問題がある。

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F. 健康危険情報

なし

G. 研究発表

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H. 知的財産権の出願・登録状況

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分担研究報告書

胃がん撲滅と次世代への感染予防を目指した中学生、高校生に対する *Helicobacter pylori* 感染率調査と除菌治療の検討

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研究要旨

Helicobacter pylori（*H. pylori*）は小児期に感染し一生持続感染する。確実な胃がん予防と次世代への感染予防を目的として、行政と連携し中学生、高校生に対する *H. pylori* 検査と陽性者に対する除菌治療を行うことを目的にモデル地区にて検討を行った。医療従事者、行政、学校関係者、市民に対する講演会、市民公開講座を行い、保健行政担当者と複数回の打ち合わせを行い、対象と方法を検討した。高校生を対象としたパイロット研究では62.7%の受診率で *H. pylori* 感染率は6例、7.7%であった。全例が除菌治療を希望し副作用なく除菌治療を行い全例が成功した。平成26年度以降、3年間をかけて中学生、高校生の全学年を対象に行うことに決定した。

A．研究目的

Helicobacter pylori（*H. pylori*）は小児期に感染し、除菌治療を行わない場合、一生持続感染し、慢性胃炎、消化性潰瘍、胃がんなど様々な胃疾患の原因となる。本邦における胃がんの99%が *H. pylori* 感染であり、健常者に対する除菌治療においても胃がん発生が抑制されることが明らかにされた。しかし、小児期に感染する *H. pylori* による胃がん発生の予防には感染早期の小児～若年層に対する介入が必要と考えられる。また、衛生環境が整備された本邦では40歳代以降の *H. pylori* 感染率が10-20%以下と低下している。現在の主な感染経路は家族内感染、母子感染であることから、子供を産む前の世代に除菌介入することにより次世代への感染を予防する効果が期待される。

H. pylori 感染早期で成人と同様の検査、治療が可能な中学生、高校生に対するtest&treat（検査と治療）を行うため、北海道のモデル地区において受診率、感染率、陽性者における除菌治療の成績を検討し、test&treatの具体的方法について検討した。

B．研究方法

北海道内のモデル地区で以下の検討を行った。

1）自治体で導入するまでの手順の作成
稚内、美幌、由仁にて実際に導入することで作成した。

2）1次スクリーニング検査の精度検定
美幌町、稚内市において1次スクリー

ニング検査の精度検定を行った。

C．研究結果

①行政、医療機関の依頼により、実際に地域に赴き、説明会の実施、1 次スクリーニングの実施、陽性者に対する精密検査、除菌治療、除菌判定の実施を行い、手順をまとめた。図 1 に示すような手順で行うが、その際に最も重要なことは、行政、医師会、学校の連携と、各者の役割分担であった。すなわち、学校は尿検査の検体を収集するのみ、行政は保護者への通知、同意書の回収、結果の通知などの管理、病院は 1 次スクリーニング陽性者への説明、希望者への精密検査と除菌治療の実施を行う。

②稚内市の高校生、美幌町の中学生を対象に同意した生徒に対して尿中抗体検査と尿素呼気試験（UBT）を同時に測定した。745 例が参加し、陽性者と両試験の結果が乖離した生徒には便中抗原、血清抗体、血清ペプシノーゲン検査を行った。

ELISA 法による尿中抗体検査の精度検定の結果、感度 100%（44/44）、特異度 96.6%(677/701)であり、陽性反応適中度 64.7%(44/68)、陰性反応適中度 100%(677/677)であった。また、尿中抗体検査の結果が一致していた症例の尿蛋白陽性者は 10%(45/449)、一致しなかった症例の陽性率は 46.2%(6/13)で有意に不一致例に尿蛋白陽性者が多く、偽陽性の原因の一つとして尿蛋白陽性があることが確認された。

陰性反応適中度が 100%であり、尿中抗体検査は 1 次スクリーニング検査として適切であり、陰性者はピロリ陰性と考えられる。一方、陽性者のうち 35%が偽陽性であることから尿中抗体陽性のみで除菌治療を行うことは不可能であり、必ず医療機関での精密検査後に行う必要があることが明らかになった。

3）受診率、感染率、除菌率の検討

受診率は尿検体の回収を学校で行ったところでは 90%前後であり、学校の協力が得られず医療機関に持参とした場合は 30%程度であった。また、中学生と高校生では中学生の受診率が高く、更に自治体の対策として行う場合、高校生は自治体を跨いで通学するものが少なくないため、課題となった。そのため、高い受診率を得るためには対象は中学生とし、学校での検体回収が重要な役割を果たすことが明らかになった。

感染率は 99/1491、6.2%と既報通りの結果であった。

除菌率は JGSG 研究の途中経過であるが、クラリスロマイシンを用いた 1 次除菌のレジメは 66.7%、メトロニダゾールを用いた 2 次除菌のレジメは 100%であった。最終報告を待つ必要があるが、中学生に対する除菌治療は 2 次除菌のレジメが良いと考えられた。

D．考察

中学生、高校生における *H. pylori* 感染率は既報通りの 6.2%と 10%を下回る結果であった。手順書を作成し、行政、学校、医療機関が協力して実施すること、特に検体回収は学校で行うことで高い受診率が得られた。中学生、高校生に対する 1 次スクリーニング検査は最も侵襲が少なく学校検診と同時に施行可能な尿中抗体検査を行い、抗体陽性者には偽陽性

が少なくないため、現在感染していることを確認するために尿素呼気試験を追加し、両者が陽性の場合に除菌治療を行うことが望ましいと考えられた。また、除菌レジメについては成人の 2 次除菌レジメの除菌率が高く服薬率、副作用は成人と同等であった。これらの結果から中高生に対するピロリ菌検査、除菌事業のガイドライン案を図 2 に示す。

