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GRIN lens rod based probe for endoscopic spectral domain optical coherence tomography with fast dynamic focus tracking

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Abstract: In this manuscript, a GRIN (gradient index) lens rod based probe for endoscopic spectral domain optical coherence tomography (OCT) with dynamic focus tracking is presented. Current endoscopic OCT systems have a fixed focal plane or working distance. In contrast, the focus of this endoscopic OCT probe can dynamically be adjusted at a high speed (500 mm/s) without changing reference arm length to obtain high quality OCT images for contact or non-contact tissue applications, or for areas of difficult access for probes. The dynamic focusing range of the probe can be from 0 to 7.5 mm without moving the probe itself. The imaging depth is 2.8 mm and the lateral scanning range is up to 2.7 mm or 4.5 mm (determined by the diameter of different GRIN lens rods). Three dimensional imaging can be performed using this system over an area of tissue corresponding to the GRIN lens surface. The experimental results demonstrate that this GRIN lens rod based OCT system can perform a high quality non-contact *in vivo* imaging. This rigid OCT probe is solid and can be adapted to safely access internal organs, to perform front or side view imaging with an imaging speed of 8 frames per second, with all moving parts proximal to the GRIN lens, and has great potential for use in extremely compact OCT endoscopes for *in vivo* imaging in both biological research and clinical applications.

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OCIS codes: (110.4500) Optical coherence tomography; (110.2760) GRIN lens; Dynamic focusing; (170.3880) medical and biological imaging; (170.0110) Imaging system; (170.2150) Endoscopic imaging.

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1. Introduction

Optical coherence tomography (OCT) has been rapidly developed and widely used to image biological tissues as a new *in vivo* noninvasive morphological imaging technique [1, 2]. The success of ophthalmic OCT in clinical diagnosis and research [3] is encouraging development of OCT for imaging other organs in clinical applications in areas such as the gastrointestinal, respiratory and urinary tracts, and coronary arteries [4, 5, 6, 7]. While significant improvement in resolution and contrast is still needed, OCT can play an important role in guiding biopsy with improved yield and reduced complications in these clinical applications.

In order to image various internal organs or tissue regions, a number of endoscopic OCT systems have been developed and reported [4, 5, 7-11]. Due to a fixed objective lens, most of the current endoscopic OCT probes have a fixed focal plane from the distal end of probe. To improve focus in tissue and obtain an optimally focused image, a high numerical aperture (NA) lens must be used, and the entire probe needs to be precisely located so that the focal spot scans into the tissue at the half imaging depth under the surface of the tissue. More importantly, some organs such as liver and larynx may require non-contact imaging in certain applications. Other tissues such as veins, intestine, cartilage, airway and colon may present curved or irregular surfaces, making it difficult or suboptimal to operate the entire probe at high speed while adjusting a fixed focal plane to encompass the entire axial scan range. In such cases the lateral resolution and the signal to noise ratio will decrease with increasing

depth from the focal plane of the probe lens. To maintain a high transverse resolution over the entire depth scan with high resolution using high NA lenses, dynamic focusing has been used with zone focusing and image fusing [12, 13]. Therefore, a method for high speed dynamic focus tracking in endoscopic probes is critical for high quality tissue imaging in real time endoscopic OCT or optical coherence microscopy (OCM) systems, in particular, for accessing some internal organs.

Several dynamic focusing methods have been reported [12-17] which could be used to perform the different depth imaging scans required for improving lateral resolution and image depth with fusing the images obtained at the different focusing zones in OCT) [14]. In addition, such approaches could be used for differential layer imaging in en-face OCM with higher lateral resolution at a given focused spot size through the entire imaging depth [15]. However, these methods are not currently suitable to be used in endoscopic OCT due to their bulk [12, 13]. A high-speed dynamic focus control system based on microelectromechanical (MEMS) mirrors could be used to perform side view imaging but will still be limited with regard to focusing range, sweep distance. In addition, MEMS based probe systems are currently expensive to design and produce, difficult to reliably preserve functionality in rigorous clinical environments, and have nonlinear relationships between the focal point shift and the voltage applied to the MEMS mirror [16].

