

Blue laser magnifying endoscopy in the diagnosis of chronic gastritis

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Abstract. The current study aimed to evaluate the clinical value of using blue laser imaging combined with magnifying endoscopy in the diagnosis of chronic gastritis (CG). The groups used were as follows: The white light group (WLI, control group), linked color imaging group (LCI, observation group 1), blue laser imaging (BLI)-bright (brt) group (BLI-brt; observation group 2), BLI + magnified imaging (ME) group (observation group 3). WLI mode initially allowed the observation of mucosal suspicious lesions on the gastric mucosa. These lesions were photographed and the mode was changed to LCI, BLI-brt and BLI + ME. Different observational patterns were compared between modes to diagnose various grades of chronic gastritis. No significant differences were observed in the baseline information of enrolled patients. The LCI mode diagnosis rate was higher for *Helicobacter pylori* (HP) infection than in any other mode. LCI exhibited a high diagnostic rate for HP, BLI-brt exhibited a high diagnostic rate for atrophy and BLI/BLI + ME exhibited a high diagnostic rate for intestinal metaplasia and intraepithelial neoplasia. All modes exhibited higher diagnostic rates compared with the WLI mode. The pathological HP diagnosis rate (consistency) of HP infection was the greatest in the LCI group (endoscopic findings and pathological consistency). The BLI-BRT mode exhibited the highest pathological diagnosis rate for atrophic gastritis and the BLI/BLI + ME mode exhibited the highest diagnostic rate for intestinal metaplasia and low-grade intraepithelial neoplasia.

Introduction

Chronic gastritis (CG) is the chronic inflammation of the gastric mucosa that is induced by a variety of factors, but mainly by infection with *Helicobacter pylori* (HP) bacteria (1,2). CG develops subsequent to the infiltration of lymphocytes and plasma cells in the gastric mucosa. Patients with CG may exhibit atrophy and intestinal metaplasia in the gastric mucosa in later stages of the condition (3,4). The incidence of CG is high in the Chinese population, with ~30% afflicted chronic gastritis. (5). Controversy exists as to the diagnosis and classification of CG, and these have resulted in varying classification methods using X-ray, immunology, endoscopy and histopathology analysis. Numerous classification schemes (>10) exist regarding chronic gastritis worldwide (6,7). The most well renowned of which is The New Sydney System Taxonomy (Updated Sydney System). However, due to the controversy over various diagnostic methods used, this system has yet to be implemented in China. The formulation of the earliest consensus opinions was undertaken in China in 1982. The consensus was updated in 2000, 2003 and 2006 and until November 2012, the national consensus conference on the diagnosis and treatment of CG was held in Shanghai. This conference provided regulations regarding the use of endoscopy in the diagnosis of this condition. An association has been previously identified between CG and gastric cancer (8,9). A number of worldwide studies have demonstrated that the chronic inflammation of the gastric mucosa is closely associated with the occurrence of gastric cancer, and that gastric cancer is one of the most common malignancies in China (10,11). The occurrence development model is as follows: (i) Normal gastric mucosa; (ii) chronic superficial gastritis; (iii) chronic atrophic gastritis; (iv) intestinal metaplasia; (v) dysplasia; and (vi) intestinal gastric cancer (12). The standard endoscopic diagnosis of chronic gastritis, the classification of endoscopy and the histological grade are essential in the discovery of early gastric cancer. Blue laser imaging with magnifying endoscopy provides endoscopic surgeons with a more accurate diagnosis of CG.

The blue laser imaging (BLI) technology was a novel treatment introduced globally in 2012 (13,14). BLI replaces the traditional xenon lamp with a laser light source and performs white light and bright, narrow-band light observations (15).