E．結論

中学生、高校生におけるにおける *H. pylori* 検査、除菌治療による胃がん撲滅対策について検討した。感染率は 10%以下と低く、行政、学校と医療機関、医師会が協力することにより、高い受診率で実施可能であること、提唱したガイドラインが有効であることが明らかになった。

F．健康危険情報

なし

G．研究発表

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ワークショップ 1：未成年者における H.pylori 検診の現状と将来
演題：北海道地区における中学生、高校生の H.pylori 対策の検討
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これまでの胃がん検診、これからの胃がん対策

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間部克裕、小野尚子、加藤元嗣、浅香正博
G.I.Research vol22. No.6 54-60, 2014

6) *Helicobacter pylori* 除菌後胃癌の頻度背景疾患の影響は?(解説/特集)
Helicobacter Research (1342-4319)18巻1号 Page34-38(2014.02)
間部 克裕(北海道大学病院 光学医療診療部), 加藤 元嗣, 津田 桃子, 大野 正芳, 大森 沙織, 松本 美櫻, 高橋 正和, 吉田 武史, 小野 尚子, 中川 学, 中川 宗一, 清水 勇一, 坂本 直哉

H. 知的財産権の出願・登録状況
なし

図 1

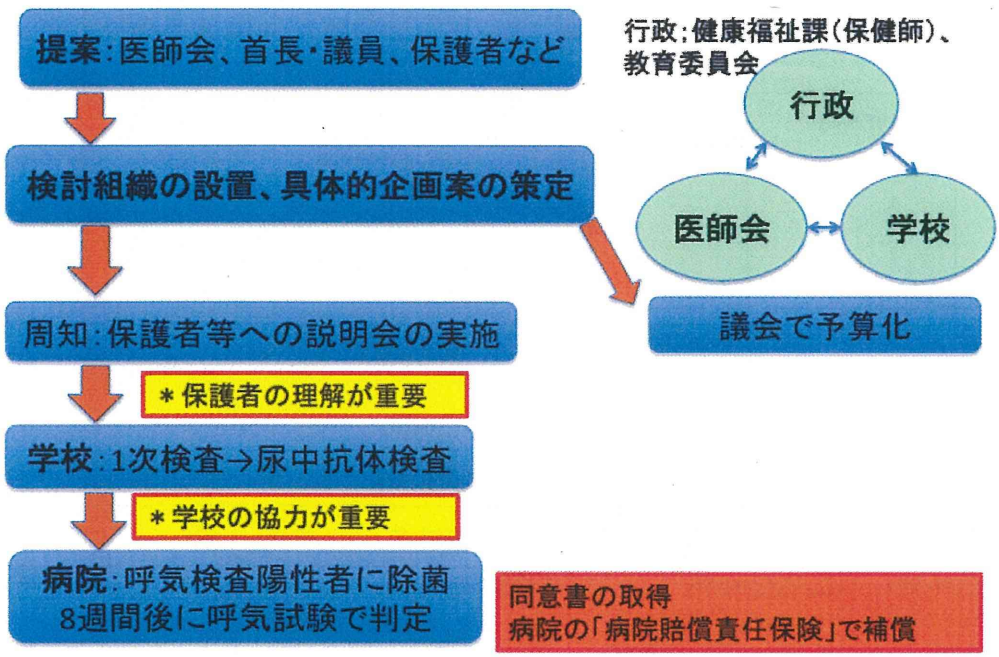
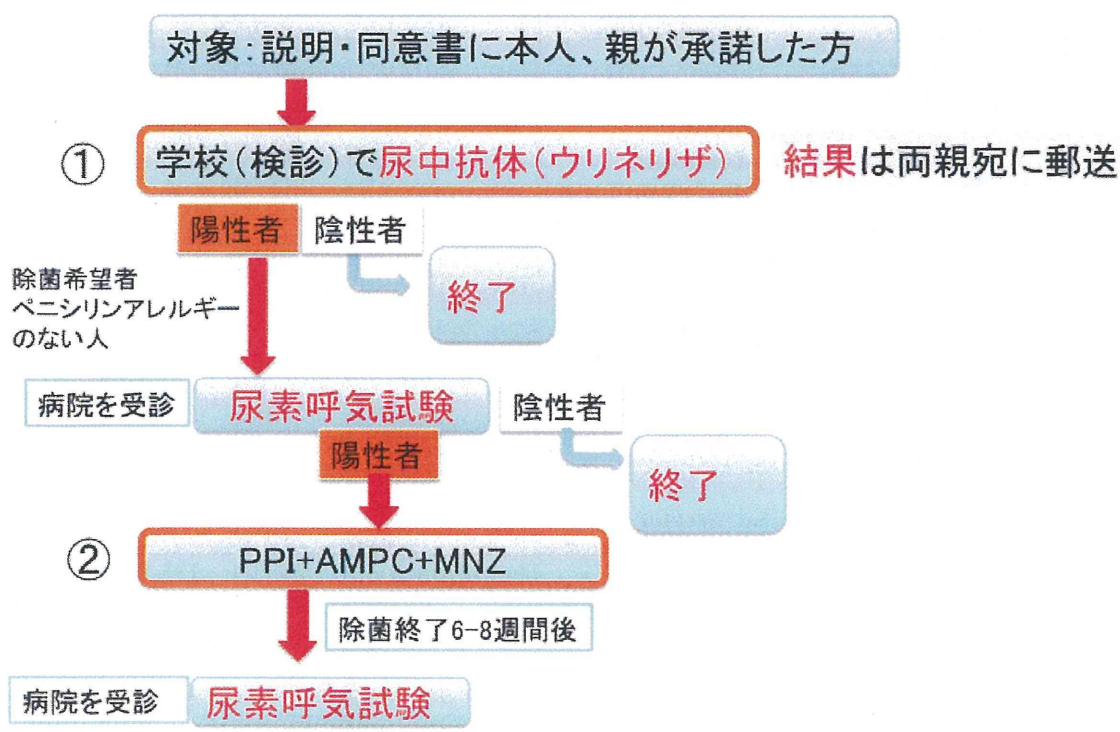

