High-resolution, wide-field, forward-viewing spectrally encoded endoscope

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Background and Objectives: Spectrally encoded endoscopy (SEE) is an optical imaging technology that uses spatial wavelength multiplexing to conduct endoscopy in miniature, small diameter probes. Contrary to previous side-viewing SEE devices, forward-viewing SEE probes are advantageous as they provide a look ahead that facilitates navigation and surveillance. The objective of this work was to develop a miniature forward-viewing SEE probe with a wide field of view and a high spatial resolution.

Results: We demonstrated a forward-viewing SEE device with an overall total diameter of 1.27 mm, which consists of a monolithic illumination probe with a length of 3.87 mm and a diameter of 500 μm , 8 multimode detection fibers that were polished at a 17° angle, a rotational scanning mechanism, and a sheath. This design resulted in a high resolution probe (best spatial resolution of 20.3 μm), a wide total angular field of view of 100°, and an effective number of imaging elements of ~344,000 pixels. The SEE probe performance was compared to a commercial color chip-on-the-tip endoscope; while monochrome, results showed better spatial resolution and a wider field of view for the SEE device. The SEE device was used for preclinical imaging of a swine joint *ex vivo*. Results demonstrate the potential of this forward-viewing SEE probe for visualization and navigation in medical imaging applications.

Key Words: Spectrally encoded endoscopy; Miniature endoscopy; Forward-viewing; Wide-field.

INTRODUCTION

Traditional endoscopy procedures have limited access to narrow anatomical structures in various organs in the human body. Miniature endoscopy has been developed to provide safer and less traumatic access by utilizing fiber-bundle (1,2) and single-fiber (3-5) endoscopes for several medical applications, such as fetoscopy (1), angioscopy (3), and bronchoscopy (4). During the last decade, chip-on-the-tip endoscopes had become attractive for various applications (6-8) as their size has reduced significantly; however, their diameter is still larger than 1 mm due to the chip size, which, in part determines the image quality as well.

Spectrally encoded endoscopy (SEE) enables macroscopic imaging in a miniature probe by using a grating to project a wavelength-dispersed line on the tissue, scanning this line along

one dimension, and spectral detection to create an image (9). SEE has been used for three-dimensional laparoscopic imaging of a mouse *in vivo* (9), subsurface imaging (10), and Doppler imaging (11). The majority of these SEE devices were designed with large side-viewing angles (9,12), which prevent their use for any application that requires navigation through confined cavities. Recently, a forward-viewing SEE device using two separate channels for illumination and detection was demonstrated to be useful for monochromatic (13) and spectral (14) imaging. In these previous SEE devices (13,14), broadband light was transmitted through the illumination channel, composed of a 200- μm -diameter multimode fiber (MMF). The detection channel consisted of a 1-mm-diameter prism-grating-prism structure. Due to the air gap between the prism and the grating, the probe was fabricated inside a holder, which increased the overall probe diameter to 1.8 mm. This design required constant overlap between the spectrally encoded line and the illumination beam during imaging. Therefore, the illumination fiber was permanently attached to the bottom of the detection probe, which prevented the probe from achieving continuous rotation and high frame rate imaging.

In this work, we demonstrate a forward-viewing SEE device with a monolithic illumination SEE probe and stationary MMF detection array that overcomes the issues that limited previous forward-viewing SEE technologies. While monochrome, the 1.27-mm forward-viewing SEE device demonstrated a wider field of view and better spatial resolution than a 1.4-mm chip-on-the-tip endoscope. The clinical potential of the SEE device was shown by conducting imaging of a swine joint *ex vivo*.

