Forward-looking OCT Probe Using Single-fiber Scanning for Transbronchial Puncturing Cytodiagnosis

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Abstract Bronchoscopic diagnosis of peripheral lung cancer with ground-glass opacity (GGO) is difficult because GGO lesions cannot be visualized using currently available radial probe endobronchial ultrasound. Therefore, a forward-looking single fiber scanning optical coherence tomography (OCT) probe with a local observation function has been developed to achieve precise sampling. The new OCT probe is only 1 mm in diameter. The probe is composed of a patterned electroplated copper coil fabricated on a polyimide tube using non-planar photofabrication technique, and an optical fiber having a permanent magnetic tube with a diameter of 0.5 mm. When an electrical alternating current is supplied to the coil, the permanent magnet vibrates electromagnetically with the optical fiber. To increase the fiber vibration amplitude, a micro gradient-index (GRIN) lens is set in front of the tip of the optical fiber. Using the micro GRIN lens, the output beam is focused, and the scanning range is enlarged. The view angle becomes approximately 45°, and image resolution becomes approximately 60 μm. The structure of grating was successfully imaged using the new OCT probe. Further improvements and animal experiments are necessary to determine the clinical application of the probe.

Keywords: transbronchial cytodiagnosis, single-fiber scanning, optical coherence tomography, electromagnetic driving.


1. Introduction
Due to the increase in mortality from lung malignant neoplasms in recent years, early detection and treatment of lung cancer are required [1, 2]. Cytodiagnosis is a prerequisite for doctors to determine whether surgery should be performed. However, no study has been conducted on cytodiagnosis by transbronchial sampling with visualization of the target lesion during sampling. Hence, whether the target tissue has been sampled with certainty is not guaranteed. Therefore, transbronchial cytodiagnosis may have to be performed several times. Despite multiple trials, a misdiagnosis may occur. Establishing a device for lesion visualization during sampling to promote diagnostic yield is urgently needed.

Endoscopes currently used in clinics are electronic and employ a small charge-coupled device (CCD) or coherent fiber-optic bundle in front of the device. A CCD as small as 1 mm is yet to be used in the clinical setting. The fiber-optic bundle consists of several thousand fibers, which translate to several thousand pixels and thus generates poor imaging resolution.

In 2010, Washington University reported the development of a 1.2-mm endoscope (catheterscope) that uses a single fiber scanner driven by a piezoelectric tube. A field of view (FOV) angle of 120° was obtained as a result of the high-quality optical design of fixing a lens assembly in front of the fiber [3]. Gluing a combination of tiny lenses onto a thin endoscope (less than 1 mm in diameter) is a complex fabrication process that unfortunately results in a low-quality optical interface.

Several reports on OCT endoscopes have been published in recent years [4]. A notable study of a forward-looking (imaging) intraocular OCT probe was conducted in 2013 [5]. The probe is driven by an electromagnetic field that is parallel to the vibrating fiber. The single-mode fiber is housed within a 34-gauge extrathin-wall stainless steel tube. The fiber tip protrudes approximately 2 to 3 mm from the tube. The front portion of the 34-gauge tube is bent into a smooth "S" shape. The mechanism to effect scanning by the fiber tip is formed by sliding a straight 28-gauge thin-wall stainless steel tube along the curved part of the 34-gauge tube. However, the above mechanism generates a length of up to 130 mm (length of the electromagnetic sliding mechanism and length of the smooth "S" shape part of the tube), although the diameter of the front part is only 0.51 mm. This probe is suitable as an intraocular imaging device but should not be used in the long and narrow bronchus, because it easily punctures the bronchial wall. In general, the probe used in transbronchial cytodiagnosis is approximately 11 mm long, which is one-tenth the length of the above-mentioned probe. A probe with a short length is preferable.

