Clinical Application of the FICE Technique for Biopsy of Bronchial Mucosal Lesions

Qing-Zhang [1], An-Na Su[1], Na Liu[1], Xiao-Han Wang[1], Chang Liu[1] and Qin-Yao Zhang[2]

[1]*Endoscopy Center, The 10th People's Hospital of Shenyang, Shenyang, China*
[2]*Department of Cardiology, Shengjing Hospital of China Medical University, Shenyang, China*

ABSTRACT

Objective: To determine the diagnostic accuracy of flexile spectral imaging color enhancement (FICE) of abnormal morphologic changes in bronchial mucosal lesions.

Study Design: Descriptive, analytical study.

Place and Duration of Study: Department of endoscopy, the 10th People's Hospital of Shenyang, China, from January 2015 to April 2016.

Methodology: Patients aged 17-71 years, who presented with abnormal lesions of lung and bronchus, were included. Patients with severe heart disease, arrhythmias, aneurysm of aorta, blood pressure >160/100 mmHg, allergic to anaesthetic drugs, and unwilling to undergo endoscopy were excluded. The bronchoscopic FICE technique was used to observe abnormal bronchial mucosa in 85 patients. Targeted brushings, lavage, and tissue biopsies were performed under the FICE mode.

Results: With routine pathological results under white light as a reference, high definition electronic bronchoscopy combined with FICE biopsy yielded a positive rate for bronchial mucosal lesions and bronchial tumors in up to (73 87%) of cases.

Conclusion: The FICE technique showed significant enhancement of bronchial mucosal lesion diagnosis, which can help endoscopists in the early and accurate diagnosis.

Key Words: *FICE, Bronchial mucosal lesions, Biopsy, Diagnostic accuracy.*

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INTRODUCTION

Tracheobronchial disease seriously affects human health, and bronchogenic and lung carcinomas are characterised by high morbidity and mortality. The biopsy positivity rates of flat bronchial mucosal lesions, hyperplasia and early tumors have remained puzzling for endoscopists. Under white light bronchoscopy (WLB), which is widely used in the clinic, these lesions lack specific bronchoscopic manifestations.[1] and the mucosal boundaries are not clearly demarcated. Furthermore, the biopsy or cytological brushings for these lesions are not always targeted, and the positive rate of biopsy could not be significantly improved. The positive rate of cancerous lesions of early central type carcinoma of lung using WLB is only about 30%.[2] The new flexile spectral imaging color enhancement (FICE) technology can provide high contrast images, and help endoscopists more accurately determine the locations of the lesions, providing a strong guarantee for the improvement of the positive rate of these tests.[2]

Correspondence to: Qing-Zhang, Endoscopy Center, The 10th People's Hospital of Shenyang, 11 Beihai Street, Dadong District, Shenyang, 110044, China
E-mail: zhangqing_76@163.com

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Nowadays, FICE technique is widely used in the gastrointestinal endoscopy diagnosis. FICE can detect changes in early gastric cancer and confirm the diagnosis of cancer with low or half magnification[2]. However, rare studies of FICE use in bronchoscopy have been published.

This study was aimed to investigate the diagnostic accuracy of the FICE technique for an early diagnosis of abnormal morphologic changes in bronchial mucosal lesions.

METHODOLOGY

This cross-sectional study was conducted in the Department of Endoscopy, The 10th People's Hospital of Shenyang, China. A total of 85 patients, who underwent electronic bronchoscopy in our Hospital from January 2015 to April 2016, were included into the present study. Among these patients, 46 patients were males and 39 were females. The age of these patients ranged from 17 to 71 years, with an average age of 41 ±2.5 years.

The inclusion criterion included patients who presented with abnormal lesions of lung and bronchus. Exclusion criterion were: (1) patients who could not tolerate the bronchoscopy; (2) with severe heart disease, arrhythmis, aneurysm of aorta, blood pressure >160/100 mmHg; (3) with chronic respiratory disease having severe respiratory insufficiency; (4) allergic to anaesthetic drugs; (5) with severe bleeding tendency and disturbances of blood coagulation; and (6) who are unwilling to undergo endoscopy.

