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Evaluation of a novel high-resolution magnifying videoendoscope that is capable of photodynamic diagnosis and therapy for gastric cancer

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Summary
Objective: To evaluate the usefulness of a novel high-resolution magnifying videoendoscope called the XG-0001 (Fujifilm, Tokyo, Japan) that is capable of PDD and PDT in experimental and clinical situations.
Materials and methods: The fluorescences of three photosensitizers (i.e., porfimer sodium (Photofrin), protoporphyrin IX and talaporfin sodium (Laserphyrin)) were studied experimentally via excitation with a purple diode laser (VDL, wavelength 405 nm). Five consecutive patients with superficial early gastric cancer not indicated for surgery or other curative endoscopic treatment due to complicated serious diseases were enrolled in this study. After close endoscopic examinations, 2 mg/kg of Photofrin were intravenously injected into the patients for PDT, and 5-aminolevulinic acid (ALA; 15—20 mg/kg) was orally taken for PDD. PDD using VDL and PDT using an excimer-dye laser (630 nm, 4 mJ, 60 Hz) were performed with the XG-0001.
Results: Photofrin and Laserphyrin had experimentally the lowest and highest fluorescence intensities, respectively. The five patients comprised four men and one woman with a mean age 75.2 year and an age range of 56—83 years. Two additional cancerous lesions were newly detected by magnifying pharmacoendoscopy. In each patient, PDD was successfully performed.

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PDT could also safely performed and CR was obtained in 71.4% (5/7) of the cancerous lesions in five patients, and no serious complications were encountered.
Conclusion: The XG-0001, which is based on a simultaneous videoendoscopy method that uses an RGB color chip CCD, proved extremely useful in routine use and also in PDD and PDT for gastric cancer.

Introduction

Gastric cancer is one of the main cause of mortality not only in Japan but also in many developing countries [1]. Recently, new endoscopic treatments for early gastric cancer, such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), have been developed [2,3]. Furthermore, new endoscopic diagnostic procedures for early gastric cancer based on magnifying endoscopes [4] and image-enhanced endoscopies (IEEs), such as narrow-band imaging (NBI) [5] and flexible spectral imaging color enhancement (FICE) [6], have been established. Subsequently, the early detection and early treatment of gastric cancer has become possible; therefore, the mortality rate of gastric cancer is gradually decreasing. However, the limitations encountered for superficial gastric cancer patients for whom endoscopic and surgical resection are contraindicated due to serious complications remain to be addressed.

Photodynamic therapy (PDT) is defined as the use of photodynamic agents in the treatment of disease. A photodynamic agent is a substance that is activated by light to cause damage to tissue. Photodynamic agents can be exogenous and absorbed preformed from the environment or endogenous and formed within the body as an abnormal metabolite, e.g., porphyrins, or as a normal metabolite, e.g., phylloerythrin, and accumulated in tissues due to faulty excretion, e.g., in hepatic disease (Sounders Comprehensive Veterinary Dictionary, 3rd edition). Therefore, photodynamic diagnosis (PDD) is defined as the use of fluorescence detection using a photodynamic agent in the diagnosis of disease. PDT is one of the non-invasive endoscopic treatments for superficial early gastric cancer, and PDT utilizing an excimer-dye laser (EDL, Hamamatsu Photonics K.K., Hamamatsu, Japan) and porfimer sodium (Photofrin, Pfizer Japan Inc., Tokyo, Japan) is approved by the Ministry of Health, Labour and Welfare in Japan. Photofrin is a photosensitizer that consists of porphyrin compounds and is also a photodynamic agent. PDD using Photofrin to detect early-stage pulmonary tumors with purple light (405 nm wavelength) excitation has previously been reported [7]. In this manuscript, PDD is defined as a procedure that uses fluorescence detection of a photodynamic agent and purple light excitation.

We have used PDT for inoperable gastric cancer patients since 1988 [8]. However, a technical problem with PDT has existed for a long time; i.e., an optic fiberscope is needed during laser irradiation because endoscopic images changes caused by whiteout due to the intense laser light (Fig. 1A) when using a conventional videoendoscope such as the GIF Q240 (Olympus Medical Systems Corp., Tokyo, Japan). In 2003, we found that the EG-485ZH magnifying videoendoscope (Fujinon, now Fujifilm, Tokyo, Japan) could be applied to both PDT (Fig. 1B) and PDD after examination of the suitability of laser light and several videoendoscopes. In 2008, a novel high-resolution magnifying videoendoscope capable of PDD and PDT called the XG-0001 (Fujifilm, Tokyo, Japan) was developed.

The aim of the present study was to evaluate usefulness of the XG-0001 in experimental and clinical use.

Materials and methods

The novel XG-0001 high-resolution magnifying videoendoscope is based on the EG-590ZW (Fujifilm, Tokyo, Japan), which is a simultaneous method videoendoscope system that uses a red, green and blue (RGB) color chip charge coupled device (CCD). The optical magnification rate of the XG-0001 is up to 135 times on 19-inch high-definition color monitor; moreover, this endoscope is capable of 10 channels of FICE [6] as an IEE.

The study protocols were planned in accordance with the Declaration of Helsinki of 1975 and were reviewed and approved by the local ethical committee (No. 2015/2008).

Experimental PDD and PDT studies

To confirm fluorescence during PDD, we studied the three photosensitizers that are available in Japan: Photofrin, protoporphyrin IX (PpIX; SBI Pharmaceuticals Co., Ltd., Tokyo, Japan) and talaporfin sodium (Laserphyrin; Meiji Seika Pharma Co., Ltd., Tokyo, Japan). The light source was a purple diode laser (VDL, 405 nm wavelength) with a spectrometer (VDL-M1/ver.3.0SP; m & m Co., Ltd., Tokyo, Japan). The three photosensitizers were diluted to physiological concentrations that are used clinically (Photofrin: 2.5 mg/mL, PpIX: 20 nmol/L, Laserphyrin: 25 mg/mL) and dropped onto black sponges. During irradiation with the VDL via the XG-0001, fluorescence on the sponge was observed on a 19-inch high-definition color monitor, digital pictures and videos were recorded. Simultaneously, the spectrum of each photosensitizer was measured with a spectrometer. We also examined which FICE channel enhanced the fluorescence by PDD.

To determine the best conditions for the XG-0001 during PDT, we adjusted the pulse rate of the EDL and the shutter speed of this novel endoscope. Additionally, we determined which FICE channel best minimized the brightness on the color monitor due to the intense laser light during PDT.

Clinical study

Five consecutive patients with superficial early gastric cancer not indicated for surgery or other curative endoscopic