MATERIALS AND METHODS

Optical Setup

The forward-viewing SEE device (Fig. 1) was designed and constructed to have a rotating illumination channel and a stationary detection channel. The illumination channel used a supercontinuum broadband light source (415 nm – 784 nm, EXU-6, NKT Photonics). The light source was coupled into a stationary single-mode fiber (630HP, Nufern), which was connected through a home-built near-contact rotary joint (RJ). The near-contact RJ design was similar in concept to the design reported in Ref. (15). Briefly, the stationary fiber and the rotating fiber were concentrically aligned facing each other with a 12- μm free space gap resulting in a 60% average throughput power. The rotating single-mode fiber was inserted into a flexible drive coil shaft (minimum bend radius of 4 mm; Asahi Intecc CO) that transmitted continuous rotation from a DC motor in the RJ to the single-mode fiber and the illumination probe at the distal end. The 500- μm illumination probe was designed to diffract and focus the broadband light into a spectrally encoded line centered around the optical axis (Fig. 1; see Section 2.2 for more details). By rotating the drive coil shaft, the spectrally encoded line illuminated a two-dimensional circular field of view (FOV).

The reflected light from the sample was collected through stationary circular MMF array (see Section 2.3 for more details). The array was composed of sixteen MMFs arranged between two pieces of flexible tubing. The lumen of the inner tubing (275-11, Microlumen), with a diameter of 700 μm , was used to house the illumination probe, while the outer tubing was a heat shrink tube (PTFE Sub-Lite-Wall, Zeus) that held the MMFs, resulting in an endoscope with an overall diameter of 1.27 mm and a minimum bend radius of about 5 mm. The illumination probe and the detection MMFs were aligned to minimize the amount of light that was directly coupled from the illumination probe to the detection MMF array. The reflected light from the sample was collected through the circular MMF array and was measured at the proximal end using a custom-fabricated spectrometer. Although sixteen MMFs were needed to fill the entire circumference of the illumination optics, eight fibers were enough to fully cover

the imaging FOV. Therefore, the light from eight fibers (Fig. 1, dark red MMFs), rearranged into a linear vertical array at the spectrometer, was detected. Light emanating from the linear MMF array was collimated by an achromatic lens (AC508-100-A, Thorlabs), diffracted by 1200 lines/mm grating (Wasatch Photonics), and focused through an imaging lens (EF35mm F/1.4L USM, Canon) over a tall pixel ($W24\mu\text{m}\times H500\mu\text{m}$, 1024 pixels) image sensor (S11490, Hamamatsu). The array of eight MMFs produced eight spectrally encoded lines on the sensor (Fig.1), which were summed at the sensor. A two-dimensional image was constructed by collecting the spectrally encoded lines at different time points, while the probe was spinning, and stitching them next to each other.

Illumination Channel

The forward-viewing SEE probe (Fig. 2a) had a monolithic structure to avoid any air gaps between the optical components, eliminating the need of assembling the optical components inside a separate housing. Broadband light from the illumination source was transferred to the probe through a single-mode fiber (630HP, Nufern), which was fusion-spliced to a 250- μm gradient-index (GRIN) lens (SilicaGRIN, 0.117 NA, Toyo Seikan Group Holdings). The GRIN lens was attached with UV-curing epoxy resin (OG142-112, Epoxy Technology) to the rear-bottom half of a 500- μm silica spacer, which coupled the light through a mirror surface into a grating at its front surface (Fig. 2a). This design resulted in an SEE probe with a rigid tip length of 3.87 mm (Fig. 2a) on the end of a long flexible drive coil shaft. The drive coil shaft was attached to the fiber-GRIN lens interface with small amount of epoxy resin, which also strengthened this interface. The rotating drive coil shaft and probe were inserted into a stationary outer tubing (PTFE Composite ID/Braid/Pebax, OD=0.95 mm, MicroLumen Inc.; See Fig.1) to protect them and isolate them from the environment.