提案:医師会、首長・議員、保護者など
検討組織の設置、具体的企画案の策定
周知:保護者等への説明会の実施
＊保護者の理解が重要
学校:1次検査→尿中抗体検査
＊学校の協力が重要
病院:呼気検査陽性者に除菌
8週間後に呼気試験で判定
行政:健康福祉課(保健師)、
教育委員会
行政
医師会
学校
議会で予算化
同意書の取得
病院の「病院賠償責任保険」で補償

図 2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①
学校(検診)で尿中抗体(ウリネリザ)
結果は両親宛に郵送
陽性者
陰性者
終了
除菌希望者
ペニシリンアレルギー
のない人
病院を受診
尿素呼気試験
陰性者
終了
陽性者
②
PPI+AMPC+MNZ
除菌終了6-8週間後
病院を受診
尿素呼気試験

研究成果の刊行に関する一覧表

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「研究成果の刊行に関する別刷り」

Tips on BLI Observation

Introduction

Conventional endoscopy systems use white light from a xenon light source for illumination. LASEREO (Fujifilm), a new-generation endoscopy system, is the world's first to use laser light for illumination. Based on a narrow-band imaging method called BLI (Blue Laser Imaging), which generates illumination using two types of laser combined with phosphor, this new system is able to image microvessels in the mucosal surface layer and the mucosal surface structures in high contrast by taking advantage of the light absorbance characteristics of hemoglobin and the light scattering characteristics of mucosa. The LASEREO series currently includes the VP-4450HD processor, the LL-4450 laser light source, the L590 series dedicated endoscopes (including the EG-L590ZW gastrointestinal magnifying endoscope, the EG-L590WR general-purpose gastrointestinal endoscope, the EC-L590ZW magnifying colonoscope and the EC-L590ZWM general-purpose colonoscope) (as of August 2013).

Until now, the illumination used to capture endoscopic images has been the white light from a xenon light source. Using laser illumination instead makes it possible to obtain endoscopic images quite different in appearance from conventional ones. Although the LASEREO system has only recently begun to be applied clinically, we will offer some tips on using BLI that have been gleaned from its use so far.

Ⅰ. Characteristics of the LASEREO system

The LASEREO light source incorporates two lasers with different wavelengths and is able to provide a range of illumination from white light imaging to BLI by changing the light emission intensities of the two lasers. The white light laser (450 nm±10 nm) is used to obtain white light with a wide spectral wavelength for normal observation by causing phosphor to emit the light. The BLI laser for narrow-band imaging (410 nm±10 nm) emits light with a shorter wavelength that is easily absorbed by blood vessels and resistant to scattering inside the mucosa. Like NBI, this improves the contrast of the microvascular architecture and fine mucosal patterns on the mucosal surface layer. The clinical significance of BLI observation is similar to NBI observation[1),2)], and it is capable of finding the brownish area that indicates a neoplastic lesion on the squamous epithelial mucosa, as well as the light blue crest (LBC) that indicates an intestinal metaplasia of the gastric mucosa.

The optical zoom function is motorized. Information on the approximate location of the lens is displayed and the shutter speed that is interlocked with the lens location is increased. Deterioration-free magnification up to 135× on a 19-inch monitor is possible with optical zoom, and magnification up to 270× can be obtained by using it in combination with the electronic zoom.

When the resolution of the EC-L590ZW was measured independently using a resolution chart (negative) (**Fig. 1**) (**Table**), we were able to resolve a thin line equivalent to 4.9 μm (6-5 in the chart) at full magnification (130×) in white-light observation. With full magnification (130×) in BLI observation, resolution is as high as 5.5 μm, which is regarded as suitable for observation of microvessels on the mucosal surface.

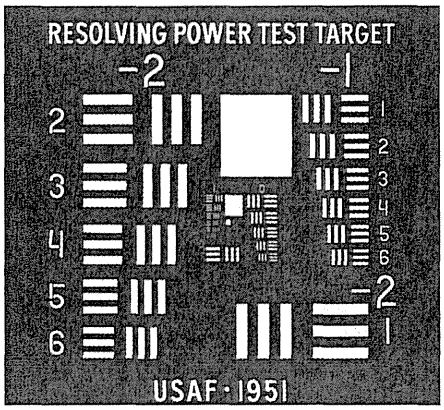

Fig. 1 Resolution Chart (Negative)

Table Resolution of the EC-L590ZW Obtained from the Resolution Chart

Magnification	Structure enhancement	White light	BLI	BLI-bright
Normal		4-3		
	A0		4-1	4-1
	B0		4-1	4-2
40×		4-6		
	A0		4-5	4-6
	B0		4-5	4-6
70×		6-3		
	A0		6-2	6-2
	B0		6-3	6-2
130×		6-5		
	A0		6-4	6-3
	B0		6-4	6-3

Ⅱ. How to use the BLI and BLI-bright modes

Narrow-band imaging is available in two modes : BLI and BLI-bright. In the BLI mode features, the ratio of BLI laser light is increased in order to maximize the contrast of microvessels on the mucosal surface layer. The BLI-bright mode combines BLI laser light with white-light laser light, providing an optimum balance between the two that enables the observer to benefit from improvements in both image brightness and vascular imaging contrast. The illumination radiated in the BLI mode is comprised almost entirely of short-wavelength components, making it suitable for observing surface structures and microvessels using mid to high magnification, while the BLI-bright mode has a slightly higher white-light component ; its high brightness is suitable for non-magnifying observation of the far view or for low- to mid-magnification observation (**Figs. 2 & 3**).