The Fujinon VP-4450HD and electron microscope EB-530H were adopted for the present study. The patients were instructed to

prepare before the operation. Electrocardiogram, coagulation time and thrombin test results were normal. The patients were fully anesthetised. Before the operation, the location and morphology of lung lesions were carefully studied through computed tomography (CT). Under the white light routine mode, the bronchoscope was inserted into the glottis, trachea, and left and right bronchis through the nasal cavity for observation. If abnormalities of the mucosa were found, it was shifted to FICE mode with a combination of 10 wavelengths for observation. After various comparisons, it was found that under the 2nd, 5th and 9th gears of the bronchoscope, the color contrast of the structures of the lesion were obvious, and the boundaries between abnormal sites and normal mucosa were obviously enhanced. Then, FICE images that highlighted the focus of these lesions were obtained. Combined with endoscopic results, blood vessel morphology and glandular openings, the morphologic patterns could be clearly observed. Furthermore, biopsy was performed at 3-4 sites of lesions under WLB mode and put it in a fixative. Then, the technique was converted to FICE mode to clamp 3-4 sites and the biopsy sites were subjected to targeted cytological brushings and lavage. In addition, blood pressure, heart rate and blood oxygen saturation were monitored during the operation. The pathological specimens of each patient were immediately sent to the Pathology Department of The Hospital and were studied by two pathologists, who were unaware of the experiment. Pathological examination was taken as the gold standard in finding abnormal morphologic changes in the bronchial mucosal lesions.

Collected data were analysed through computer software SPSS 22.0. Mean and standard deviations were calculated for quantitative variables. Frequency and percentage was calculated for qualitative variables. For the determination of lung cancer diagnosis, WLB and FICE methods were compared by using 2×2 tables; and paired Chi-square test (McNemar test) was used to compare the accuracy of the two methods. $P < 0.05$ was considered statistically significant.

This study was conducted in accordance with the Helsinki Declaration and conducted with approval from the Ethics Committee of The 10th People's Hospital of Shenyang. Written informed consents were obtained from all participants.

Table I: The positive rate of 85 patients using FICE.

Results	Number	Rate
Positive	73	86%
Bronchial tuberculosis	42	49%
Bronchiogenic cancer	31	36%
Negative	12	14%
Total	85	100%

RESULTS

During the bronchoscopy, 85 patients underwent biopsy, cytological brushings and lavage under the FICE mode, and 73 (87%) patients achieved a definite diagnosis. Among these patients, 42 were diagnosed with bronchial tuberculosis, and 31 were diagnosed with early bronchiogenic cancer (Table I). Pathology revealed tuberculous granuloma in 10 patients (24%), adenocarcinoma in 11 patients (35%), small cell carcinoma in nine patients (29%), squamous cell carcinoma in eight patients (26%), squamous cell carcinoma with severe atypical hyperplasia in three patients (10%), and squamous cell carcinoma with moderate atypical hyperplasia in two patients. (Table II). In 10 patients, pathology did not reveal a definite result; while in 62 patients, cytological brushings and lavage fluid cytology revealed a positive result.

Table II: Pathology results of all patients.

Results	Number	Rate
Bronchial tuberculosis	42	
Tuberculous granuloma	10	24%
Bronchiogenic cancer	31	
Adenocarcinoma	11	35%
Small cell carcinoma	9	29%
Squamous cell carcinoma	8	26%
Squamous cell carcinoma with severe atypical hyperplasia	3	10%
Squamous cell carcinoma with moderate atypical hyperplasia	2	6%

Table III: Comparison of positive rate of WLB and FICE in 31 patients.

WLB (n)	FICE (n)		Total (n)
	Positive	Negative	
Positive	21	1	22
Negative	8	1	9
Total	29	2	31

Three representative cases are illustrated here:Of the 31 cases diagnosed with bronchial lung cancer, 29 were positive and 2 were negative under FICE mode. In WLB mode, 22 cases were positive and 9 cases were negative (Table III). The FICE sampling accuracy was 93.5%, as compered with 71% on WLB. The Chi-square test P value was 0.039, indicating that the difference was statistically significant, and the FICE sampling accuracy was significantly improved. From this set of data, the results of the histology and cytology suggested that the positive rate of diagnosis (more than 87% and 73%, respectively) was significantly improved.

Case 1: Small cell carcinoma:

As shown in Figure 1A, there were changes in the mucosa and blood vessels under white light during the first examination. There were protrusions in the surrounding mucosa, and the boundaries were not obvious. No abnormal results were reported by pathology. The second examination revealed that under the enhancement of the FICE technique (Figures 1B, 1C and 1D), the surrounding mucosa was enhanced, and the crowding, distortion and distribution of blood vessels were clear. Then, 4-5 targeted pices of tissues were sampled, and cytological brushings and lavage were performed. Histopathological report was strongly suggestive of small cell carcinoma.