The forward-viewing design was achieved by polishing the 500- μm spacer rod at its bottom and front surfaces. The bottom surface was angle-polished, so that the incident light angle was larger than the critical angle; this surface thus functioned as a mirror and the light was reflected from the bottom surface towards the front surface. The 250- μm front surface was angle-polished and a grating pattern was stamped over it using the following procedure: 1) adding a small amount of UV-curing acrylate resin (OG603, Epoxy Technology) to the front surface, 2) stamping it with a master grating (2000 l/mm, Canon) coated with a single layer of hydrophobic chemical (Trichlorosilane, Gelest Inc.), 3) curing the acrylate with UV light, and 4) detaching the master grating to obtain a 2000 l/mm acrylate grating at the front surface of the spacer. The polishing angles of the bottom and the front surfaces were 17.6° and 9.2° with respect to the major and minor optical axes, respectively. These values were chosen so that the grating would diffract the incident light and emanate the shortest wavelength (blue) parallel to the major optical axis, while the longest wavelength (red) would emanate with a 55° angle with respect to the major optical axis. In practice, due to inaccuracies in the polishing and the fabrication processes, the diffracted light from the SEE probe (Fig. 2b) had a blue wavelength that was slightly shifted from the optical axis, which resulted in a small signal gap at the center of the image, and a red wavelength that emanated at an angle of about 51° . In addition, the measured focal shift between the shortest and longest wavelengths was about 1 mm. Rotating the illumination probe resulted in two-dimensional illumination of a circular region with a total angular FOV of approximately 102° .

Detection Channel

Using multiple MMFs for light detection reduced speckle noise and increased the signal-to-noise ratio (SNR). In addition, the fixed circular array structure did not require detection

channel scanning, which made detection simpler than prior SEE probe designs. In the current device, the light was collected through 185- μm MMFs with a numerical aperture (NA) of 0.66 (FSUA125145185, Polymicro Technologies). With the MMFs polished flat, at a 0° angle, a circular detection spot with a theoretical total angular FOV of 82.6° was achieved (Fig. 3a). Since the distance between each opposing MMF was about $800\mu\text{m}$, a substantial overlap between the collection spots at the center of the FOV occurred. In addition, because the illumination probe's half angular FOV (51°) was larger than the 0° angle MMF (41.3°), light was not detected from the outer circumference of the illuminated FOV. Therefore, the 0° angle polished MMF array caused the SEE device's total angle of view to be approximately 80° .

To increase the detection angular FOV, the distal ends of the MMFs were angle-polished, resulting in an elongated detection spot that was slightly shifted outwards from the center (Fig. 3b). A polishing angle of 17° provided the largest detection area with theoretical total angular FOV of 102.5° . The MMFs were polished together with 17° angle tilt and inserted as a circular array between the inner and outer tubing (Fig. 1, Fig. 3d). Each one of the fibers was manually aligned so that the circular edge of the detection spot (Fig. 3b, right inset) pointed towards the center of the illumination FOV (Fig. 3c). Then, the MMFs were fixed by applying hot air flow to the heat shrinkable outer tubing. The final SEE device configuration is shown in Fig. 3d.

RESULTS

Optical Performance

The optical performance of the SEE device was evaluated using a USAF resolution target (#53-715, Edmund Optics). The resolution target (Fig. 4a) was placed about 5.2 mm from the probe's distal tip so the middle circular region of the FOV is in focus. As the probe spun, the spectrally encoded lines were continuously acquired by the sensor, stitched together to reconstruct the two-dimensional image, and normalized by a calibration spectrum (an averaged spectrally encoded line over an entire image). The images were acquired at a frame rate of 15 Hz, where each image was comprised of 1000 spectrally encoded lines. The acquired image (Fig. 4a) has a total angular FOV of 100° . The spatial resolution and the SNR were not uniform across this FOV. These parameters were not constant across the image because of optical aberration, the nonuniform density distribution of the detection spot (Fig. 3b, right inset), and higher illumination at the center relative to the periphery (due to increased sampling at the center relative to the edges). To further analyze the resolution of the SEE image, the FOV was divided into innermost, middle, and outermost circular regions. The averaged radial/angular spatial resolutions (edge response, FWHM) were $20.3\ \mu\text{m}/21.2\ \mu\text{m}$, $22.5\ \mu\text{m}/24.8\ \mu\text{m}$, and $27.9\ \mu\text{m}/34.8\ \mu\text{m}$ for the innermost, middle, and outermost circular regions, respectively. The total number of resolvable points was calculated as:

