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Fiber Bundle Fluorescence Endomicroscopy

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Abstract: An improved design for fiber bundle fluorescence endomicroscopy is demonstrated. Scanned illumination and detection using coherent fiber bundles with 30,000 elements with 3 μm resolution enables high speed imaging with reduced pixel cross talk.

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OCIS codes: (110.2350) Fiber optics imaging; (170.2150) Endoscopic imaging; (170.2520) Fluorescence microscopy

Fiber optics based endoscopy has a long history of clinical applications in the gastrointestinal (GI) tract [1, 2]. The recent development of imaging fiber bundles enables the combination of endoscopy with microscopy technologies, including confocal and fluorescence microscopy [3-6]. Among various fluorescence endomicroscopy techniques, line illumination is especially attractive as it provides simpler scanning mechanism compared to point illumination and less signal crosstalk compared to full-field illumination [7, 8]. Line illumination fiber bundle fluorescence endomicroscopy has been reported recently with a full field detection scheme [3, 9]. In this paper, we demonstrate a novel fiber bundle fluorescence endomicroscopy system incorporating both line illumination and line detection techniques. The use of a line scan camera as the detector enables confocal detection as well as the rejection of unwanted scattered light, which is important for reducing crosstalk from adjacent lines and therefore improving signal-to-noise ratio in the image. The imaging speed using line detection can be significantly higher compared to point scanning and detection. In addition, line scan imaging provides better immunity to motion artifacts compared with full field illumination and detection. Line scan cameras provide parallel data acquisition from multiple pixels at line rates of 50 kHz or more. High speed imaging is important for *in vivo* applications to minimize motion artifacts and enable high magnification.

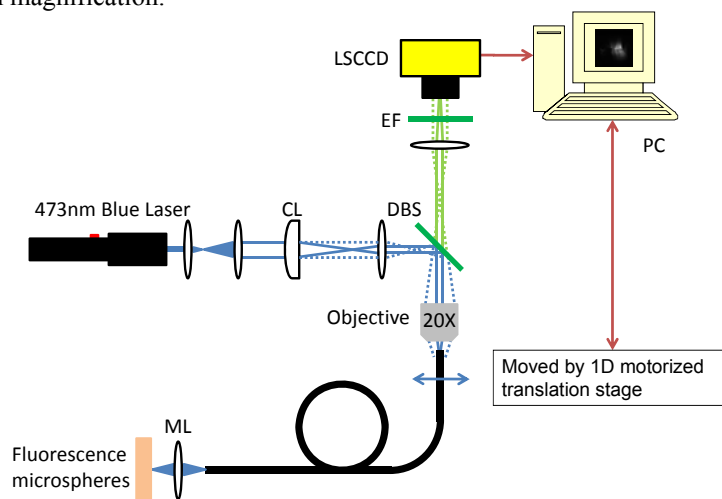


Fig. 1. Preliminary line scan endomicroscopy system. CL: cylindrical lens; DBS: dichroic beam splitter; EF: edge filter; ML: microlens.

Fig. 1 shows the setup of the line scan endomicroscopy system. The light source is a portable diode pumped, frequency doubled blue laser with a center wavelength of 473nm. The beam is expanded using a telescope, focused in one dimension with a cylindrical doublet lens, and collimated in the same dimension by a spherical lens. The beam then is reflected by a dichroic beam splitter and coupled into a 30,000-pixel fiber bundle (FIGH-30-650S, Fujikura) using a 20X objective. Each fiber in the fiber bundle has diameter of 3 μm and the core-to-core spacing between fibers is 3.3-4 μm and the outer diameter of the fiber bundle is 750 μm . A microlens is placed at the distal end of the fiber bundle to achieve 1X magnification on the imaging plane. The excited fluorescence is collected by the fiber bundle and imaged on the line scan camera. The combination of the objective and the tube lens gives a 20X magnification from the fiber proximal end to the line scan CCD camera (M2CL1014, e2V), which has 1024 pixels of 14x14 μm size. The fiber bundle is scanned by a one-dimensional linear translation stage which is