In 2008, our group at Tohoku University developed a 1-mm forward-looking OCT endoscope with an electromagnetically driven single-fiber scanner [6]. Using a 125-μm diameter lens welded onto the optical fiber tip, OCT imaging was achieved. However, the half amplitude of fiber vibration was only 54.5 μm. Therefore, the corresponding FOV angle was only 3.7°. OCT is able to image a section plane in the depth of biolog-
ical tissue. Thus, it is a useful tool for observing neoplasm spread across the transbronchial mucosa, and is the top ranking method for early diagnosis of lung cancer [7, 8]. In this study, we developed an OCT probe that employs a scanning fiber endoscope (with a diameter of 1 mm) and an electromagnetic mechanism [6]. The endoscope is able to detect idiopathic adenocarcinomas with hypertrophied alveolar walls (more than 60 μm), and detect a puncture needle simultaneously. In this case, an imaging depth of 1.5 to 2.0 mm, FOV angle of 45°, and resolution of less than 60 μm (lateral and depth) are required for used in clinical setting. To obtain this imaging depth, FOV and lateral resolution, a single gradient-index (GRIN) lens is feasible, instead of combined lenses. Joos and Shen [5] also developed an OCT probe with a GRIN lens, which permits a chosen working distance of 3 to 4 mm from the outer surface of the GRIN lens to the target. In our study, a GRIN lens is used to allow continuous imaging depth of 1.5 mm from the outer surface of the GRIN lens. It also increases the FOV and realizes lateral resolution of less than 60 μm. Depth resolution depends on the OCT imaging system and the resolution of a conventional OCT system is sufficiently small.

In this study, the design of the driving coil is improved and the fiber vibration amplitude increased. We examined the optical design that is appropriate for transbronchial puncturing cytdiagnosis. The fabricated electromagnetic driving single fiber scanner was then optically connected to the OCT imaging system, and used for imaging a grating.

2. Structure of transbronchial puncture probe

The basic design of a transbronchial puncture probe is shown in Fig. 1. The forward-looking fiber scanner functions as the OCT probe, and is parallel to the puncture needle inserted into the working channel of the bronchoscope (BF-MP60, Olympus Co.). Instead of an ordinary lens, a GRIN lens is fixed to the front end of the puncture device, the probe has a diameter of 1 mm and a length of 11 mm. A 9-mm-long optical fiber 125 μm in diameter (mode field diameter of 9.3 μm) with its rear-end fixed by a jig is placed inside the probe. In addition, the optical fiber is inserted into a permanent magnetic tube with a diameter of 0.5 mm and a length of 2 mm (Adamant Co., Ltd.). The saddle-shaped driving coils with line widths of 100 μm, spaces of 50 μm, and 4.5 turns are patterned on the PI tube surface fabricated using non-planar photofabrication technique [3]. The electrical resistance of the coil is 2.7 Ω, and the power consumption under fiber resonant condition is less than 100 mW. A light beam with a center wavelength of 1310 nm and spectral width of 100 nm is directed to the optical fiber.

To observe the puncture needle as it protrudes at a length of 1.7 mm, the FOV angle of the probe should be 45° and the imaging depth 1.7 mm. This depth is measured from the surface of the GRIN lens to the tissue, as shown in Fig. 1.

3. Design of the OCT probe

3.1 Design for FOV

To obtain an FOV angle of 45°, a GRIN lens is used to enlarge the optical scanning range and focus the emitted light beam. The GRIN lens has the advantages of small size and columnar shape. It is generally less than 1 mm in diameter with flat faces at both ends. Therefore, this lens is easier to assemble than the ordinary combination of micro lenses. More importantly, a single GRIN lens is sufficient to obtain an FOV angle of 45°.

Technical parameters of the GRIN lens are as follows: 350-μm diameter, 1/4 pitch (lens length 745 μm, gradient of refractive index in radial direction g = 2.082), and refractive index in the axis n0 = 1.636 (Go!Foton Co.).

The geometric optics track for normal incident beams that pass through the GRIN lens is simulated using an optical design software CODE V program (Synopsys Inc.).