$$\frac{A_n}{R_n} \cdot 2 \quad \{n=0,1,2\},$$

where A_n was the area of each region, R_n was the resel area within each region, and $\{n = 0,1,2\}$ corresponded to the innermost, middle, and outermost regions of the image. The ratio was multiplied by a factor of two to account for the fact that the radial dimension was Nyquist sampled. Therefore, the total effective number of imaging elements was estimated to be $\sim 344,000$. The SNR of the SEE image was 25 dB, 14 dB, and 3 dB at the innermost, middle, and outermost circular regions, respectively. In addition, the SEE image had a small dark spot at the center of the FOV, which was caused by the spectrally encoded line shift described in Section 2.2, and some circular and radial stripe artifacts. The circular stripe artifact was caused

by inadequate spectral compensation. The radial stripe artifact (e.g. top-right part of Fig. 4a) was caused by changes in the baseline signal measured through the MMF array while the SEE probe was spinning.

To evaluate the SEE performance and quality compared to other technologies, we chose one of the smallest commercial chip-on-the-tip endoscopes (MinnieScope-XS, Enable Inc. (16)) with an outer diameter of 1.4 mm and an effective number of pixels of 160,000 (400x400), which is approximately 2-fold smaller than the SEE probe's effective number of imaging elements. Figure 4b shows a USAF image that was captured using the chip-on-the-tip endoscope at a working distance of 5.2 mm. In the vertical/horizontal direction, the total angular FOV at the center and at the edges of the chip-on-the-tip endoscope image was about 62.2° and 66.5°, respectively, while in the diagonal direction, the total angular FOV was about 85.7°. The spatial resolution (edge response, FWHM) was calculated by examining each RGB channel separately; the best spatial resolution was 36.6 μm and 33.9 μm at the horizontal and vertical directions, respectively. However, when examining the smallest object in the USAF target (Group 4, element 3; line width of 24.8 μm), the lines can be still resolved by the human eye in the RGB image. Figure 4c shows a zoom-in of the smallest objects in the USAF target for both the SEE device (Fig. 4c, top inset) and the chip-on-the-tip endoscope (Fig. 4c, bottom inset). The working distance was modified in both devices to achieve the best image of these objects. In both devices the smallest spaced objects (24.8 μm ; Group 4, element 3) were still resolvable, however, the SEE device provided clearer and sharper images.

Swine Joint Imaging

To demonstrate the capacity of the forward-viewing SEE probe to image clinically relevant anatomic structures, it was used to image a swine knee joint *ex vivo* (Partners IRB protocol #2015N000144). The target joint was the Intertarsal joint that joins the distal part of the Calcaneus bone and the 4th Tarsal bone (Fig. 5a). The swine skin and tissue were dissected to enable access to the Intertarsal joint. The SEE device was placed about 5 mm from the lateral side of the Intertarsal joint when the images (Fig. 5b; Visualization 1) were acquired with a frame rate of 15 Hz. Color images (Fig. 5c; Visualization 2) of the same Intertarsal joint were acquired, with a frame rate of 30 Hz, using the chip-on-the-tip endoscope. All images were acquired after the insertion of the endoscopes. While the chip-on-the-tip endoscope was inserted from a closer point to the joint level, the SEE device was inserted from a lower point and had a larger insertion angle relative to the joint.