synchronized to the imaging frame rate to generate images with 1024x640 pixels. Scanning the fiber bundle in one dimension can avoid beam aberration at focal plane compared to scanning using a galvanometer mirror and lens. In the current experiment, the camera exposure time is 50 μ s per line and a rate of 7 frames per second (fps) was used to demonstrate the feasibility of the imaging system. Depending on fluorescence signal levels, a much high rate (up to ~50fps) might be obtained with a shorter exposure time (~20 μ s) and a higher speed linear translation stage.

Fig. 2 shows images from a sample with fluorescent microspheres obtained with the line scan fiber bundle system. The excitation peak of the microspheres is at 488nm and the emission peak is at 560nm. The average diameter of the microspheres is 1 μ m. Figs. 2(B) and (C) are the enlarged views in Fig. 2(A) and these figures show the distribution of the fiber pixels clearly. In fig. 2(C), fluorescence from individual pixels can be observed, indicating that the imaging system can distinguish fluorescence from microspheres smaller than the 3 μ m diameter of an individual fiber. Crosstalk between adjacent fibers is very small. This result shows the capability of the line scan endomicroscopy system to distinguish small fluorescence sources from the sample, suggesting its potential for visualizing cellular structures.

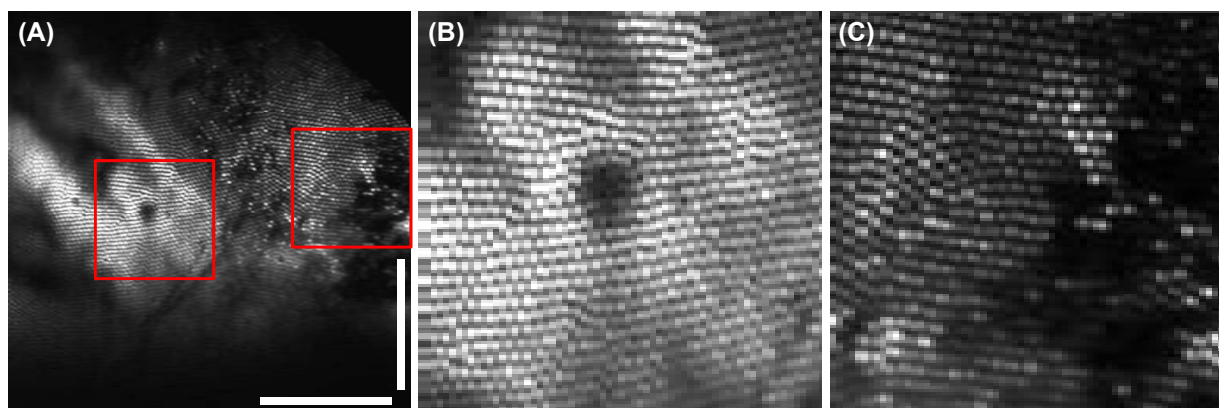


Fig. 2. Images from the fluorescence microsphere sample. (B) and (C) are enlarged views from the left and right boxes in (A). Scale bar: 100 μ m.

We demonstrated a novel fiber bundle endomicroscopy system which utilizes both line illumination and line detection technique. The use of line illumination and detection promises to enable higher imaging speed, as well as reduced crosstalk and improved signal to noise ratio. These advantages are especially important when imaging scattering tissue, since they reduce the background scattering present in full field illumination and detection. The coherent fiber bundle is small enough to be introduced through the accessory port of a standard endoscope. This new line scan fiber bundle endomicroscopy system is promising for clinical applications which require real-time imaging with cellular level resolution. This research is sponsored by NIH 5R01-CA075289-13 and AFOSR FA9550-07-1-0101. T. Tsai acknowledges fellowship support from the Center for Integration of Medicine and Innovative Technology.

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