A dual mode imaging fiberscope system for colon cancer diagnosis

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ABSTRACT

This paper presents an all fiber optic endoscope system working in double modalities of normal imaging and fluorescence spectrum analysis, for the diagnosis of colon cancer. A coherent laser source is used here for providing the simultaneous illumination (for normal imaging mode) and excitation of fluorophores (for fluorescence spectrum analysis mode). The design aspects of the fiberscope distal end with two illumination/excitation fibers for large area interrogation and a fiber bundle based imaging system is discussed here. The two illumination/excitation fibers are oriented at equal angles from their respective optic axis for providing the maximum illumination/excitation of the test target area in line with the optic axis of the fiberscope probe. The probe elements consist of a ball lens at the probe distal end, a high resolution image fiber, and an objective lens at the probe proximal end. Separate detection systems are provided for displaying the image / analyzing the fluorescence spectrum. Experiments were carried out with the developed fiberscope system by employing a prototype colon phantom sample as the test specimen. In the normal imaging mode, the abnormal areas in the phantom colon model are identified by looking at the protrusions in the reflected image. In the fluorescence spectrum analysis mode, these areas of abnormalities depicting cancerous growths showed a decrease in emitted intensity as compared to the normal areas.

Keywords: endo-fluoroscope, dual modality imaging, bio-imaging, fluorescence analysis

1. INTRODUCTION

Flexible fiber optic endoscopes permit visualization of normally inaccessible areas of human body, such as body cavities [1, 2]. Due to the unlimited length provided by such endoscopes, demands on design and performance of endoscopic instruments; including very small diameters and extreme flexibility have increased over the last decade. Most of the flexible endoscopes adopt an optical fiber based illumination scheme. Besides the transmission of white light images of the internal body parts, such endoscopes can also be made useful for medical applications such as fluorescence diagnostic techniques [3]. Also, in the field of cancer diagnosis, fluorescence techniques overcome the size limitations of detected polyp, with conventional white light endoscopy. White light endoscopy cannot be used to identify the abnormalities unless there is some topographic alteration on the tissue [3] and thus is not useful in diagnosing flat dysplasia. On the other hand, fluorescence techniques in endoscopy are of great diagnostic value, as the qualitative differences in tissue fluorescence intensity are used to identify the presence of cancer during endoscopy. Fluorescence intensity of cancerous tissue will be less as compared to that of normal tissue and thus the fluorescence spectrum collected from body cavities can normally highlight regions of suspicious tissue providing biopsy guidance. Since the use of external drugs to induce tissue fluorescence is having undesired side effects, fluorescence techniques based on the autofluorescence of the endogenous fluorophores contained in the tissue provides a more promising way of disease detection [3]. Since the tissue autofluorescence intensity is weak, the selection and use of proper imaging elements is having vital importance for the maximum collection of the emitted intensity.

Most of the reported and commercial fluoroscopes (endoscopic instruments used for fluorescence image collection / spectrum analysis) make use of a single light source (coherent and incoherent) in order to provide the necessary excitation
for inducing fluorescence [4-7]. Different arrangements of the excitation and collection fibers have been reported in the literature that make use of the following geometries (i) single fiber for excitation and collection [4] and (ii) single fiber for excitation and multiple fibers for collection [5,6]. The use of dual excitation in fluorescence spectroscopy will enhance the interrogated tissue area, thus maximizing the emitted fluorescence [8]. For all types of fluoroscopes mentioned above, the collection optics is designed for maximizing the emitted fluorescence, while the reflected laser light is normally ignored. In this context, an all fiber optic endoscope is discussed here, which can be operated in dual modalities of imaging the inner body cavity walls as well as for the fluorescence signal collection from the cavity tissue sites.

2. METHODOLOGY

The schematic diagram representing the developed fiberscope system with associated detection systems for imaging the colon inner cavity walls and for fluorescence collection is shown in Fig. 1.