Both SEE and chip-on-the-tip endoscope images revealed the joint structure including articular cartilages of the Calcaneus bone and the 4th Tarsal bone, the gap between them, the inner edge of the Calcaneus bone (red arrow), and tissue that blocked the endoscope view (yellow arrow). While the chip-on-the-tip endoscope images suffered more from the specular reflections, the SEE images had circular and radial stripe artifacts due to spectral non-uniformity that were not compensated. In addition, as described in Section 2.2, the SEE images had a small dark speckled signal gap in the center of the images that resulted from a slight deviation of the spectrally encoded line from the center of the probe's rotational axis. The FOV of the SEE and the chip-on-the-tip endoscope images were slightly different due to the different insertion position and angle relative to the joint, the different imaging distance from the joint, and the different FOV of each endoscope. Comparing the images acquired with a similar imaging distance (Fig. 5b, c) shows the wider FOV of the SEE device, which revealed larger areas of the Calcaneus and the 4th Tarsal bones. In addition, the wider SEE imaging angle relative to the joint had emphasized the crinkled surface of the 4th Tarsal bone (Fig. 5b). However, the chip-on-the-tip endoscope provided a color image that emphasizes the difference

between the white articular cartilages at the tip of the condyles and the pinkish tissue beneath it, while the monochromatic SEE image lacks these details.

DISCUSSION

The current forward-viewing SEE device overcomes many of the limitations of the previous forward-viewing SEE probe (13,14); it has a smaller diameter, the probe is monolithic, the device forms an image by continuous scanning, and the frame rate is sufficiently high to enable seamless real-time imaging. The combination of the two separate channels – a rotating illumination probe and a stationary MMF detection array – reduced complexity, eliminated back reflection and cross-talk between channels, reduced speckle noise, and increased the SNR. Indeed, imaging and navigating in narrow cavities, for various clinical applications, could be attainable using the miniature forward-viewing SEE device described here.

One missing element that would be required for use *in vivo* is an optical window to protect the optics at the tip of the device. The current device did not contain this window, as we used the device in a controlled, *ex vivo* setting. However, our next generation device, which will be used for *in vivo* imaging, will have an end window while maintaining the same outer diameter. Another area of improvement would be to increase SEE detection speeds to allow video rate imaging. The SEE images were acquired at a frame rate of 15 Hz, which is sufficiently high to enable seamless real-time video. The camera that was used to grab and process the signal in the current system limited the frame rate to 15 Hz. In the future, the camera can be upgraded to achieve video-rate (30 Hz) imaging.

SEE image quality differed across the FOV due to several reasons. First, the center of the image was angularly oversampled while the periphery was undersampled. Peripheral sampling can be increased by sampling more spectrally encoded lines using a faster camera. Second, the light collection efficiency was lower at the periphery in part because of the nonuniform detection density distribution (Fig. 3b, c). In addition, the detection regions for the different MMFs overlapped much more near the center than in the periphery. Third, the field curvature and the resolution drop, caused by the GRIN lens aberrations, reduced the image quality at periphery of the image. This effect could be addressed in the future by modifying the lens design to correct for these aberrations. Fourth, the focal shift between the center and periphery was about 1 mm, caused mainly by the chromatic aberration of the GRIN lens. Again, this issue could be abrogated by an improved lens design. Fifth, the SEE images, especially the swine joint images, had circular and radial stripe artifacts due to spectral non-uniformity that were not compensated. These stripe artifacts can be addressed through more sophisticated image processing algorithms. In the future, if all of these aberrations and artifacts are corrected and the sampling in both the radial and angular coordinates is performed at Nyquist rate, the effective number of imaging elements for this probe could exceed a megapixel.

Comparing the forward-viewing SEE device and the commercial chip-on-the-tip endoscope, the SEE device has a smaller diameter, wider FOV, higher effective number of imaging elements, and better spatial resolution. In addition, the SEE device compares directly to other state-of-the-art single-fiber endoscopes, such as the scanning fiber endoscope (SFE) (17). The SFE illumination probe consists of a static two-lens assembly placed in front of a single-mode fiber that is resonantly scanned by a piezoelectric actuator in a spiral pattern. The illumination light combines red, green, and blue laser light. The reflected light is collected through MMF array that surrounds the illumination probe. To our knowledge, the smallest SFE device reported to date (17) has an outer diameter of 1.2 mm, a maximum FOV of 100°, and full color 30 Hz video with a spatial resolution of about 20 μm . Despite the similar SFE optical performance and diameter to the SEE device, the SFE has a longer rigid tip of 9 mm, which presumably decreases its bend radius.