The authors interviewed endoscopists experienced in the use of BLI and asked them to describe the appropriate uses of the BLI and BLI-bright modes. Most reported that in routine observation of the laryngopharynx and esophagus, they would switch to the BLI-bright mode during endoscope insertion and use white-light imaging for endoscope withdrawal. In routine observation of the stomach, some said they did not use the BLI mode because it was not bright enough, while others reported using the BLI-bright mode in about half of all examinations they performed. While use of the BLI mode in magnifying observation is standard, many considered high magnification observation in the BLI-bright mode to be of comparable quality to that in the BLI mode. It was also found that in order to maintain brightness in the BLI mode, the shutter speed was normally set to 1/100, whereas in the BLI-bright mode, image quality can be maintained with higher shutter speeds, meaning that shutter speed can be increased to 1/200 when necessary without compromising image quality.

Ⅲ. Setting the structure enhancement

Endoscopy covers a broad range of observation targets, from the background mucosa to microlesions. In magnifying observation, it is also necessary to observe the microstructures and microvessels in the superficial mucosa. To deal with various observation conditions and targets, the structure enhancement of BLI provides two enhancement modes with different enhanced frequency bands, the A mode and the B mode. Each mode has nine enhancement

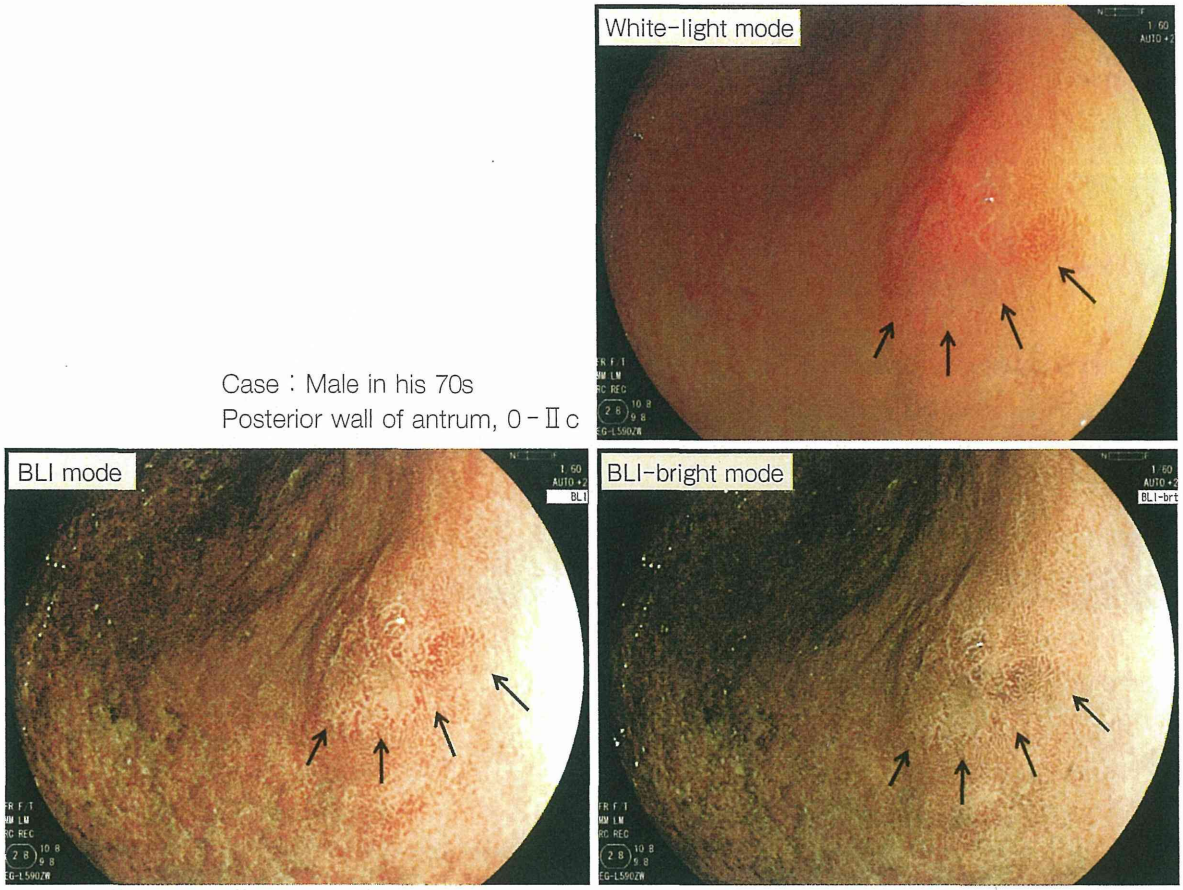

Fig. 2 Comparison of Non-Magnifying Observation between BLI and BLI-bright Modes

steps from 0 to 8 (A0 to A8 and B0 to B8). The A mode is designed to enhance lower frequency bands than the B mode and is therefore considered best for structure enhancement in colonoscopies, while the B mode is designed to enhance only thin lines, making it more suitable for microvascular observation (**Fig. 4**).
In fact, general opinion has it that there is not much difference between the A and B modes. Many endoscopists say that they utilize the capabilities of both settings. For example, prior to endoscopic observation of the stomach, structure enhancement is set to B8 and B6 of the B mode so that they can be switched on the front panel as required. Usually B6 is used, as B8's stronger image enhancement often results in more noticeable noise such as graininess or glittering.