Light from the laser source (532nm, used as the illumination/excitation source) is coupled into a sheathed single mode optical fiber, which is then split into two using a 1 x 2 fiber splitter. The two split fibers are provided with FC connector at the end port. The fibers are connected to two single mode bare fibers (each having a 1mm diameter removable sheath) by making use of a bare fiber adapters, and theses bare fibers are fed to the illumination / excitation channels (F) of the fiberscope. The use of a bare fiber adapter allowed the easy plug-in and plug-out of the excitation source from the fiberscope probe. A ball lens placed at the front end of the fiberscope collects the reflected image as well as the tissue fluorescence so as to pass through the image fiber (IF). At the receiving end of the probe, an objective lens is used to collect the emitted light as well as the image of the tissue wall. In the imaging mode, the objective lens output is imaged using the CCD camera that is integrated to a PC, and images of the cavity wall are displayed on the monitor in real-time (Scheme A). A band pass filter placed in front of the CCD camera filters out the emission, from the fiberscope output. In the fluorescence spectrum analysis mode, the objective lens output is fed to the monochromator [Dongwoo Optron, DM 150], which is integrated to a PC and the emission spectrum is analyzed with the use of related software (Scheme B).
2.1 Design considerations of the fiberscope distal end

The design details as well as the dimensions (see Fig. 2) of the probe distal end and its constituent elements’ selection and integration of optics to facilitate the examination of large intestine are discussed here.

The distal end of the probe consists mainly of the excitation fiber ports and the image fiber-imaging lens unit. The excitation fiber ports are provided with an angle of inclination of 2.86 degrees for providing maximum illumination / excitation of the test target area, the center of which is lying in line with the probe axis. The selection of image fiber is to be done keeping in mind, the required increase in the flexibility of the probe and also the miniaturization aspects of the whole image collection scheme. Moreover, such schemes allow all the detection electronics to remain outside the human body to facilitate the requirements of a change of imaging schemes more easily. An appropriate probe is designed to incorporate the illumination / excitation fiber (single mode, 1mm diameter including the sheath), imaging lens (ball lens of 3mm diameter) and imaging fiber (15,000 pixels, 600µm diameter) as shown in Fig. 2. The choice of the ball lens as the imaging lens was made due to its uniformity and symmetry in all directions. The diameter of the ball lens was selected according to the criteria that too small diameters will cause barrel distortion in the collected image and too large diameters will increase the overall probe diameter. The excitation port center in the probe is oriented at a distance of 2.5mm from the image fiber/imaging lens center. The diameter of the imaging port end was fixed at 3.1mm in order to fix the imaging lens, allowing a tolerance of 0.1mm. The total length of the distal end is set to 20mm. The image fiber, which performs the double role of image transmission as well as an emitted fluorescence collection and guidance, is positioned at the focal plane of the imaging lens.

Figure 2: Dimensions of the fiberscope distal end

2.2 Fluorescence analysis using the designed fiberscope

An efficient endoscopic system for biomedical applications requires the optimum design parameters such as excitation energy, distance between the endoscope distal end to the test tissue surface, spatial distribution of the emitted signal intensity in order to have a better fluorescence signal from the concerned biological tissue and the signal intensity collected through the probe. Exact information and knowledge regarding the excitation energy is needed for deciding its optimum level as too much energy causes tissue damage and too little energy gives only undetectable signals. This also determines the closeness of the distal end to the tissue wall. As absorption coefficient is a dependant parameter with wavelength, use of different excitation wavelengths requires different optimum excitation energy level for better performance. By considering all these points, a theoretical model is developed to determine the role of axial distance dependence of the probe in the spatial intensity distribution of the collected emission.
Imagine an endoscope with the distal end oriented at normal incidence to the colon wall as shown in Fig. 3.

Let us assume that the different points in the curved surface shown in Fig. 3 are at different planes. Let P be such a point distant $\delta$ from the plane containing the curved surface point that lies in the image fiber axis.

The excitation fluence and the collected emission with respect to the point P can be analyzed as follows.