In this study, a GRIN (gradient index) lens rod based probe for spectral domain OCT with dynamic focusing is presented. This GRIN lens based probe can dynamically adjust focus very rapidly at the proximal end of the probe, outside the body, to improve lateral resolution and obtain the high quality OCT images in 2 or 3 dimensions. This is particularly important when non-contact mode imaging is needed or when areas that are difficult to access or have irregular surface topography must be imaged. The dynamic focusing probe is compact and does not require any moving parts or electrical elements at distal ends. The probe can image frontal or side viewing for OCT or en-face OCM if it is connected to a time-domain OCT.

2. Materials and methods

The schematic diagram of the GRIN lens rod based dynamic focusing 2-D spectral domain OCT system is shown in Fig. 1. A low coherence light from a superluminescent diode (SLD) with polarized power of 10 mW and a full width at half maximum (FWHM) spectral width of 80 nm centered at 1.3 μm , corresponding to a round trip coherence length of 10 μm , illuminates a Michelson interferometer where it is split by a 2×2 coupler into a reference arm and a sample arm. A grating based rapid scanning optical delay line (RSOD) is inserted in the reference arm only for dispersion compensation purposes, with a matched optical path length without any movement for scanning delay. Backreflected or backscattered light signals from different depths within tissue that correspond to different delays in the sample arm interfere with light from a reference path with a known delay in the detector arm. In the detector arm, a spectrometer consisting of a diffraction grating (500 lines/mm) and a photodiode array (1024 pixels) was used to detect the spectral interference signal to measure the echo time delay and magnitude of backreflected and backscattered light by Fourier transformation and generate cross-sectional images at 8 frames/s. The dynamic range is 72 dB.

In the sample arm, light from the single mode fiber was collimated to a Gaussian beam, which was steered by a servo mirror to perform the lateral scan. The beam is then focused by an achromatic objective lens to a beam spot that was laterally scanned onto the entrance plane of the GRIN lens rod (Gradient Lens Corporation, Rochester, NY). The scan rates of the servo mirror (Model 6210H, Cambridge Tech., Cambridge, MA) could be up to at 500 Hz over a scan of ± 6 degrees of optical scan if driven by a triangle wave. The laterally scanning light beam illuminated the sample after the GRIN lens relay. If a prism is mounted on the distal end surface of the GRIN lens rod, the viewing direction can be easily changed. The image position of the light focus spot as shown in Fig. 2 could be calculated by [18]

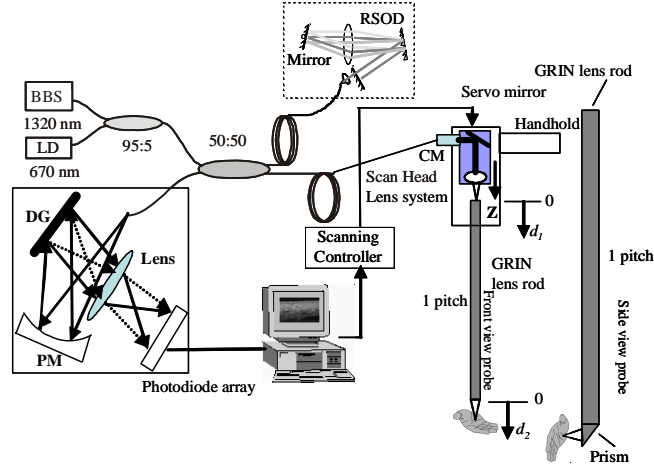


Fig. 1. Schematic diagram of a GRIN lens rod based dynamic focusing 2-D spectral domain optical coherence tomography system. PM: parabolic mirror; DG: diffractive grating; RSOD: rapid-scanning optical delay line for dispersion compensation.