The main drawback of the current SEE device compared to chip-on-the-tip endoscope and SFE is its lack of color imaging capability. Examining the tissue in color can provide valuable diagnostic information and in many cases is essential. Recently, a single-beam benchtop color SEE system was reported (18). The color SEE system used a single broadband light beam with a custom grating that diffracted the light beam into three overlapping orders; red, green, and blue spectral bands from the third, fourth, and fifth orders, respectively. Using this configuration, each point over the line was illuminated with three different wavelengths, enabling the reconstruction of RGB information. In the future, combining this technique with the current forward-viewing SEE probe design could provide a miniature color SEE device with distinct advantages in resolution and image quality.

In summary, a forward-viewing SEE probe was designed, fabricated, and demonstrated to be suitable for imaging within narrow spaces such as joints. Although the chip-on-the-tip endoscope provided color imaging, the miniature SEE probe showed a better spatial resolution, a wider total angular FOV of 100°, and a larger effective number of imaging elements. These results along with the smaller diameter of the SEE device will potentially make it useful for various applications that require high quality endoscopic imaging within confined cavities.

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FIGURES

Fig. 1. Schematic of the forward-viewing SEE device. SMF - single-mode fiber; MMF - multimode fiber.

Fig. 2. Forward-viewing SEE illumination probe. (a) The optical assembled components of the 500- μm monolithic probe. (b) A photograph of the spectrally dispersed light from the forward-viewing SEE illumination probe. SM – single-mode; GRIN – gradient index; FOV – field of view.

Fig. 3. SEE detection fibers. (a) Multimode fiber with 0.66 NA and a 0° angled tip (left inset) resulting in a circular detection spot (right inset) with a total angle of view of 82.6°. (b) By polishing the multimode fiber tip with a 17° angle (left inset), the detection spot (right inset) was elongated to cover a total angular field of view of 102.5°. The lower and upper part of the detection spot (right inset) collected light from the center and the outer circumference (edge) of the SEE illumination probe's field of view, respectively. (c) Illumination through one of the fibers in the circular MMF array shows the detection area covered in practice by the polished MMF. (d) A front view of the 1.27-mm SEE device including the illumination probe and the circular multimode fiber (MMF) array. The heat shrinkable outer tubing (red arrow), the MMFs (black arrow), the inner tubing (yellow arrow), and the grating at the tip of the illumination probe (white arrow), can be clearly seen from this vantage point.

Fig. 4. USAF resolution target imaging obtained using the SEE device (a; c, top inset) and a commercial chip-on-the-tip endoscope (b; c, bottom inset). (a) and (b) demonstrate the full FOV of each endoscope and were imaged with the same working distance (5.2 mm) demonstrating a larger angular FOV for SEE. (c) SEE (top inset) and chip-on-the-tip endoscope (bottom inset) zoomed-in images of the smallest objects in the USAF resolution target, which are located at the center of the full FOV. The working distances were slightly modified to achieve the best image quality. The magnified images qualitatively show a better resolution for the SEE device. The illumination optical power of both endoscopes ranged between 0.8-1.5 mW; the power was adjusted each time to avoid specular reflection.

Fig. 5. *Ex vivo* imaging of swine Intertarsal joint, which joins between the Calcaneus bone (top) and the 4th Tarsal bone (bottom), using smartphone camera (a), the SEE device (b), and the chip-on-the-tip endoscope (c). The joint bones were moved relative to each other between the acquisition of image (a) and images (b, c). Red and yellow arrows point at the inner part of the Calcaneus bone and some of the surrounding tissue that blocks the endoscope view, respectively. The different FOV of (b) and (c) is due to the larger SEE FOV and the different insertion position and angle relative to the joint. Scale bars, 5mm for (a) and 1 mm for (b, c).