The incident energy on the tissue surface from excitation ports $\equiv P \Delta t \cos \theta$, where $P$ is the incident source power at a certain specified wavelength, $\Delta t$ is the corresponding excitation time and $\theta$ the excitation angle for at point P, for both excitations ($\theta_1' \equiv \theta_2' \equiv \theta$). This energy from the excitation fiber port end is delivered over a solid angle $2\pi (1 - \cos \theta_{\text{max}})$.

Here $\theta_{\text{max}}$ represents the maximum excitation angle of excitation port 1 / excitation port 2.

The total excitation fluence $F$, due to excitation 1 and excitation 2 is given by

$$
F = \frac{P \Delta t}{2\pi (1 - \cos \theta_{\text{max}})(d - \delta)^2} \left( \frac{1}{1 + \left( \frac{(l - \Delta x)}{(d - \delta)} \right)^2} \right)^{3/2} + \frac{1}{1 + \left( \frac{(l + \Delta x)}{(d - \delta)} \right)^2}^{3/2}
$$

where $d$, $\Delta x$ and $l$ are the probe distance from the colon wall, the vertical distance of point P from the fiberscope optical axis, and the distance of imaging unit center to the center of the excitation port 1/ excitation port 2 respectively.
Now, $\delta = R - R \cos \beta = R - (R^2 - (\Delta x)^2)^{1/2}$ where $R$ is the radius of curvature of the tissue surface and $\beta$ is the sector angle including the point P and the tissue surface point, which lies in the image fiber axis.

The collected energy using the probe can be expressed as [8]

$$E_c = \left( \frac{\tan \alpha_{max}^2 F \eta \pi i^2 \tan^2 \theta_f}{N 2[1+(\Delta x / (d - \delta))^2]} \right)$$

where $\eta$ is the fluorescence energy conversion efficiency of the biological tissue, $\alpha_{max}$ is the maximum collection angle of the imaging unit, $I$ is the image distance of the ball lens, $\theta_f$ is half the collection angle of the image fiber, and $N$ is the total number of pixels in the image fiber. The approximate number of photons collected using the probe can be determined from $E_c$ by the use of energy per photon ($hc/\lambda$) where $h$, $c$, and $\lambda$ are the Planck’s constant, velocity of light and the emission wavelength respectively. Considering the transmission coefficient ($T_\theta$) and the packing fraction ($f_p$) of the image fiber, the total number of photons collected is given by,

$$N = \frac{\lambda T_\theta f_p E_c N}{hc}$$

3. RESULTS AND DISCUSSIONS

The designed and developed fiberscope system as shown in Fig 1 was tested in both modes (imaging mode and fluorescence analysis mode) employing a phantom colon surface (model from Buy-a-Mag corporation, USA) for estimating the ability of the probe for imaging the inner cavity as well as collecting the fluorescence emission. For checking the image collection efficiency using the laser light as the illumination source, the experimental setup was arranged as shown in the scheme ‘A’ of Fig. 1. The images of the phantom model of colon, obtained using the system are shown in Fig. 4, which illustrate the usefulness of the probe in imaging the inner body cavities with laser light. The abnormal regions of the phantom model are observed clearly as depicted in Fig. 4. In the second modality as shown in scheme ‘B’ of Fig 1, the same laser source is used for providing necessary excitation to analyze the fluorophores present in the same phantom model (fluorescent dyes that has the emission wavelength range as endogenous fluorophores present in the colon [7], were stained in the test phantom model). The obtained excitation-emission fluorescence spectrum is shown in Fig. 5. It can be observed that the detected signal efficiency is quite good and a reduction in emission intensity can be seen at the abnormal region representing cancerous growth, where disease abnormality is simulated.

![Figure 4: Image of the colon phantom showing the position of cancer growth taken using the fiberscope system](image)
4. CONCLUSIONS

It is illustrated that the use of an image fiber to carry the image along the endoscope flexible body can facilitate the operation of the endoscope in multiple modes of diagnosis, as the entire detection system is kept outside the body. This proposed system and concepts can be applied for in vitro and in vivo minimal 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. The use of a single laser as an illumination source for cavity imaging and as an excitation source for inducing fluorescence emission from the test target makes the system further compact.

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