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Through the use of lasers, new methods have been established for the diagnosis of various diseases using endoscopy. In recent years, narrow-band imaging (NBI) has been the most sophisticated gastroscopy method, which is used in clinical practice, in the endoscopic diagnosis of CG and early gastric cancer (16,17). The high diagnostic value of NBI in the diagnosis of early gastrointestinal cancer has also been supported (18). However, due to the low brightness of NBI, wide gastric cavity and the limited mucosa visibility, various limitations of using this method in the diagnosis of gastric mucosal lesions exist. In BLI, the laser is the light source and the fusion images of the digestive tract mucosa are captured at wavelengths of 415 and 450 nm and provide increased penetration (13,14). In addition to clear and high quality images produced by blue laser imaging, magnified observations can allow the assessment of deeper blood vessel structures in the mucosal membrane (15). This aids in the discovery of subtle structural changes in the mucosal surface and can help endoscopic doctors to accurately evaluate the lesions nature (19). In 2015, BLI endoscopy was introduced in various large and medium-sized urban hospitals in China (20). According to current data, compared with traditional endoscopy, BLI endoscopy diagnostic rate of the upper gastrointestinal tract and colorectal cancer was significantly increased, especially in younger patients (21,22). The use of blue laser endoscopy has enabled doctors to make a more accurate diagnosis of observed lesions. Therefore, this imaging technique is clinically useful for the diagnosis of CG and for providing an accurate endoscopic classification and histological grade.

Materials and methods

Patients and grouping. The current study is a prospective study. Patients were selected if they had undergone blue laser magnifying endoscopy from August 2017 to July 2018 in the outpatient department at the Shenzhen Hospital of Southern Medical University (Shenzhen, China). Endoscopy and pathological biopsy were used to diagnose CG in 120 patients (60 male and 60 female), aged 26-79 years old. Four modes were used to observe all patients, which were divided into four groups. The groups were as follows: i) white light group (control group); ii) Linked color imaging (LCI) group (observation 1 group); iii) BLI-bright (BLI-brt) group (observation 2 group) and the iv) BLI+ magnified imaging (ME) group (observation 3 group). The diagnostic criteria used were based on the 'Consensus Opinion for Chronic Gastritis in China, 2012' of the Chinese Medical Association Gastroenterology Section (23). Endoscopic classification and histological grading were performed in 120 patients (23). All participants in the current study signed written informed consent. The current study is in full compliance with the ethical standards established by The Human Body Testing Committee of China.

Inclusion criteria. Patients meeting the diagnostic criteria were potentially eligible for the study if they met the following criteria: i) Aged between 26-79 years old; ii) being diagnosed as CG by western medicine procedures; iii) being diagnosed as CG according to syndrome differentiation in traditional Chinese medicine; and iv) voluntary submission of written informed consent prior to enrollment (24).

Exclusion criteria. The exclusion criteria were as follows: i) Functional dyspepsia (ruled out using medical history and endoscopy); ii) gastric and duodenal ulcers (ruled out using endoscopy); iii) gastric cancer (ruled out using endoscopic and pathological examination); iv) pancreatic and biliary diseases (ruled out using abdominal doppler ultrasonography) and partial computerized tomography and magnetic resonance were excluded if necessary; v) serum liver function was measured in all patients and 8 patients were excluded due to hepatitis; (vi) age <25 years, age >79 years, pregnant or lactating women; vii) cardiac, pulmonary and neuropsychiatric disorders, patients which cannot tolerate gastroscopy or patients who disagree with endoscopy; and viii) patients who had received anticoagulant drugs in preceding 2 weeks, or patients who exhibited coagulation dysfunction (25).

Inspection method. Using the EG-L590ZW electronic magnifying endoscope (FUJIFILM), combined with the LL-4450 laser light source (FUJIFILM Corporation) of the LASEREO blue laser endoscope system (FUJIFILM Corporation) and the VP-4450 HD image processing device (FUJIFILM Corporation), the gastric mucosa was initially observed using white light, and the mucosal suspicious lesions were photographed and observed using LCI. BLI-brt, BLI + ME images, biopsy under different observation methods, histopathological results and any necessary additional immunohistochemical examinations were performed to confirm the diagnosis.