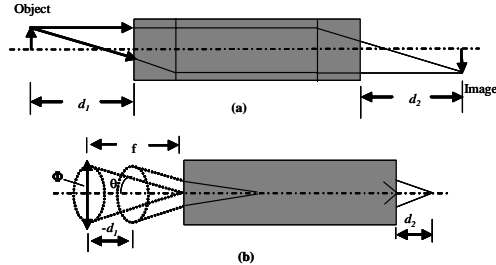


Fig. 2. Diagram of image formation by a GRIN lens rod (a), objective lens focusing and focus shift (b).

$$d_2 = \frac{1}{n_0 \sqrt{A}} \left[\frac{\sin \sqrt{AL} + n_0 \sqrt{Ad_1} \cos \sqrt{AL}}{n_0 \sqrt{Ad_1} \sin \sqrt{AL} - \cos \sqrt{AL}} \right] \quad (1)$$

Where A is a constant for a particular lens, n_0 is the refractive index on the optical axis of the lens, d_2 is the image position corresponding to an object at a distance d_1 in front of the lens. L is the length of the GRIN lens ($L_0 = 2\pi/\sqrt{A}$ when the length of the GRIN lens is one pitch). When the length is exactly one pitch, the image position of the light focus spot is simplified into $d_2 = -d_1$. Since the GRIN lens we designed is one pitch, light emerging on the distal end surface of the GRIN lens is the same as on the entrance surface of the GRIN lens. If the position of light beam spot in the entrance of the GRIN lens rod in the z direction (the axis of the rod) is changed, the image position of the light beam spot after a one pitch GRIN lens relay is changed the same corresponding distance and in the same direction as the entry site. This relationship is used to perform dynamic focusing. However, if the length of the GRIN lens selected is not exactly one pitch, the d_2 to d_1 ratio can be smaller or greater than -1 (which is determined by the length in the commercially produced lenses). In the system we designed for these studies, a small high speed linear motor (M-663, Physik Instrumente GmbH & Co. KG, Palmbach, Germany) is used to adjust the distance between the scan head lens system and the entrance surface of GRIN lens rod in order to change the focal position of the sample beam exiting the distal end of the probe. The motor can move at a velocity up to 500 mm/s with a resolution of 1 μm and maximal normal load capacity of 5 N. This motor

can be driven to relocate the focal plane so that the image could be registered for image fusion to maintain high lateral resolution over the whole image depth.

Based on the access requirements of specific applications, the probe length could be increased by half pitch increments, such as 0.5, 1, 1.5 and 2 pitches to create dynamic focus tracking based OCT probes. We tested 2 commercial GRIN lens rods which are approximately one pitch; one with a diameter of 2.7 mm, and the other, 4.58 mm with NA of 0.1. The pitch lengths are 128.5 mm and 220.5 mm and the length of GRIN lenses are 127 mm and 219 mm, respectively. The refractive index on the optical axis of the lens n_0 is 1.542. For a side view probe, a right angle 5 mm prism was glued on the distal end surface of the larger GRIN lens rod.

In the scan head lens system, the beam diameter of the collimated light is $\Phi=1.5$ mm and the focus length of the objective is $f = 10$ mm, therefore, the lateral resolution or focused beam spot is $\Delta r=4\lambda_0f/(\pi\Phi)=11 \mu\text{m}$ where λ_0 is the central wavelength of the illuminating light. The maximum acceptance angle of GRIN lens rod θ is determined by the NA of the GRIN lens rod. In our system, the maximum angle (φ) of the focused light beam on the entrance of the GRIN lens rod can be determined by the collimated beam size and the focal length of the objective lens and is calculated as $\sin\varphi=\Phi/2f=0.08$. It should be smaller than the NA of GRIN lens rod in Fig. 2(b) and be expressed by

$$\Phi/2f \leq NA_{GL} \quad (2)$$

where NA_{GL} is the NA of the GRIN lens rod, so that the incident light from the scan head lens system could be accepted and transmitted in the GRIN lens rod. The lateral resolution will be limited by NA_{GL} as follows:

$$\Delta r \geq \frac{2\lambda_0}{\pi \cdot NA_{GL}} \quad (3)$$

The *in vivo* animal study was performed in rabbits in which hematogenous metastatic lung tumors had been previously induced using a VX2 sarcoma cell line model. These studies were approved by the local IACUC committee in compliance with all state and federal regulations. After anesthesia induction with 1cc of a 2:1 cocktail mixture of Ketamine/Xylazine, a 24 gauge catheter was placed in a marginal ear vein. A moderate inoculum of 20×10^6 VX2 sarcoma tumor cells were injected intravenously through the catheter followed by 2-3 cc heparin flush. Two to four weeks later the tumor is mature for examination.

