Integrated simultaneous dual-modality imaging endospeckle fluoroscope system for early colon cancer diagnosis

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Abstract. An integrated and flexible fiber optic endoscope system for diagnostic investigations in medical cavities using specially designed probe distal and proximal ends so as to facilitate simultaneous speckle correlation analysis and fluorescence spectroscopic imaging is presented. © *2005 Society of Photo-Optical Instrumentation Engineers.*
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Minimally invasive intracavity investigations play an important role in disease diagnosis in body cavities, such as detection of cancerous growths in the gastrointestinal path.[1] Normal white light imaging that has been used until now fails normally in identifying the presence of flat dysplacia or any growths beneath the mucosal surface.[2] The imaging electronics are allowed to go inside the human body through the endoscope in such conventional systems. Hence any change or modification in the detection electronics requires pulling out the entire endoscope probe from the human body, which add to the injury of the tissue walls and discomfort of the patient. Also, conventional external and internal imaging methods employed in colon inspection have the limitation of being able to detect only large polyps and abnormality. Such conventional endoscopy (colonoscopy) followed by biopsy is used as today's gold standard for colon cancer diagnosis. Once a suspicious growth is found in the colonoscopy, a sample of the tissue is taken out of the body for examination (biopsy procedures). However, a probe system that can detect growth and simultaneously confirm the presence of cancer could be possible if the entire diagnosis can be done during an endoscopic examination itself. Such a system can help avoid the complications and errors due to the tissue sampling. In this context, we are introducing an all-fiber-optic endoscope probe system called an endospeckle fluoroscope, which can work simultaneously in two modalities of (1) digital speckle shearographic imaging modality for identifying the abnormal growths and (2) laser-induced fluorescence spectral imaging modality for cancer diagnosis.

This developed system consists of (1) the fiberscope probe, (2) the collection lens, (3) the optical component selection unit (OCSU), consisting of a beam combiner/splitter, filter, and biprism, to facilitate the respective imaging modality, (4) a digital speckle correlation unit (DSU) that consists of a CCD camera and the associated image processing system, and (5) a monochromator unit for spectral analysis. A schematic diagram of the endofiberscope system is shown in Fig. 1. Laser light of 10 mW from the laser source (λ=532 nm) is coupled into a sheathed single mode fiber, which is then connected to a bare fiber end (with 1-mm removable sheath) of another length of same type of fiber via a connector known as a finger splice (FC). The sheathed length of this bare fiber is then fed into the illumination channel of the probe. This type of arrangement allows easy plug-in and plug-out of the probe and the source. The source light is delivered to the colon surface from the fiber port at the probe distal end. The return light from the cavity surface is collected by an imaging lens and is transmitted through an image fiber (Fujikura 15-600N, 600-μm diameter, 15,000 pixels). A ball lens (diameter =3 mm) at the image fiber end is used as the imaging lens due to its excellent symmetry along the probe axis and its ability to eliminate barrel distortion. An objective lens (Mitutoyo infinity corrected 20X objective with 20-mm working distance) placed at the proximal end of the probe collects the return image from the image fiber. The OCSU directs the collected return speckle pattern and emitted fluorescence into the two respective channels A and B as shown in Fig. 1.

A phantom colon model (purchased from Buy-A-Mag Co.[3]) that resembles the human colon with simulated growth and cancerous abnormalities is employed as the test specimen in this investigation. At different locations inside this phantom colon, layers of phantom tissues were pasted (purchased from Simulab Corp.[4]). The tissue layers each have a thickness equal to the layer thickness of the real colon (approximately 1 mm). Phantom tissue material representing abnormality is introduced between the first and second tissue layers. The size of the tissue material to represent the abnormality is chosen to be either 1 mm (to represent small abnormality) or 3 mm (to represent larger abnormality). Also, exogenous fluorochromes that have the same emission wavelength range as endogenous fluorophores present in normal and abnormal colons[5] were simulated in the test phantom model.