Ⅳ. Setting the color enhancement

Lesions in the gastrointestinal tracts can cause variations in mucosal epithelium and vascular densities that cause a similarly wide variation in the reproduced color tones. To obtain the best lesion imaging effects in different regions, BLI provides three color tones : C1, which was originally intended for the esophagus ; C2 for the stomach ; and C3 for the colon (**Fig. 5**). Furthermore, the BLI-bright mode provides an additional color tone that closely resembles white-light imaging, called "no color enhancement". The color tone becomes increasingly green as the tone is stepped up from C1 to C2 and C3. Many endoscopists employ C1, which has a strong brownish tone similar to NBI, in upper gastrointestinal observations, and C2 in the lower gastrointestinal observations.

Ⅴ. Features of BLI observation

The laser light source has some features not available with conventional xenon light sources, which include a monochromatic property thanks to the very narrow wavelength band,

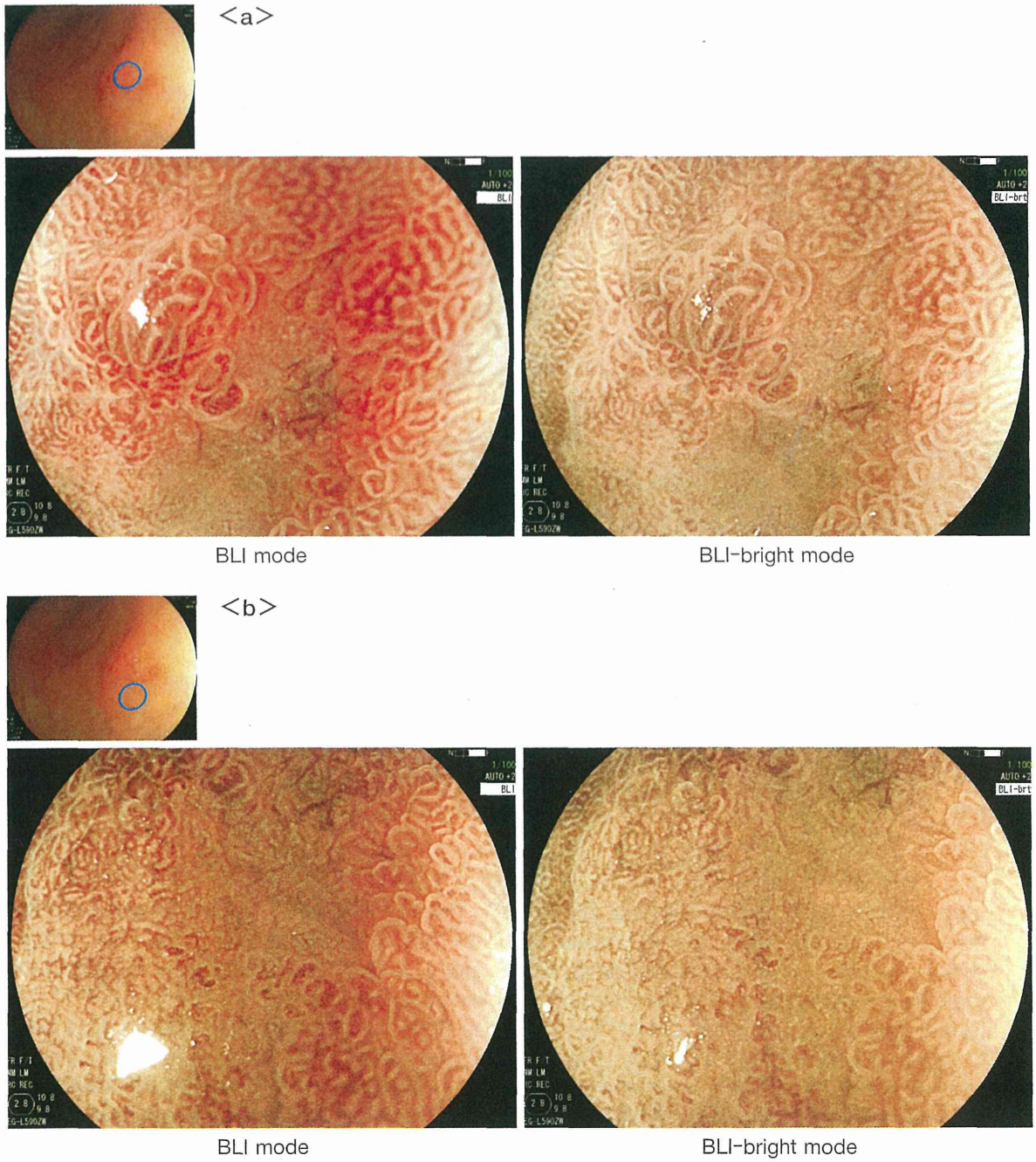

Fig. 3 Comparison of Magnifying Observation between BLI and BLI-bright Modes (same case as Fig. 2)

directivity that does not cause scattering or expansion of light, and economy thanks to the compact size, light weight, low power consumption and long service life. These features lead to certain differences between BLI observation and NBI observation. Instead of producing narrow-band light by using a filter like the NBI system, the BLI system can emit narrow-band light directly so that bright images can be obtained even from a far view, the light source does not need to be replaced, and the low power consumption helps reduce the running cost.

