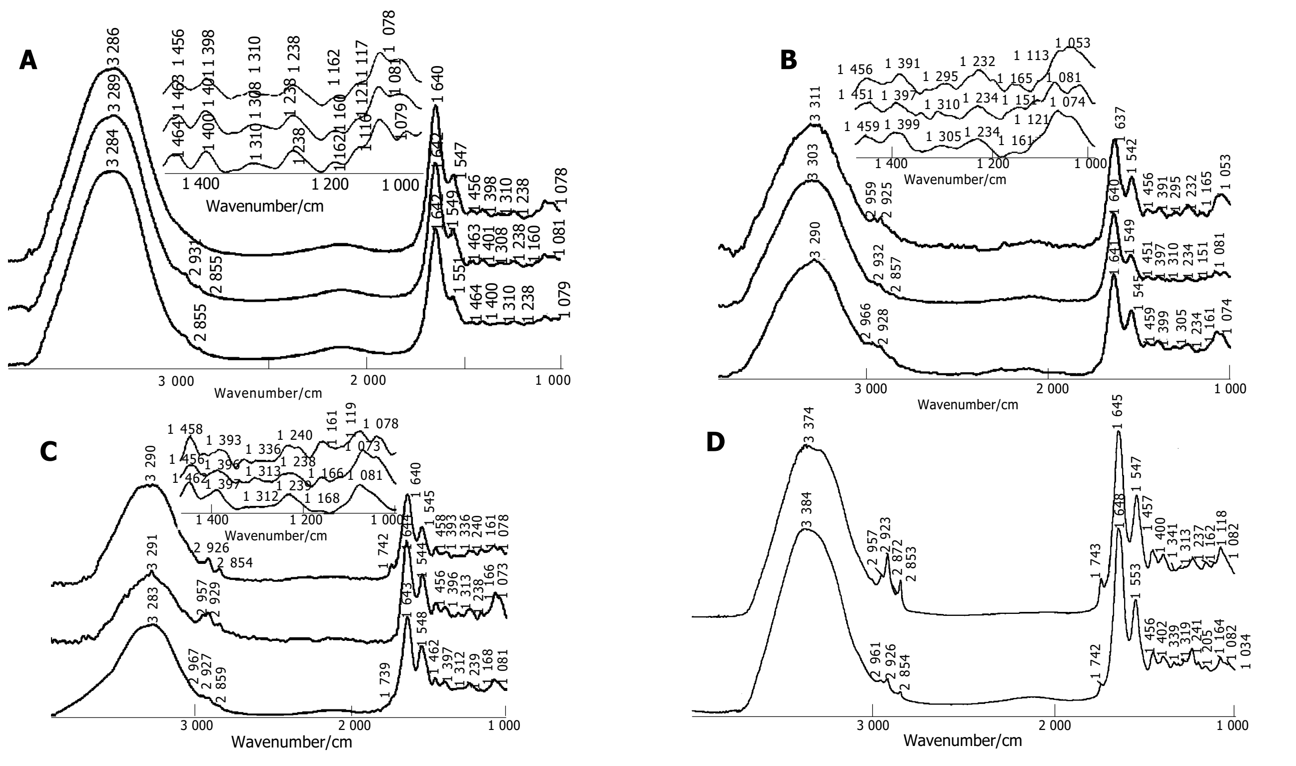

Figure 1 Typical FT-IR spectra of gastric endoscopy samples. **A:** Spectrum of malignant gastric tissue sample; **B:** spectrum of chronic atrophic gastritis tissue sample; **C:** spectrum of chronic superficial gastritis tissue sample; **D:** spectrum of normal gastric tissue sample.