To illustrate the functioning of the proposed probe system, first the working principle of the shear configuration (section A in Fig. 1) is explained here. The reflected speckle pattern is collected by the ball lens and transmitted through the image fiber. The collection lens after the probe proximal end collects the speckle pattern transmitted through the image fiber. This collected speckle pattern, which is passed through a bandpass filter (to filter out the emitted fluorescent light), is sheared into two by means of a custom-made biprism (1-deg wedge angle) inserted between the collection lens and the CCD camera. The sheared speckle patterns are captured by the CCD camera and stored in frame buffers of the image processing system for further processing in the DSU. Frame corresponding to the nondeformed state of the phantom colon model is stored as the reference frame. Frames corresponding to the deformed state of the
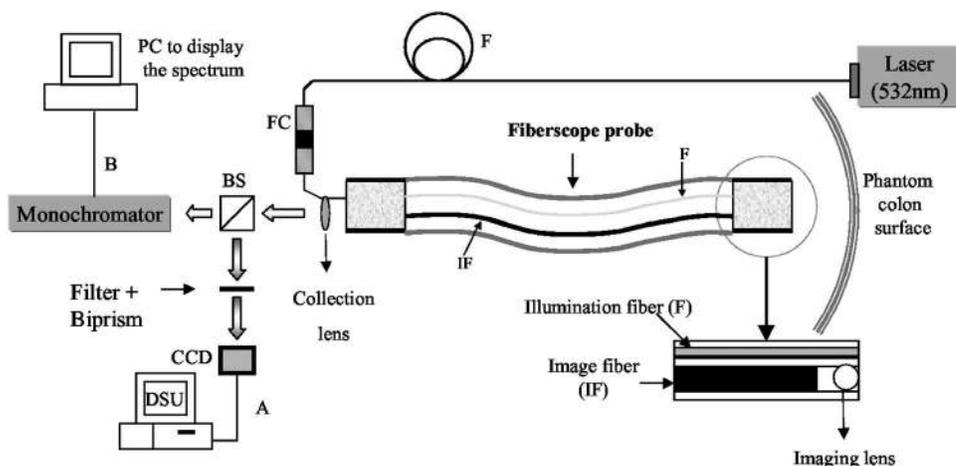
Fig. 1 Schematic of the integrated dual-modality imaging endospeckle fluoroscope system.

object are subtracted from the first frame at the rate of 25 frames per second. The evolution of fringes is observed on a PC monitor in real time, using the developed software and EDC 2000N image-processing card.

A fringe pattern in the shape of a butterfly was expected to be formed from the phantom model, when the endoscope system was set up in the shear configuration.[6] However, when the endoscope was set in the shear configuration, the imaged area falls under the central region of the butterfly fringe pattern, due to the smaller interrogation (imaged) area. The shear fringe pattern obtained at the abnormality site for the abnormal colon phantom (cancer growth size 3 mm) using the fiberscope is shown in Fig. 2, as an illustrative example. It represents a separate fringe system formed at the position of the abnormality upon induced displacement of the phantom specimen. In this modality, the presence of abnormality created a separate fringe system upon the decorrelation of the original fringe system. In this way, identification of smaller abnormalities (≈ 1 mm) was also possible with the endoscope system in the shear configuration.

In the second modality as shown in scheme B of Fig. 1, the same laser source is used for providing necessary excitation to the fluorophores present in the same phantom

model (exogenous fluorochromes that have the same emission wavelength range as endogenous fluorophores present in normal and abnormal colons were simulated in the test phantom model). Here, Rhodamine 6G was selected as the staining agent (fluorochrome) for the phantom tissue, whose emission corresponds to that of the colon fluorophore. In this modality, the collection lens output is directed toward a PC-Monochromator system (Dongwoo optron, DM 150), where the OCSU output is scanned according to the set resolution of the monochromator. The obtained excitation-emission fluorescence spectra, which is displayed on the PC monitor, are shown in Fig. 3. The diagnosis of cancerous regions in the colon tissue was made by looking into the difference in emitted intensity of normal and cancerous regions. A reduction in emission intensity is observed at the abnormal region representing cancerous growth, as compared to the normal region.

In conclusion, we have experimentally illustrated a novel dual-modality endospeckle fluoroscope system for simultaneously identifying the presence of abnormalities and for diagnosis of suspicious cancerous growth at the detected abnormality sites. The abnormalities simulated in the phantom colon model resembled the early stages of cancer growth, thus making the endoscope system effective in
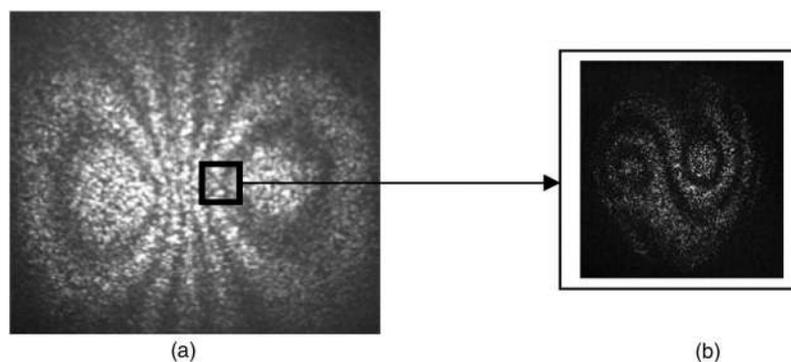