Image analysis. The diagnosis concluded from endoscopy is subjective. Therefore, to avoid the selective bias in the current study, scientific and objective diagnoses were made. Two experienced endoscopists performed the endoscopies and two additional senior endoscopists randomly reviewed the results. Photographs, final endoscopic diagnosis and pathological results after review were used to measure the consistency between endoscopic diagnosis. When the endoscopic or pathological findings are controversial, an additional immunization group is used. The parameters of the immunization group were serum gastrin 17 (G-17), pepsinogen (PG I, PG II) and T cell subsets (CD4+T, CD8+T).

Pathological diagnosis. The gastric mucosa was observed using blue light and lesions were examined using four observational modes: The white light model (WLI); LCI; BLI-BRT; and the BLI/BLI + ME. The suspicious lesion sites were observed using these four observational modes aforementioned and any pathological signs: i) *Helicobacter pylori* infection; ii) chronic inflammatory response (mononuclear cell infiltration) and activity (neutrophil infiltration); iii) atrophy (decrease of inherent glands); and iv) and intestinal metaplasia were recorded. Comparative studies were subsequently performed. Images were first captured at typical locations of observed lesions, the samples of diseased tissues were then taken and stained using heterochromic reaction by toluidine blue, which is followed by pathological analysis. Comparative analysis of the diagnostic accuracy of the three examination methods (LCI, BLI-BRT and BLI/BLI + MI) was performed, and four methods (WLI, LCI, BLI-BRT and BLI/BLI + MI) were used for the endoscopic classification of chronic gastritis (based on the CG classification in 2012) into superficial gastritis, erosive gastritis,

Table I. Predicting and population distribution of various gastritis grades in each group of patients.

Group	Pathological typing							
	Intestinalization		Chronic atrophic gastritis		<i>Helicobacter pylori</i> infection +/-++		Intraepithelial neoplasia	
	Number of forecast cases	Actual number of cases	Number of forecast cases	Actual number of cases	Number of forecast cases	Actual number of cases	Number of forecast cases	Actual number of cases
White light mode	12	4	12	3	23	4	5	1
Linked color imaging	12	6	10	6	51	42	6	3
Blue laser imaging-bright	14	11	44	41	19	7	12	11
Blue laser imaging/ Blue laser imaging + magnified imaging	61	55	14	12	15	4	34	31

hemorrhagic gastritis and atrophic gastritis. Histological changes were also used in the disease classification: Chronic inflammatory response (+), active inflammation (++) and atrophy (+++) and intestinal metaplasia (+++++) based on the degree of pathological changes (26,27). *Helicobacter pylori* infection was considered as +/-++ according to the literature (28).

Diagnosis. Chronic gastritis is currently considered to be indicated by a mucositis change, which can be observed by the naked eye or using special imaging methods under endoscopy. The final diagnosis should be concluded in conjunction with a pathological examination.

Statistical analysis. Data are presented as the mean \pm standard deviation. Statistical analysis was performed using SPSS version 13.0 (SPSS, Inc.). One-way ANOVA was used to detect the differences between groups of various treatments after establishing the distribution of the data and the equivalency of variances using SPSS version 13.0. The Student-Newman-Keuls test was used as the post-hoc test. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. The same mode was used to observe the same 120 patients. Combined with pathological biopsy results, the diagnostic rate of blue laser magnifying endoscopy was evaluated and compared with that of normal white light imaging. The baseline information of the patient, including sex, age, severity of the disease, living environment and habits among the enrolled patients is shown in Tables I-VII. However, no significant differences were observed ($P > 0.05$).

Images of the LCI pattern exhibited by HP infection. A representative image of a patient of each group in this study was selected for observation (Fig. 1). The current study revealed that the diagnosis of HP infection using LCI was higher compared with the other modes. The red-white boundary and abnormal redness can be observed under endoscopy. The abnormal redness is divided into four appearances: Stove-like redness, flat erosion, uplift erosion and diffuse redness.

Low-level intraepithelial neoplasia. A representative image of a patient was selected in this study for observation (Fig. 2). The WLI and LCI model observation revealed inflammation. Lesions were rough compared with the surrounding mucosa. The BLI-brt model observed the lesions in comparison with the background and revealed a brown color, which determined the extent of lesions. The BLI + ME observation model showed no obvious demarcation line (DL), regular micro surface (MS) patterns, micro vascular (MV) patterns, distortions or irregularities or low-grade intraepithelial neoplasia (LGIN).