Many endoscopists also found focus adjustment easy with the BLI system. Though when considered from a photographic standpoint, the images lack depth and do not clearly represent surface irregularities ; they offer an improved view of surface microstructures and make it possible to observe microvessels at a deeper location. On the other hand, the clear

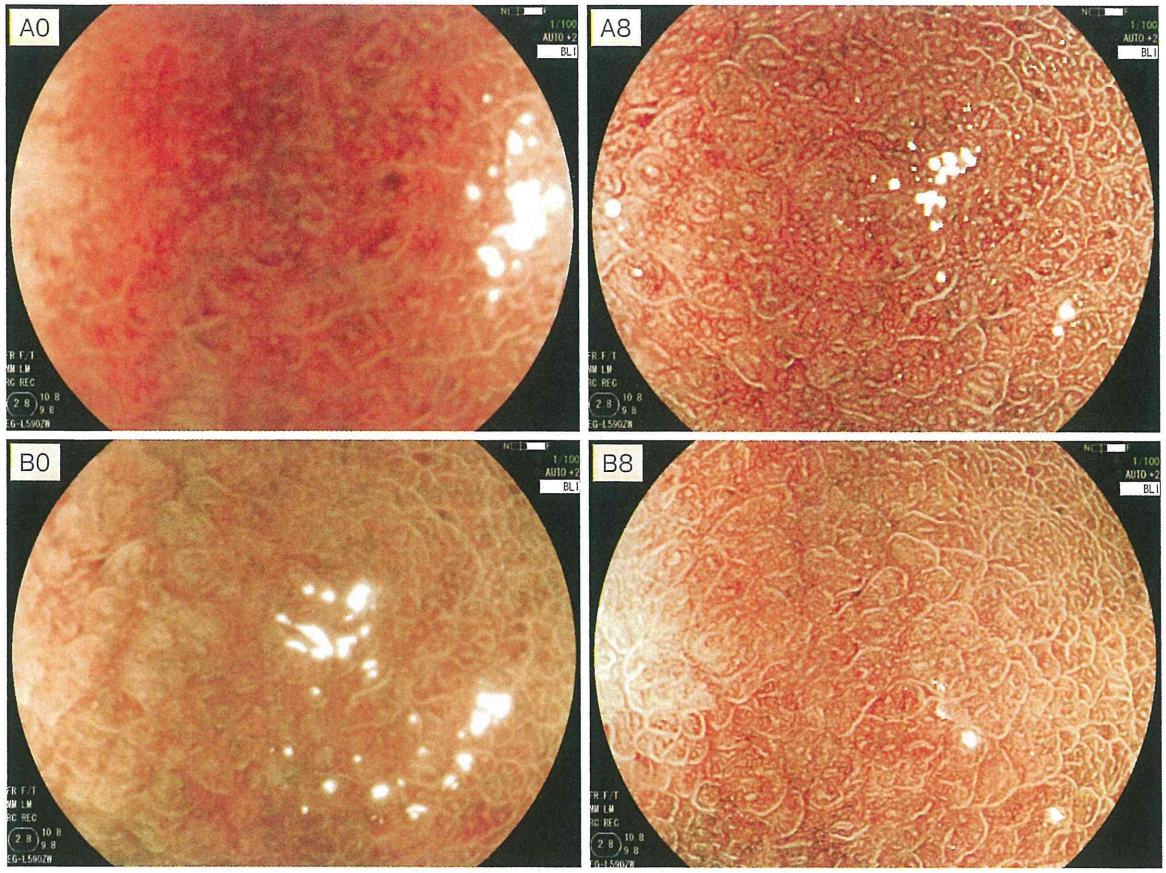

Fig. 4　Comparison of Structure Enhancement

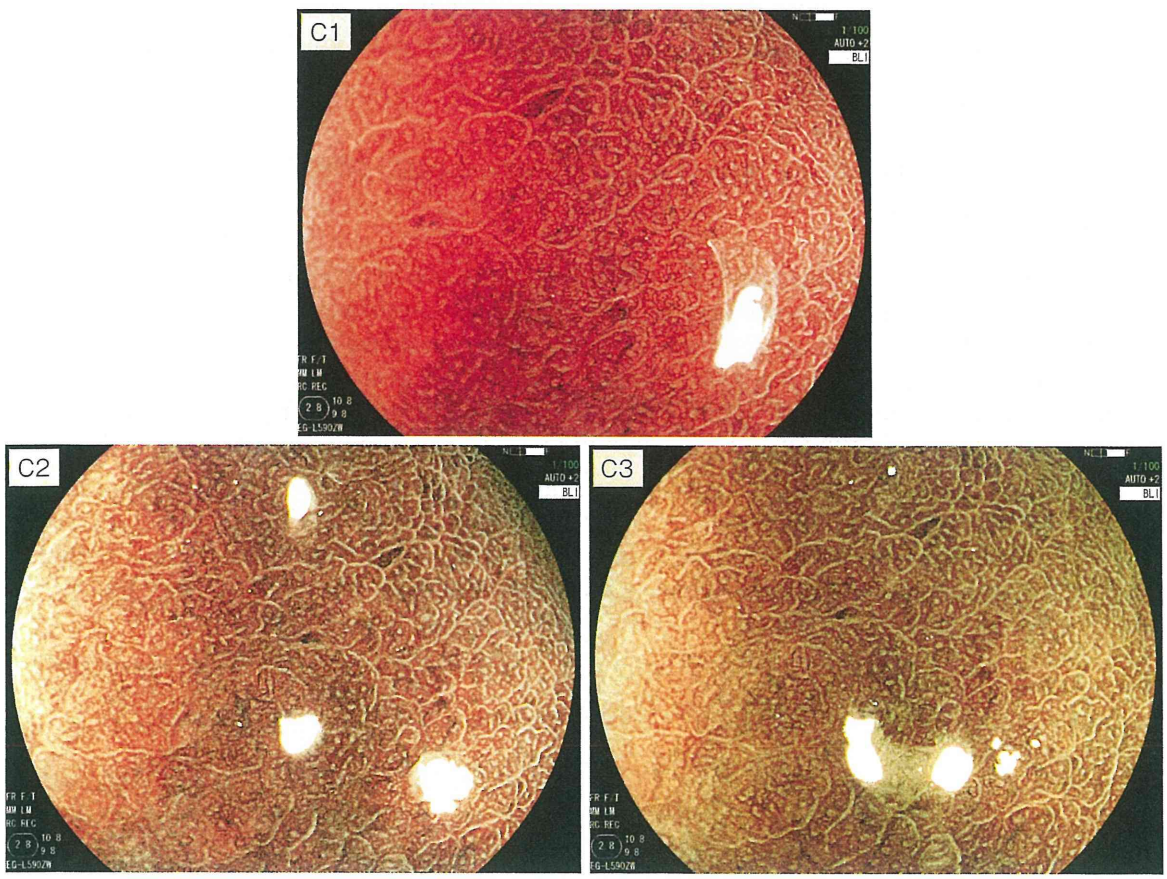

Fig. 5　Comparison of Color Enhancement

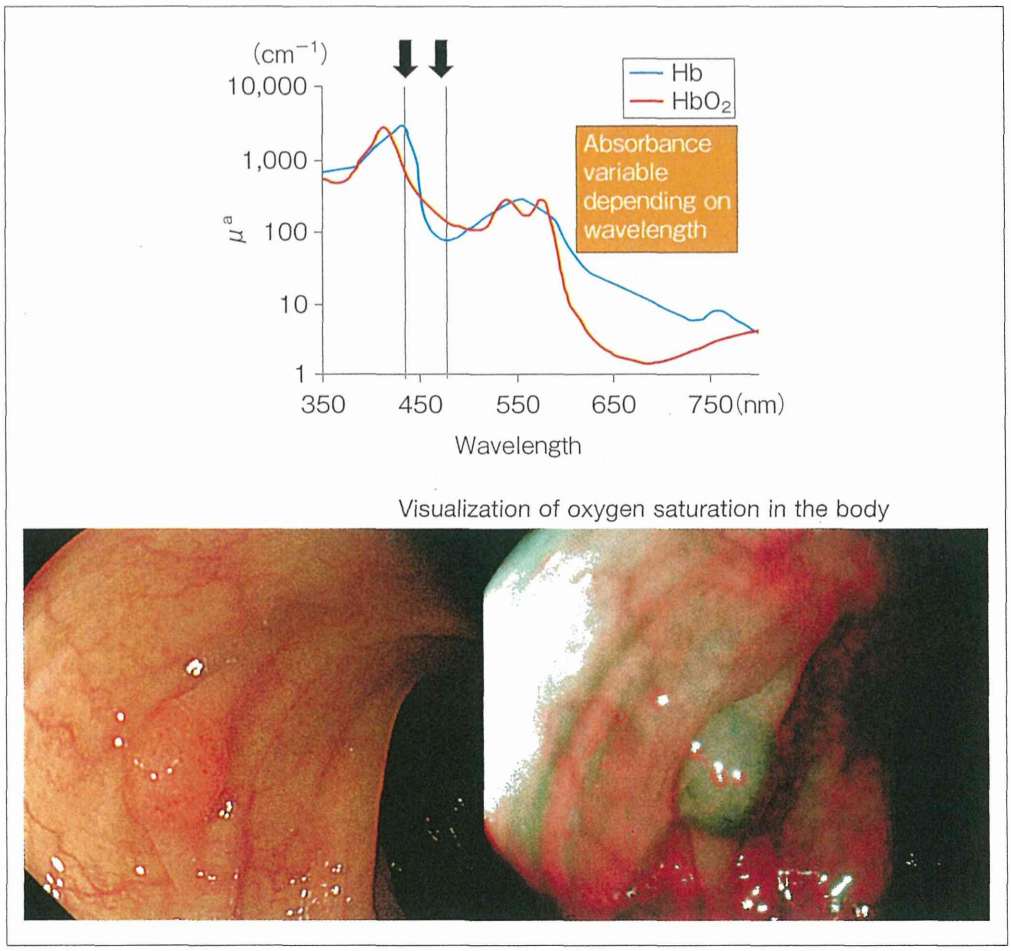

Fig. 6 Low-Oxygen Imaging

Two kinds of laser light (↓ ↓) for low-oxygen imaging are irradiated in the living body.

view of microvessels makes identification of demarcations difficult in some cases.

Conclusion

The LASEREO system has been designed to incorporate laser light with any wavelength, so it can be developed into a new endoscopic diagnosis system by creating observation modes for specific functionality, as well as for specific target tissue and target molecules. At this time, a low-oxygen imaging system has been put to practical use, which visualizes the oxygen saturation in the living body by irradiating the laser light specialized for low-oxygen imaging in the body (**Fig. 6**).

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(Kato, M., Ono, S., Yagi, N., Yoshida, S.)

Digestive Endoscopy 2013; ••: ••–•• doi: 10.1111/den.12183

Guideline

Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment

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[1]*The Japan Gastroenterological Endoscopy Society,* [2]*The Japanese Society of Neurology,* [3]*The Japan Stroke Society,* [4]*The Japanese Society on Thrombosis and Hemostasis,* [5]*The Japan Diabetes Society, and* [6]*The Japan Circulation Society, Tokyo, Japan*

Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment have been produced by the Japan Gastroenterological Endoscopy Society in collaboration with the Japan Circulation Society, the Japanese Society of Neurology, the Japan Stroke Society, the Japanese Society on Thrombosis and Hemostasis and the Japan Diabetes Society. Previous guidelines from the Japan Gastroenterological Endoscopy Society have focused primarily on prevention of hemorrhage after gastroenterological endoscopy as a result of continuation of antithrombotic therapy, without considering the associated risk of thrombosis. The new edition of the guidelines includes discussions of gastroenterological hemorrhage associated with continuation of antithrombotic therapy, as well as thromboembolism associated with withdrawal of antithrombotic therapy.

Key words: anticoagulant, antiplatelet agent, gastroenterological endoscopic examination and treatment, gastroenterological hemorrhage, thromboembolism

INTRODUCTION

IN THE MIDST of rapid advances in the medical and healthcare fields, Japan has achieved impressive progress in the development of gastroenterological endoscopy techniques that have been adopted around the world. The history of research in this field shows major breakthroughs in recent years in both endoscopic diagnosis and treatment, driven mainly by advances in medical equipment. These breakthroughs are dependent on rising standards in endoscopic diagnosis and treatment, and in the field of endoscopy in general.