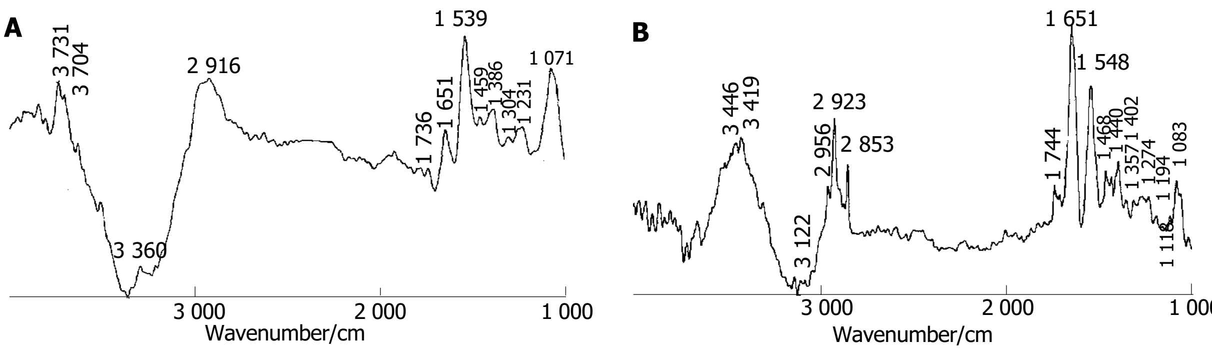

Figure 2 Subtraction spectra of gastric endoscopy samples. **A:** Spectrum of chronic atrophic gastritis tissue minus that of malignant gastric tissue; **B:** spectrum of normal gastric tissue minus that of chronic superficial gastritis tissue.

the peak position was lower than 1 310/cm for 73% of atrophic gastritis tissues.

The spectra of chronic superficial gastritis tissues (Figure 1C) were similar to those of normal stomach tissues[15] (Figure 1D). The spectral features were as follows. CH stretching vibrational band near 3 000-2 800/cm and C = O vibrational band at about 1 740/cm were strong in the spectra of superficial gastritis samples. In general, there existed strong and broad amide II bands in the spectra of superficial gastritis samples. The peak at 1 460/cm was stronger than that at 1 400/cm. The relative intensity of $I_{1\,460}/I_{1\,400}$ was higher than 1 in about 78% of superficial gastritis samples. The peak at about 1 250/cm was stronger, and the band near 1 308/cm disappeared or became weak and the position of this band often shifted to a high wave number, indicating that the peak position was higher than 1 310/cm in 80% of superficial gastritis tissues. Similar to normal gastric tissues, the intensity of peak near 1 160/cm increased and often became stronger than that at about 1 120/cm.

DISCUSSION

To enhance our understanding, the subtraction technique was performed in the spectral analysis[16]. The subtraction spectra (Figures 2A and B) could highlight spectral differences between chronic atrophic gastritis tissue and malignant gastric tissue, and between normal gastric tissue and chronic superficial gastritis tissue. From the two subtraction spectra, some new information could be observed.

Figure 2A illustrates the subtraction result of the spectrum of chronic atrophic gastritis tissue minus that of malignant gastric tissue. It verified that chronic atrophic gastritis tissues exhibited relatively stronger C-H stretching vibration, C = O stretching band, amide I, amide II than gastric cancer tissue. In addition, there was more water in gastric cancer tissue due to the strong negative band located near 3 360/cm in the spectrum of subtraction malignant tissue from chronic atrophic gastritis tissue.

Figure 2B shows the spectral differences between normal gastric tissue and chronic superficial gastritis tissue. The positive peaks in the region of 2 800-3 000/cm and near 1 740/cm were observed in the subtraction spectrum, suggesting that normal gastric tissue contains more components of long-chain C-H and C = O bonds. However, these peaks often decrease and even disappear in the spectra of gastritis and malignant tissues. Because triglyceride contains a large proportion of methyl, methylene and carbonyl, and fat in the region of malignant tissue is consumed because of the necessary nutritional and energy requirement in the development of carcinoma. At the same time, amide I and amide II bands are stronger in the spectrum of normal gastric tissue than in that of chronic superficial gastritis tissue, indicating that normal gastric tissue has more regular protein secondary structures, such as α helical structure.

In conclusion, the results in our study demonstrate that the sensitivity of FT-IR detection to gastric cancer, chronic atrophic gastritis and superficial gastritis is 90.9%, 82.5%, 91.5%, and specificity is 97.3%, 91.7%, 89.5% respectively. FT-IR spectroscopy is effective in distinguishing gastric inflammation from malignancy.

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