During the OCT experiments, male New Zealand White rabbits (Western Oregon Rabbit Company) weighing 4.0 ± 1 kg were anesthetized with a 2:1 ratio of Ketamine HCl (100mg/ml) (Ketaject, Phoenix Pharmaceutical Inc., St. Joseph, MI): Xylazine (20mg/ml) (Anased, Lloyed Laboratories, Shenandoa, IA) at a dose of 0.75 cc/kg IM. The depth of anesthesia was evaluated by monitoring the physiologic parameters and reflexes of the animal. Maintenance anesthetic was dosed at 0.3 cc of a 1:1 mixture of Ketamine: Xylazine (Ketamine 100 mg/ml:Xylazine 20 mg/ml) was administered accordingly. The animals were intubated with a 3.0 cuffed endotracheal tube, and mechanically ventilated (dual phase control respirator, model 32A4BEPM-5R, Harvard Apparatus, Chicago, IL) at a respiration rate of 32/min and a tidal volume of 50 cc and FiO_2 of 100%. A thoracotomy was performed to allow access for OCT imaging of the thorax and lungs. Upon completion of the experiment, the subjects were euthanized with an intravenous injection of Eutha-6 (1.0-2.0 cc) administered through the marginal ear vein.

3. Results

To test the ability to dynamically change focus depth, a section of normal fresh trachea was excised from a euthanized rabbit and pinned onto a silicone pad. The tracheal specimen was then placed on a micro-stage and under the OCT probe for *ex vivo* OCT imaging. The objective lens was mounted on a micro-positioner and could be adjusted in the axial direction of the GRIN lens rod. When the light focal spot of the objective lens adjusted by the micro-positioner was just at the entrance surface of the GRIN lens rod, the off-focus was zero ($d_1=0$). When the objective lens was adjusted by the micro-positioner, its focal plane within the GRIN lens was changed and the whole probe focal plane after the GRIN lens rod delaying was also changed. The sample was adjusted by a micro-stage in the axial direction of the GRIN lens rod so that the sample is within the scanning beam focus. The axial optical path length from the distal end surface of the GRIN lens to the focus within the tissue is d_2 . The theoretical relationship between the incident focus plane change and illuminating focus plane change of the GRIN lens rod can be calculated from Eq. (1) where d_1 is negative indicating a focal point inside the rod. The experimental and theoretical results for the GRIN lens rod with diameter of 2.7 mm are shown in Fig. 3 and are almost linear. Since the length of the GRIN lens rod (127 mm) is slightly shorter than one pitch (128.5 mm) after polishing of both ends, the slope is larger than one. The dynamic focusing range can be up to 7.5 mm.

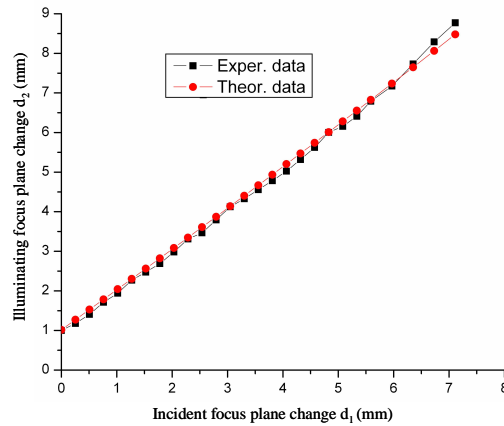


Fig. 3. Relationship between the incident focus change d_1 and illuminating focus change d_2 in GRIN lens rod with the diameter of 2.7 mm and length of 127 mm.