The calculation result is shown in Fig. 2, when the distance between the fiber and GRIN-lens inputting plane is 80 μm. As the scanning beam passes through the GRIN lens, three beams appear successively at different times. The middle beam is the axial beam. The distance between the upper and bottom beams corresponds to the scanning amplitude, and both beams always converge at the axial entrance of the GRIN-lens outputting plane. The
The upper and bottom beams are set apart from the outputting plane through cross shot, and then form an enlarged FOV angle.

The relationship between the FOV angle and the half amplitude of fiber vibration is calculated. The result is shown in Fig. 3. An FOV angle of 45° can be achieved when the half amplitude of fiber vibration reaches 120 μm, thus indicating that the GRIN lens greatly increases the beam scanning amplitude.

One conclusion that can be drawn from Fig. 3 is that the FOV angle can reach 45° if the half amplitude of fiber vibration is 120 μm. This condition is not difficult to achieve.

### 3.2 Design for imaging depth

In practice, idiopathic adenocarcinomas in the lung first replace the alveolar epithelium even in early stages. This process causes the alveolar wall to undergo hypertrophy and become several times thicker than normal [10]. Imaging the hypertrophied alveolar walls leads to detection of lung cancer during the early stages. Irregular alveolar walls are thicker than 60 μm. Thus, the imaging beam diameter related to the lateral resolution should be less than 60 μm in diameter and the depth resolution should be less than 60 μm.

The alveolar layer should be observed using an OCT probe through the bronchial mucosa which normally is approximately 0.5 mm in thickness [11]. The imaging depth should be greater than 0.5 mm. As previously mentioned, imaging depth from 1.5 to 2.0 mm is required clinically. In this case, the imaging depth of the OCT probe is selected as 1.5 mm.

The aforementioned analysis indicates that the optical design should maintain an imaging beam diameter within 60 μm with an outputting length of 1.5 mm.

The light beam emitted from the optical fiber is a Gaussian beam that is self-focused through the GRIN lens. The result calculated using CODE V is shown in Fig. 2. A schematic of the self-focused beam is depicted in Fig. 4. The outputting beam from the GRIN lens has a beam waist, which is shown as Wz. The length from the beam waist to the outputting plane of the GRIN lens is f. The diameter of the beam (the beam spot at every point) is expressed as d, whereas L0 is the distance from the fiber to the GRIN-lens inputting plane, labeled as fiber space.

The imaging depth approximates D_i during insufficient beam penetration when the beam spot at the GRIN-lens outputting plane is less than 60 μm. Given that the intrinsic character of the GRIN lens is fixed and no other suitable product is currently available, we mainly simulated the dependence of D_i on the parameter L0 to obtain the maximum D_i based on the condition that the beam spot is within 60 μm [12], using CODE V. The simulated curve of D_i that varies depending on the fiber space L0 is presented in Fig. 5. D_i can reach 1.7 mm when L0 is 50 μm. However, we should not set L0 to less than 80 μm in practice, as the installation will be too difficult. Therefore, L0 = 80 μm is fixed. In this case (L0 = 80 μm), the outputting beam spot varies with the distance from the GRIN-lens outputting plane. This distance is called distance from lens, as indicated in Fig. 6, where the blue line denotes the axial beam, and the red line represents the 45° abaxial beam. The beam spot curves under 45°abaxial condition suggest that the beam spots become as large as 85 μm when the beam is 1.7 mm from the lens. The beams can approach the puncture needle and an image of the needle can be captured with the help of strong reflection from the stainless needle. Therefore, D_i basically meets the required imaging depth.