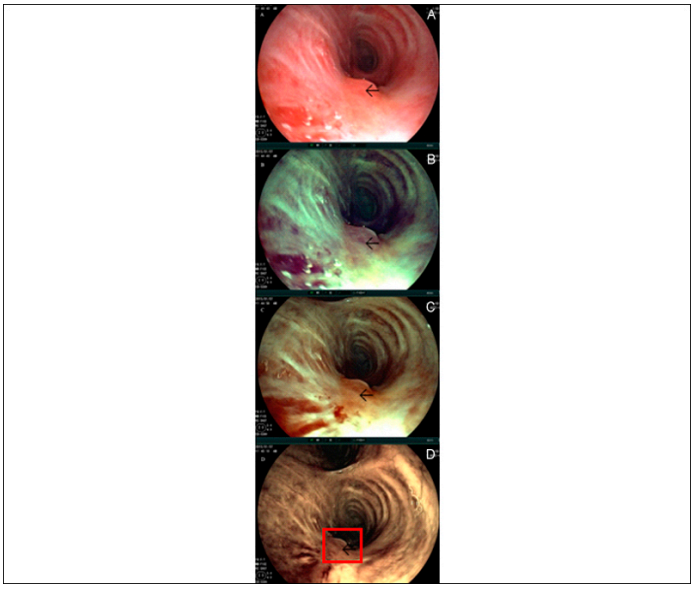

Figure 1: Small cell carcinoma mucosal changes under the FICE mode of the bronchoscope.
(A) WLB: Eminence lesion on the right lateral wall at the upper margin of the opening of the upper lobe of the right lung.
(B) FICE: Nodules clearly visible and blood vessels well demarcated.|
(C) FICE: Eminence lesion with brown red, and blood vessels clearly visible.
(D) FICE: Proximal nodules clearly visible.

Figure 2: Granulomatous inflammation mucosal changes under the FICE mode of the bronchoscope.
(A) WLB: Prominent of the opening membrane of the middle bronchus in the right lung, vascular disturbances, external pressure on the anterior wall of the B5 bronchial opening nodules, eminenece of mucous membrane of the superior wall.r wall.
(B) FICE: Nodules clearly visible and blood vessels well demarcated.
(C) FICE: Eminence lesion wiht brown red, and blood vessels clearly visible.
(D) FICE: Vascfular disturbances of the upper wall of the middle bronchus opening in the right lung.

Case 2: Granulation nodules:

As shown in Figure 2A, the first examination revealed that under white light, granulation protrusion could be observed in the mucosa. Biopsy revealed a small amount of mucosal epithelium, with interstitial inflammatory cell infiltration observed in the pathology. During the second examination under the enhancement of the FICE technique (Figures 2B, 2C and 2D), 4-5 pieces of tissues were sampled. The biopsy results met the criteria of granuloma.

Case 3: Vessel convergence:

As shown in Figures 3A, the first examination revealed the morphology and blood supply of the tumor under white light. However, the pathological results were not clear. During the second examination, under the 2nd, 5th and 9th gears of FICE mode (Figures 3B, 3C and 3D), tissues were sampled. Biopsy result revealed adenocarcinoma.

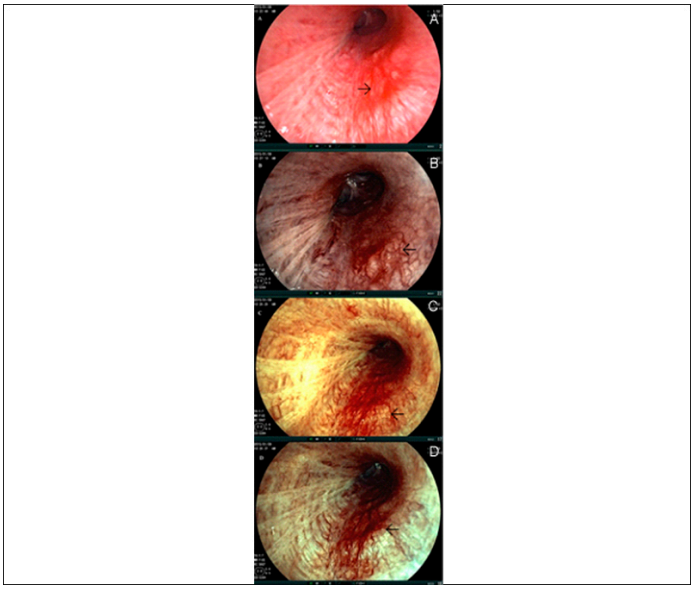

Figure 3: Blood vessel convergence mucosal changes under the FICE mode of the bronchoscope.
(A) WLB: The vascular network in the left common bronchomembrane is distorted.
(B) FICE: The vascular network with brown, proximal nodules clearly visible, active blood vessels.
(C) FICE: The vascular network clearly visible, clear boundaries with surrounding mucous.
(D) FICE: Proximal blood vessels clearly visible, clear boundaries with surrounding mucous.

DISCUSSION

Our results indicate that the FICE technique can significantly improve the accuracy of bronchial lung cancer biopsy by 93.5%, while WLB can only achieve 71% accuracy.