Chronic atrophic gastritis observation modes. A representative image of a patient was selected in this study for observation (Fig. 3). The WLI, LCI, BLI-brt observation model showed that the lesions were slightly rough compared with the surrounding mucosa. The mucosa color appeared

Table II. Distribution of gastritis grading in each group of patients.

Group	Pathological typing (n)			
	None	Mild	Moderate	Severe
White light mode	0	116	4	0
Linked color imaging	0	78	38	4
Blue laser imaging-bright	0	113	5	2
Blue laser imaging/ Blue laser imaging + magnified imaging	0	116	4	0

Table III. Distribution of gastritis activity classification in each group of patients.

Group	Pathological typing (n)			
	None	Mild	Moderate	Severe
White light mode	116	0	113	116
Linked color imaging	78	35	3	0
Blue laser imaging-bright	113	4	2	2
Blue laser imaging/ Blue laser imaging + magnified imaging	116	3	2	2

Table IV. Distribution of HP classification in each group of patients.

Group	Pathological typing (n)			
	None	Mild	Moderate	Severe
White light mode	116	0	2	3
Linked color imaging	78	35	4	3
Blue laser imaging-bright	113	3	2	2
Blue laser imaging/ Blue laser imaging + magnified imaging	116	0	2	2

Table V. Distribution of intestinal differentiation grading in each group of patients.

Group	Pathological typing (n)			
	None	Mild	Moderate	Severe
White light mode	116	0	2	2
Linked color imaging	114	1	3	2
Blue laser imaging-bright	109	3	6	2
Blue laser imaging/ Blue laser imaging + magnified imaging	65	44	8	3

to be different in the different modes. However, in all cases, an obvious color difference was observed compared with the surrounding normal mucosa. Under the BLI + ME observation mode, regular MS pattern, gland shortening and a spiral blood vessel were observed between the fossa.

Various observational modes of intestinal metaplasia (GIM). A representative image of a patient was selected in this study for observation (Fig. 4). LCI mode observation revealed rough lesions, uneven color, BLI + ME weakly magnified the visible DL, a strong amplifying gland typical finger shape and regular MV pattern.

Table VI. Distribution of stomach atrophy grading in each group of patients.

Group	Pathological typing (n)			
	None	Mild	Moderate	Severe
White light mode	117	0	1	2
Linked color imaging	114	1	2	3
Blue laser imaging-bright	79	34	3	4
Blue laser imaging/ Blue laser imaging + magnified imaging	108	7	2	3

Table VII. Distribution of epithelial sarcoma grading in each group of patients.

Group	Pathological typing (n)	
	None	Mild
White light mode	0	1
Linked color imaging	0	3
Blue laser imaging-bright	0	11
Blue laser imaging/ Blue laser imaging + magnified imaging	0	31

Discussion

In the present study, BLI technology was used to aid in the accurate diagnosis and classification of chronic gastritis via endoscopy, standardize histological grading, establish contrast imaging with traditional white light, in combination with histopathology. The current study assessed the clinical value of this technology. BLI remains to be a novel technology, therefore, the number of cases of its use are insufficient. Studies assessing a large sample size of multi-center clinical studies are required to further support the use of this technique clinically.

An LCI pattern was observed in patients exhibiting HP infection. In this mode, the sinusoidal junction demonstrated a clear red-white boundary, and the targeted biopsy results suggested the presence of a HP infection. Additionally, the mucosa at the gastric fundus was diffuse and red. In the WLI mode, mucosal roughness was observed in the central stomach angle, which suggested the presence of inflammation. Irregular redness was observed in the central stomach angle, and the center was slightly depressed, which may have been caused by the inflammatory reaction. In the BLI-brt mode, the middle part of the stomach was brown with no obvious observed boundaries. In the BLI + ME mode, no DL, regular MS pattern, MV irregularity, distortion, targeted pathology or low-grade intraepithelial neoplasia.

