

# 学位論文の要旨

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学位論文名      Bronchial Physiological Saline Injection to Visualize  
Peripheral Pulmonary Lesions in Ultrathin Bronchoscopy

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## 論文内容の要旨

### INTRODUCTION

In the 1960s, the flexible bronchial fibroscope was developed, and with its widespread adoption, improvements in performance and reductions in diameter were achieved. The use of thin bronchoscopes with an outer diameter of 4 mm and ultrathin bronchoscopes with an outer diameter of 3 mm has enabled access to peripheral pulmonary lesions; however, direct visualization of the bronchial lumen remains difficult.

We have experienced that, during bronchoalveolar lavage performed using bronchoscopy for diffuse lung diseases, instillation of normal saline into the bronchial lumen leads to luminal expansion and improved visibility. Based on this experience, we hypothesized that instillation of normal saline into the peripheral bronchi would similarly allow direct visualization of the luminal findings and thereby potentially improve the diagnostic yield.

### MATERIALS AND METHODS

To quantitatively evaluate how image resolution changes when imaging with an ultrathin bronchoscope under conventional air conditions versus under saline immersion, we assessed the signal-to-noise ratio (SNR). A USAF 1951 resolution test target (Group 2, Element 2; Edmund Optics) was used. While gradually reducing the distance between the bronchoscope and the target, videos were recorded under white-light illumination and narrow-band imaging (NBI). Evaluation images were generated from the recorded videos using ImageJ software. White and black line profiles in the evaluation images were plotted, and the areas corresponding to signal (S1, S2, S3) and noise (N1, N2, N3) were measured. The SNR was calculated using the following formula to assess image resolution. Statistical analyses were performed using R software, and a p value of <0.05 was considered statistically significant.

$$\text{SNR} = 10 \times \log_{10} \left[ \frac{\{(S1 + S2)/2 + S3\}}{\{(N1 + N2)/2 + N3\}} \right] \text{ (dB)}.$$

In addition, 40 patients undergoing bronchoscopy for the diagnosis of peripheral pulmonary lesions were enrolled. Using an ultrathin bronchoscope, the scope was advanced in close proximity to the peripheral pulmonary lesions, and normal saline was instilled through the working channel to observe and record images of the bronchial lumen under white-light and NBI modes. After these observations, the bronchoscope was exchanged for a thin bronchoscope, and endobronchial ultrasound-guided biopsy with a guide sheath was performed. Histopathological diagnoses were then compared with the directly visualized bronchial luminal findings.

The study protocol was approved by the Research Ethics Committee of Shimane University.

## **RESULTS AND DISCUSSION**

### **① Quantitative evaluation**

In the quantitative evaluation, the target was more easily visualized under saline immersion than under air. Under saline immersion, the image size was increased by a factor of 1.33. The SNR under white-light imaging increased from 3.12 to 3.77 dB (1.21-fold), and under NBI from 5.18 to 6.44 dB (1.24-fold). Moreover, the distance between the bronchoscope and the target at which the maximum SNR was obtained increased from 3.0 to 4.5 mm.

Reported advantages of the immersion technique include: (1) the removal of light reflection and lens flare by water makes it easy to observe micro-vessel construction and mucosal surface microstructure; (2) the depth of observation becomes deeper at maximum magnification; and (3) the resolution tends to increase. Because the refractive index of normal saline is 1.33, which is higher than that of air (1.00), even when the distance between the lens and the target is identical, the field of view under saline immersion becomes approximately three-quarters that under air, resulting in a 1.33-fold magnification. Consequently, spatial resolution is enhanced, leading to a 1.21-fold increase in SNR under white-light imaging and a 1.24-fold increase under NBI. Furthermore, calculation of the focal lengths of a thin lens without saline ( $f_A$ ) and with saline ( $f_S$ ) yielded a ratio of  $f_S/f_A = 1.49$ , which is consistent with the approximately 1.5-fold increase in the bronchoscope-target distance at which the maximum SNR was observed in this study.

### **② Peripheral Bronchial Findings**

Forty patients were enrolled in this study. Two patients were not examined according to the established protocol because a thin bronchoscope could not be used; therefore, 38 patients were examined according to the protocol. In eight patients, we could not directly observe the peripheral lesion because the lesion was not reachable, or the bronchial lumen was occupied by sputum or a clot. Using an ultrathin bronchoscope, bronchoscopic observation of the peripheral lesion was successful in 78.9% of patients (30/38). We excluded four patients. In three patients, a definite diagnosis could not be obtained. One patient was excluded because the bronchoscopy was performed during ongoing chemotherapy, which might have affected the bronchoscopic findings. Among these, 26 patients with a definitive final histopathological diagnosis were included in the analysis of the relationship between luminal findings and histological subtype. Of the 26 patients, the final diagnosis was confirmed by bronchoscopy in 20 patients, bronchoscopy was repeated in two patients, and surgery after bronchoscopy without a confirmed

diagnosis was performed in four patients. The median number of bronchial generations close to the peripheral lesion on HR-CT images was six. The median number of generations reached by the ultrathin bronchoscope was also 5.5, whereas that reached by the thin bronchoscope was four.

The border between the normal bronchial area and the lesion was unclear in the subepithelial type. Of the five squamous cell carcinomas (SCCs), three were epithelial, two were subepithelial, two were flat, two were raised, and one was obstructive. Of the 13 adenocarcinoma lesions, one was epithelial and 12 were subepithelial; eight were flat, four were raised, and one was obstructive. Even for peripheral pulmonary lesions, adenocarcinomas were of the subepithelial type (92.3%, 12/13 cases), whereas SCCs were of various types.

It has been reported that the mucosal invasive type is usually observed in hilar-type SCC, and the submucosal invasive type is mainly observed in peripheral adenocarcinoma, SCC, large cell carcinoma, and small cell carcinoma. However, the relationship between peripheral bronchial findings and histological type has not yet been investigated. In our study, we suspected that the border between lesions and the normal bronchus would be clear for epithelial-type lesions, whereas the border would be unclear for subepithelial-type lesions. Even peripheral pulmonary lesions, similar to central lesions, adenocarcinomas are of the subepithelial type, whereas SCCs are of various types. When an ultrathin bronchoscope reached the inside of the SCC lesion, we directly observed the exposed part of the epithelium. In contrast, when the ultrathin bronchoscope reached only the margin of the SCC lesion, we occasionally observed a subepithelial type extending under the epithelium. Therefore, we suspected that various luminal findings were present in the SCC.

The diagnostic yields of ultrathin bronchoscopy and EBUS-GS were reportedly 60–74% and 59–77%, respectively. In our study, observation of the bronchus leading to the peripheral lesion using the ultrathin bronchoscope was successful in 78.9% of patients (30/38). When malignancy is strongly suspected based on bronchoscopic findings, the diagnostic yield of lung cancer can be further improved if a biopsy can be performed from a site with abnormal findings under direct vision. By including observational findings, such as NBI with saline injection, it may be possible to further improve the diagnostic yield. Even for peripheral lesions, we believe that it is important to closely observe the bronchus in the same manner as for central lesions.

The limitations of this study are as follows. The sample size was small because the study was conducted at a single institution. In addition, pure ground-glass nodules were difficult to detect using endobronchial ultrasonography after saline was injected into the bronchus around the lesion; therefore, only solid lesions were analyzed in our study. This study could not evaluate whether saline injection improved the cytological or histological diagnostic yield.

### **CONCLUSION**

In conclusion, injecting saline into the peripheral bronchus is useful for direct bronchoscopic observation in both quantitative experiments and clinical studies. Ultrathin bronchoscopic findings indicate the histological type in some cases.