At present, bronchoscopy is the most effective examination tool for the diagnosis of bronchial mucosal lesions, which can accurately realize the diagnosis, location and biopsy of lung cancer. However, for early lung cancer and precancerous lesions, such as squamous dysplasia and carcinoma *in situ*, WLB alone is often inadequate. Only 29% of cancers *in situ* and 69% of microinvasive cancers were detected by WLB examination, according to the study.[3]

FICE is a new endoscopic diagnostic technique, and a technique of image enhancement that utilises spectral reflectance. The main principle is that the full spectrum white light image is subjected to light decomposition, and the extraction and recombination of the spectrum, in order to enhance the lesions. The single wavelength of this spectral image is endowed with red (R), green (G), or blue (B). Different combinations of RGB spectral images are processed to produce specific FICE images. Since a large amount of blood in

the blood vessels of the mucosa is the medium for propagating and diffusing light and hemoglobin is more prone to the absorption of a specific light wavelength, it thereby has asynchronous scattering and wavelength-dependence in the absorption and reflection of light. In a wavelength range of 400-700 nm, FICE technology can set arbitrary wavelengths with a width of 5 nm. Since different wavelengths can penetrate into different depths of bronchial mucosa, an ordinary electronic bronchoscopic color image can be decomposed into multiple single-wavelength spectral images. Using the advanced electronic spectral technique, different depths of bronchial mucosa can be observed by selecting any combination of RGB light at any wavelength, and different spectral images can be selected according to the different lesions observed. Then, the selected spectral images are reduced to the FICE images, achieving the purpose of the electron staining. FICE technology can utilise up to 50 different wavelength combinations, and different combinations of RGB can present different colors and depths of different layers. This would be helpful in observing the mucosal surface structure and capillary morphologic structure, and reflecting the change of mucosal micro-concave and -convex, which in turn enhances the visibility of blood vessels and other structures on the mucosal surface. Furthermore, this would help in the analysis and evaluation of the boundaries of lesions, and in more accurately diagnosing histological mucosal changes, dysplasia and early bronchiogenic cancer. This technique can detect subtle changes in the location of bronchial mucosal lesions, help observe the surface structure, capillary texture and shape of the mucosa, enhance the visibility of blood vessels and other structures on the tumor or mucosal surface, and clearly display the boundaries between the lesion and surrounding mucosa. In addition, this technology plays a decisive role in the analysis and judgment of the sampling or cytological brushing sites. FICE has a chromoendoscopic and narrow-wave imaging function.[4-7]

FICE technique is widely used in the gastrointestinal endoscopy diagnosis. In the study by Pittayanon *et al*., the accuracy of FICE for intestinal metaplasia was 85.5%, and the accuracy with the observation of a light blue crest was 95.2%, and that with the observation of a long large crest, 96.8%[8]. In addition, studies have shown that some cases of early flat gastric cancer are missed by routine white light endoscopy, which is detected and confirmed by FICE. The results showed that compared with ordinary white gastroscopy, the result was clear in image.

A variety of studies have confirmed that FICE technology plays an important role in locating the target sites for the diagnosis of bronchial mucosal lesions and early bronchogenic carcinoma.[9-11] High definition electronic bronchoscopy aided with the FICE technique has a definite advantage in improving the diagnostic yield of bronchial mucosal lesions and early bronchogenic carcinoma, and the diagnosis was accurate. The positive rates of biopsy and cytological brushing sites were improved with the use of high definition electronic bronchoscopy aided with the FICE technique. Hence, this has solved the thorny conundrum that has puzzled endoscopists,[12-14] reducing the risk in selecting sampling sites for endoscopists.

Because FICE is relatively a new technique in bronchoscopy, relevant studies are rare. Hence, there are no consensus guideliness about vessel structure and morphology of bronchial mucosal lesions using FICE. This study referred to previous studies to distinguish abnormal morphology and lesions of bronchial mucosa, soit needs more exploration.

CONCLUSION

FICE is user-friendly and novel image processing technique, which can help detect abnormal morphology and lesions of bronchial mucosal lesions, and for targeting the site of biopsy. The emergence of this technology provides a break-through in clinical tool for accurately diagnosing the bronchoscopic changes of various bronchial lesions and early cancers.

PATIENTS' CONSENT:

Consent for publication Consent for publication was obtained from every individual whose data are included in this manuscript.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

QZ: Involved in the conception and design of experiment, the technology and materials provide administrative support to draft articles and critical review of the informative content of article.
QYZ: Participated in experiment design, participate in data analysis and summary.
ANS, NL, XHW: Involved in providing learning materials and patient data, at the same time to participate in the article summary for the data collection and analysis.
CL: Providing learning materials and patient data, and to participate in the data collecting and analyzing data.

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