Fig. 2 Detection of growth using speckle correlation modality (Fig. 1, section A): (a) butterfly fringe pattern corresponding to the normal surface and (b) fringe pattern developed at the growth (of 3-mm size) using the endospeckle fluoroscope system. The simulated growth site is depicted as a square in (a).
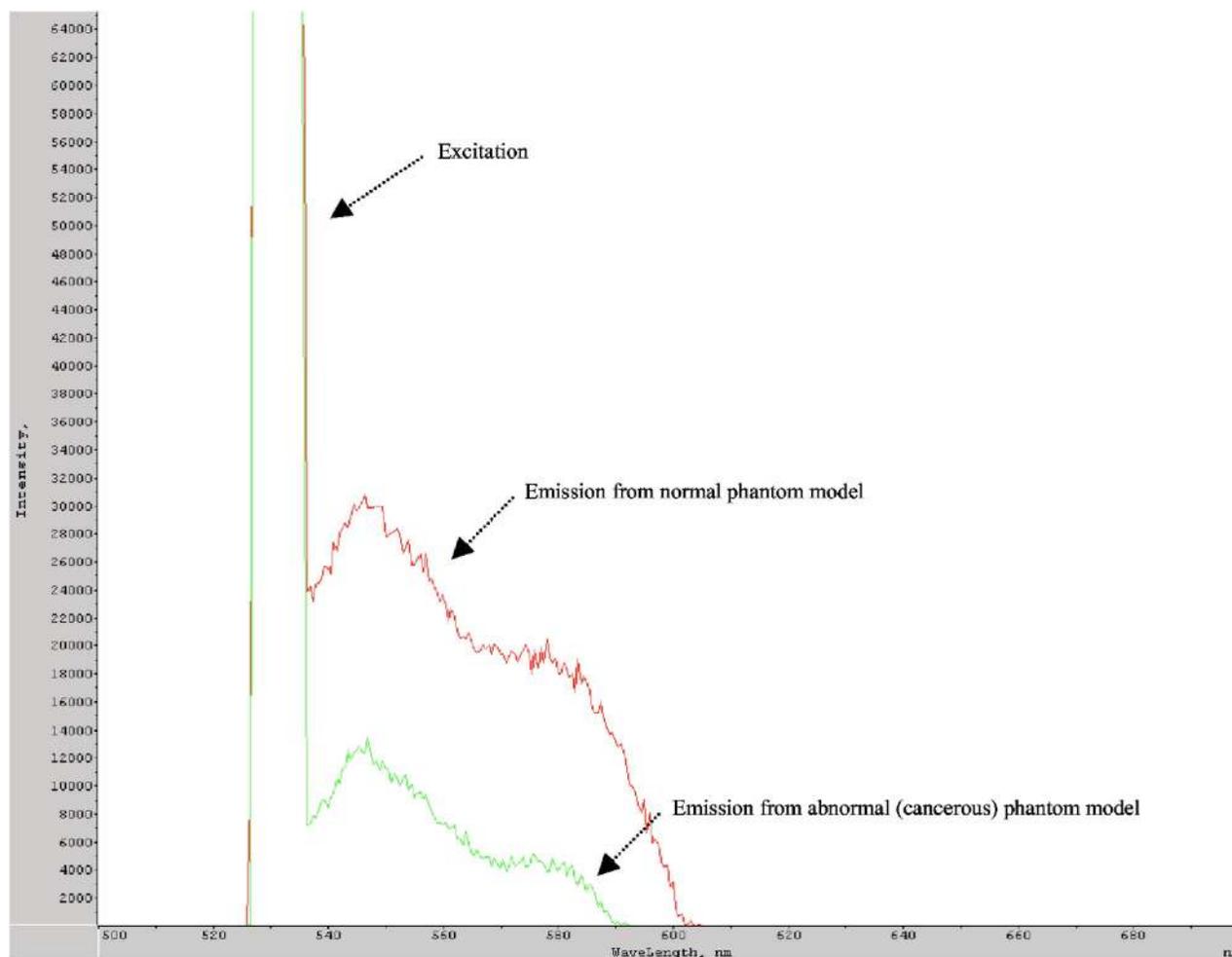
Fig. 3 Excitation-emission spectrum collected using the fiberscope.

identifying the presence of cancer at an early stage. We have compared the detection efficiency for both modalities. In the speckle modality, as already mentioned earlier, we can detect the abnormality with size 1 mm (which is our minimum detectable size). However, we found that the when the size is very small, the fluorescence emission intensity (fluorescence modality) also reduces. The proposed system can be applied for *in vitro* and *in vivo* minimally invasive medical diagnostics for understanding the tissue biochemistry, which may in the long run provide an answer to the replacement for current surgical biopsy approaches. For the laser illumination and excitation, the threshold fluence limits normally applicable to soft tissues have been considered. It should be mentioned that at the moment the developed probe does not have the locomotion integrated into it, and future work will concentrate on these aspects. There is a renewed interest in using speckle techniques, holography, etc. integrated into the commercial probe where fiber optics are used for illumination and micro-CCD or other optical imaging is used for microscopic examination of tissues.[7] In this context this proposed technique has

real relevance apart from its novelty as illustrated in this paper.

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