### 4. Imaging results

To evaluate the imaging resolution in the Y direction and the FOV angle of the OCT probe, a grating was fabricated using permanent
photoresist SU-8 (Nippon Kayaku Co., Ltd.) on a 1.1-mm-thick glass plate by photolithography. The grating had 60-μm-wide and 20-μm-thick strips with intervals of 140 μm. The period length was 200 μm. The shape of the grating was measured using a surface profiler (P-16+ Stylus Profiler, KLA-Tencor Co.), as shown in the upper panel of Fig. 7. However, etching bevels of the photoresist were observed. Slight protrusion of the photoresist was also present between two strips.

In the test, the fiber scanner was optically connected to a commercial swept source OCT system (HLS-2100, Santec Co.) used in clinical imaging. The OCT system has a light source with a center wavelength of 1310 nm, spectral width of 100 nm, and maximum luminous power of 20 mW. The depth resolution was 12 μm. Data acquisition speed of the system was 100 MHz, 12 bit.

The grating was set up in front of the OCT probe. During the test, a 605-μm gap was maintained between the OCT probe and the grating.

The optical fiber started the scan, which was driven by an alternating current of 300 mA at a frequency of 21 Hz. The scanning frequency of the optical fiber was also 21 Hz, which is consistent with the frequency of the OCT imaging program but not the resonant frequency of the fiber (160 Hz).

The scanning image was obtained with normal incidence (Fig. 7). The shortest and longest bright horizontal lines were alternately aligned. The lengths of the longest and shortest bright lines were approximately 70 and 45 μm, respectively. These dimensions indicate the patterns of the grating strips.

Because 2.5 periods of grating stripes were shown in the scanning image, the beam vibration amplitude was estimated to be 500 μm, corresponding to a maximum view angle of 44.9°.

The distance between the bright line produced by the GRIN-lens surface and the bright line generated by grating strips was 0.6 mm. A bright line produced by the glass plate surface was observed at the lower part of the scanning image. Because the glass plate was 1.1 mm thick, the distance between the glass plate and gratings was approximately 1.1 mm. Thus, the imaging depth of the scanning image was estimated to be 1.7 mm.

5. Discussion

The longest bright lines in the scanning image are assumed to be the upper flat surfaces of the 60-μm-wide strips. The shorter bright lines in the scanning image are assumed to be the bottom flat surfaces with slight protrusion of photoresist between the two strips. The interval between the bright lines is assumed to be etching bevel that reflects light at an oblique angle. The difference in length between the flat surface of the photoresist and bright lines may be caused by measurement error of the OCT system, fabrication error of the photoresist pattern, and estimation error of the length of blurred bright lines on the scanning image.

This result suggests that the novel OCT probe can distinguish strips that are approximately 60 μm wide. Thus, the clinically required lateral resolution of less than 60 μm is satisfied.

The maximum view angle of 44.9° achieved by the probe meets the clinically required FOV angle of 45°. From the correlation between the FOV and the half amplitude of fiber vibration (Fig. 3), the half amplitude of fiber vibration is estimated to be approximately 120 μm. This result suggests that the improved design of the driving coil effectively increases fiber vibration amplitude.

In our study, the imaging depth of the scanning image was approximately 1.7 mm. This result meets the clinically required imaging depth of 1.5 mm. However, absorption and scattering of lung tissue are greater than those of the glass plate. Therefore, imaging depth will decrease when imaging lung tissue. High optical intensity and deep beam penetration into the tissue can be achieved by welding a GRIN lens with a small diameter onto the optical fiber tip to focus a light beam [6].

6. Conclusion

This report presents the development of a 1-mm-diameter scanning fiber endoscope driven by electromagnetic vibration for transbronchial puncturing cytodiagnosis. A GRIN lens was used...
to achieve a continuous 1.5-mm imaging depth from its outer surface, as well as to increase the FOV and realize lateral resolution of less than 60 μm. The fabricated electromagnetic driven single fiber scanner is optically connected to the OCT imaging system.

The structure of photorefrist grating was imaged with the novel OCT probe. The results verify that the lateral resolution, imaging depth, and FOV angle meet the clinical requirements.

For clinical applications, further improvements and animal experiments should be considered in future research.

References


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