The above developments have prompted a complete revision of the Guidelines for Gastroenterological Endoscopy issued by the Japan Gastroenterological Endoscopy Society along with other guidelines appearing in academic journals. The fundamental expertise built up over many years of work on gastroenterological endoscopy in Japan will now be presented as a Handbook on Gastroenterological Endoscopy, while the latest advances in the rapidly evolving field of endoscopic treatment will be issued in the form of legitimate guidelines based on evidence based medicine (EBM) and consensus.

The Guidelines for Gastroenterological Endoscopy in Patients undergoing Antithrombotic Treatments represents the first set of Guidelines issued in accordance with this new approach. I would like to take this opportunity to express my appreciation to the editorial team led by Professor Kazuma Fujimoto and the evaluation team led by Professor Yoshikazu Kinoshita, whose tireless efforts helped bring the Guidelines to fruition. I should also like to extend my thanks to Professor Shinichiro Uchiyama of Tokyo Women's Medical University Department of Neurology, Professor Atsunori Kashiwagi of Shiga University Hospital, and Professor Hisao Ogawa of Kumamoto University Department of Cardiovascular Medicine for their invaluable contributions.

We are planning to produce many more Guidelines in areas such as endoscopic mucosal resection and endoscopic submucosal dissection of the esophagus, stomach and bowel; anesthetics and sedatives; and training and education. Given that guidelines are designed to present both standard medical

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knowledge and recent developments, they are subject to periodical reassessment, review and revision as required. The Handbook on Gastroenterological Endoscopy, meanwhile, presents the fundamental principles and established understandings of gastroenterological endoscopy. The Handbook and the various Guidelines are thus equivalent to 'pure' and 'applied' endoscopic theory respectively, and should be read in conjunction rather than in isolation. In this way, we hope to enhance the standards of gastroenterological endoscopy in this country.

Finally, I would like to once again extend my heartfelt thanks to Professor Masao Ichinose, Director, and Professor Toshiyuki Matsui, Chair of the Steering Committee, for their work in the production of the Guidelines.

Michio Kaminishi
The then Chair of Board of Directors, The Japan Gastroenterological Endoscopy Society (JGES)

BASIC PRINCIPLES UNDERPINNING THE JAPAN GASTROENTEROLOGICAL ENDOSCOPY SOCIETY GUIDELINES

WITH THE INCREASING need for endoscopic examination and treatment, and the increasing complexity of procedures, there is a need to standardize protocols to raise overall standards of endoscopic examination and treatment, and thus improve patient outcomes. A committee was established by the Japan Gastroenterological Endoscopy Society (JGES) in January 2010 to produce an updated version of its evidence-based guidelines. The six basic principles of the guidelines are:

1. They should be based on solid scientific foundations.
2. Where the literature does not provide sufficient evidence – for example, in relation to endoscopic techniques – the guidelines should be supplemented through consensus (formation of a joint position based on scientific methodology to make recommendations when the level of evidence is low).
3. They should make clear and specific recommendations about therapeutic options, especially in high-priority areas.
4. Given the wide scope of the literature, the criteria and methodology for literature searches will be determined by individual working committees.
5. Because the guidelines are intended for Japanese readers, Japanese and English language versions should be produced.
6. They should provide a general overview.

The guidelines have been produced in accordance with the approach espoused by the Medical Information Network Distribution Service (MINDS), using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument for the research and evaluation process. Care has been taken to ensure consistency with other guidelines in related areas. Given the rapid pace of change in this field, the guidelines will need to be reviewed in several years to reflect the latest developments in diagnostic and therapeutic techniques. The guidelines are intended as a decision-making tool for use by medical professionals in clinical practice.

HISTORY AND BACKGROUND

IN 2010, THE JGES decided to produce and/or update a number of guidelines related to gastroenterological endoscopy. The 1999 version of the *Guidelines for Gastroenterological Endoscopy*[1] provided general guidance for the conduct of gastroenterological endoscopy in patients taking antithrombotic therapy. These were followed in 2005 by guidelines on the *Use of Anticoagulants and Antiplatelet Agents During Endoscopic Procedures*,[2] which formed the basis of the third version of the *Guidelines for Gastroenterological Endoscopy*[3] released in 2006. The latter was used as a key source of information concerning gastroenterological endoscopy in patients taking antithrombotics, and the principles were adopted in other guidelines from academic associations published in Japan, including the *Guidelines on Anticoagulant and Antiplatelet Therapy for Cardiovascular Illnesses*[4] (revised edition, 2009) and the *2009 Stroke Therapy Guidelines*.[5]

The 2010 update to the guidelines was prompted by recent advances in gastroenterological endoscopic examination and treatment techniques. Some of the updated information has been adapted from similar guidelines in the USA[6–8] and Europe.[9,10]

In July 2010, the board of directors of JGES established editorial and evaluation committees to oversee the production of the updated guidelines; the first committee meeting was convened in October 2010. Agreement was reached with other academic bodies to collaborate in the production process. Searches of the literature included in the PubMed and Japan Centra Revuo Medicina (the Japan Medical Abstracts Society) databases were undertaken, covering the period 1983 to 2011 using the keywords 'endoscopy', 'anticoagulant', 'antiplatelet' and 'antithrombotic' in PubMed and the equivalent Japanese terms in the Japan Medical Abstracts Society search engine.

A draft was produced and reviewed in line with feedback from the peer review committee (Table 1) before final approval at a consensus meeting in June 2011, attended by nine members of the editorial committee, four members of the evaluation committee and the two directors responsible for the project. The team used Delphi Answerpad[11–13] to produce the consensus statements. Where consensus could

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