The focal plane of the scan head lens system was axially moved more distally from the entrance of GRIN lens rod to change the focus plane of the OCT probe in order to obtain the *ex vivo* OCT images of a fresh rabbit trachea. The GRIN lens rod with a diameter of 2.7 mm and length of 127 mm was used to test image quality at three different focusing distances, $d_2=1$ mm, $d_2=4.5$ mm and $d_2=8.5$ mm, respectively. By this method, we demonstrated that the OCT images obtained can delineate the micro morphology of normal rabbit trachea including mucosa, submucosa, glands and cartilage rings as seen in Fig. 4. Comparing OCT images [Fig. 4(a), (b) and (c)] obtained at the different focusing distances, the image fidelity including resolution, image depth, and contrast is not appreciably different. Since the rod length was not exactly one pitch and the slope was slightly larger than one, the coherence gate was changed slightly with the focal plane change and the OCT images were shifted from high to low on the screen as shown in Fig. 4(a, b, and c).

The lungs of a New Zealand rabbit as described above were imaged *in vivo* by the side-view GRIN lens rod probe. The probe was located close to the lung sample, which could be brought into the focus by adjusting the high speed linear motor to change the focal plane of

the objective lens. The coherent gate is not changed with the beam focus in the sample without changing the preset reference arm length. The OCT image is shown in Fig. 5. Because the scanning range was controlled at 5 mm and the diameter of GRIN lens rod is 4.58 mm, the left and right side of the image is without signal and appears black in the image with size of 5 mm \times 2.8 mm. The image in Fig. 5 demonstrates that the pleura and alveoli of the rabbit lung are clearly delineated and the early tumor can be seen.

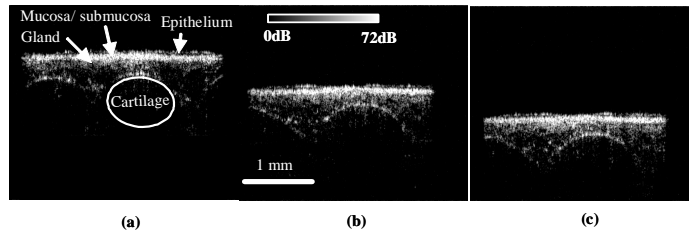


Fig. 4. *Ex vivo* OCT images of a normal fresh rabbit tracheal tissue obtained by the GRIN lens rod based dynamic focus endoscopic OCT at different focus plane of $d_2=1$ mm (a), 4.5 mm (b) and 8.5 mm (c), respectively. The diameter of GRIN lens: 2.7 mm; Image size: 3 mm \times 2.8 mm.

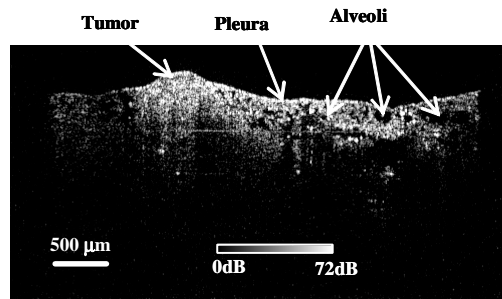


Fig. 5. In-vivo OCT image of rabbit lung obtained by a side-view GRIN lens rod based dynamic focus endoscopic FDOCT system. The diameter of GRIN lens rod: 4.58 mm; Image size: 5 mm \times 2.8 mm.

4. Discussion and conclusions

The GRIN lens rod based dynamic focus endoscopic OCT system can axially change the focal plane of the scanning light beam within the range of 7.5 mm by a linear motor at the entrance end of a one pitch GRIN lens rod. If a longer focus objective lens in the scan head lens system is used, adjustable focus range of the OCT probe can be further increased. Additionally, the probe can be longer if the GRIN lens rod is 1.5, 2, 2.5 or 3 pitches according to the requirements of different applications. If the rod is exactly one pitch at the central wavelength of the light source, the slope in Fig. 3 should be one, and the optical path length in the sample arm is unchanged. When the scan head lens system is adjusted axially, the focal plane shifts. Therefore, the coherence gate will keep at the beam focus without the path changing in the reference arm. However, if this probe is used in OCM with high lateral resolution to keep constant lateral resolution through the whole tissue depth using image fusing, the path length in the sample arm will change with the focus shifting within tissue due to the change of refractive index of tissue. Therefore, the reference arm would need to be readjusted to keep the fixed coherence gate. Compared with other endoscopic OCT probes [4, 5, 7-11], this probe can be made more compact, and perform 2 or 3 dimensional scanning over the entire surface of the probe area. Since there are no moving parts in the distal end of the probe, it can be readily adapted to various sites, sterilized, and will be robust to tolerate the rigors of surgical applications. The imaging speed of this system is 8 frames per second at the image

size of 512 pixels by 512 pixels and the probe itself could actually scan much faster if desired. The frame rate of current system is limited by the speed of photodiode array at 1.3 μm .

In this study, the dispersion from the GRIN lens rod was compensated by the RSOD. More complete compensation could be attained by adding another GRIN lens rod in the reference arm with the same size and optical properties as used in the probe. Since the NA of GRIN lens rods can be larger than the NA of the one used in this study, lateral resolution could be made even higher by decreasing the light focal spot size of the objective lens in the scan head lens system if a rod and an objective lens with large NA are incorporated into the probe. Due to the chromatic dispersion introduced by the GRIN lens rod, the focus planes for various wavelengths may be displaced from each other, in particular, for very broadband light source used in high resolution OCT imaging. It might affect the quality of the images in the lateral axial resolution. In our system set up, the FWHM spectral width of the light reflected from a mirror on the focus of the GRIN lens rod in the sample arm is 6% narrower than one back from reference arm. The axial resolution degraded by 6% (from 9.5 μm to 10.1 μm). To verify the possible effect on lateral resolution from aberrations of GRIN lens rod, a variable resolution target (Edmund Optics, NJ, USA) was imaged under the GRIN lens probe and OCT image of the target area with 100 line pairs/mm is shown in Fig. 6. The OCT image demonstrates that the lateral resolution of 10 μm can be maintained with GRIN lens as did in the bench-top system without GRIN lens rod. For an ultra-high resolution OCT system with very broadband light source, the chromatic aberration of GRIN Lens can be minimized by selecting an ion-exchange pair for producing achromatized radial gradients [19].

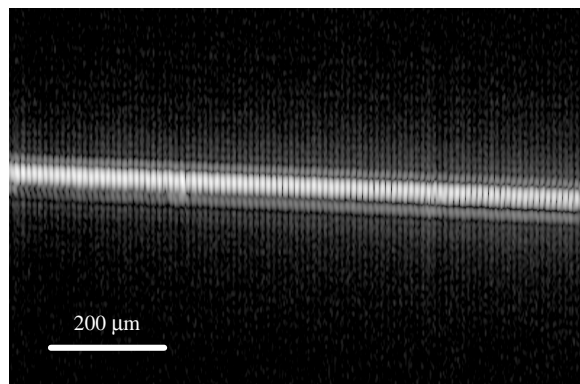


Fig. 6. OCT image of resolution target of 100 line pairs/mm obtained by the GRIN lens rod based dynamic focus endoscopic OCT, the lateral resolution of 10 μm is maintained.

In summary, a GRIN lens rod based dynamic focusing spectral domain optical coherence tomography (OCT) system has been presented. The focus of this OCT system could be dynamically adjusted at up to the speed of 500 mm/s since the coherent gate coincides with the beam focus in the sample without changing reference arm length. Two or three dimensional scanning can be accomplished endoscopically with this approach. The experimental results demonstrate that this GRIN lens rod based OCT system can perform high quality non-contact *in vivo* imaging due to its dynamic focusing. This OCT probe is solid, safe, and is capable of performing frontal or side view imaging in this system at speeds of 8 frames per second. It has great potential for use in extremely compact OCT endoscopes to image internal organs *in vivo* in both biological research and clinical applications. It also has excellent potential to be used for en-face OCT imaging and OCM as a dynamic focusing probe for high lateral resolution and to simultaneously perform both 3D imaging and surface imaging in the same channel.

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