In the WLI mode, the gastric mucosa was not smooth. In the LCI mode, the gastric mucosa was not smooth, uneven, with some of the mucous membranes exhibiting an orange

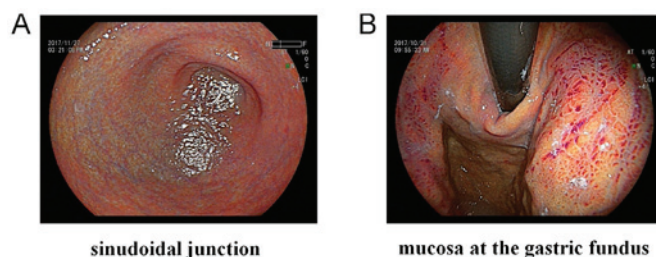


Figure 1. Typical image of a *Helicobacter pylori* infection, observed using linked color imaging. Images using the linked color imaging mode of (A) the sinusoidal junction and (B) the mucosa at the gastric fundus. Both images were taken from the same patient.

color. The BLI-brt mode revealed that the lesions in the stomach horn were rougher than the surrounding mucosa and indicated a brown color. Under the BLI magnification mode, the MS pattern of the gastrointestinal angle was observed, the gland was shortened and the pathology showed atrophy.

From the various observational modes of visualizing GIM in the present study, it has been revealed that the mucosa of the gastric antrum anterior wall was white in the WLI mode. In the LCI mode, the mucosa of the antral antrum anterior wall was swollen and rough. DL was observed in the BLI weak amplification mode and the lesions center exhibited a brown color. BLI was clear in the strong amplification mode, the glands were observed to be finger-like, the MV pattern was regular and the targeted biopsy indicated intestinal metaplasia.

The diagnosis of chronic gastritis is commonly based on pathological diagnosis (29). The coincidence rate of endoscopic and pathological diagnosis of atrophic gastritis is low. The reason for this is the subjective analysis by endoscopic surgeons, the selection of endoscopic examination and sampling site inaccuracy (30). Blue laser magnifying endoscopy (BLI-bright/BLI + amplification) allows a clear observation of the fine morphology of blood vessels and glands and, combined with the clinical classification, can help doctors to accurately determine the nature of lesions, reduce biopsy sites, increase the positive rate of biopsy, reduce the rate of missed diagnosis and increase the detection of early stage gastric cancer.

The use of blue laser technology can increase the diagnostic rate of chronic gastritis under endoscopy, and can also increase the diagnostic rate of early gastric cancer,

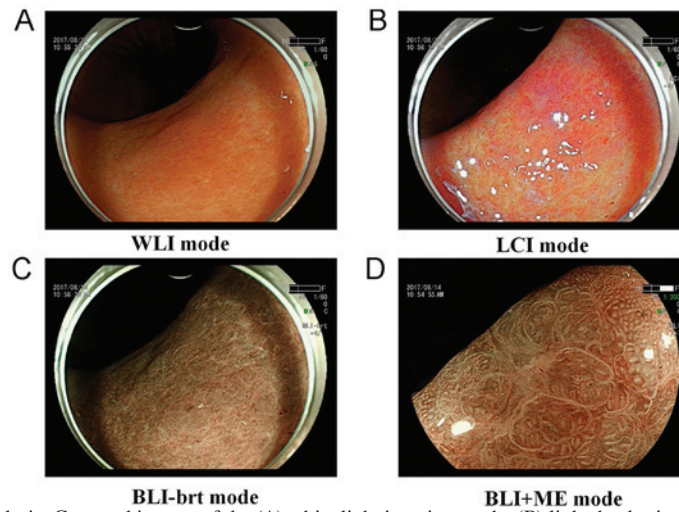


Figure 2. Low-level intraepithelial neoplasia. Captured images of the (A) white light imaging mode, (B) linked color imaging mode, (C) blue laser imaging-bright mode and (D) blue laser imaging + magnified imaging mode used on the central stomach angle. All images were taken from the same patient.

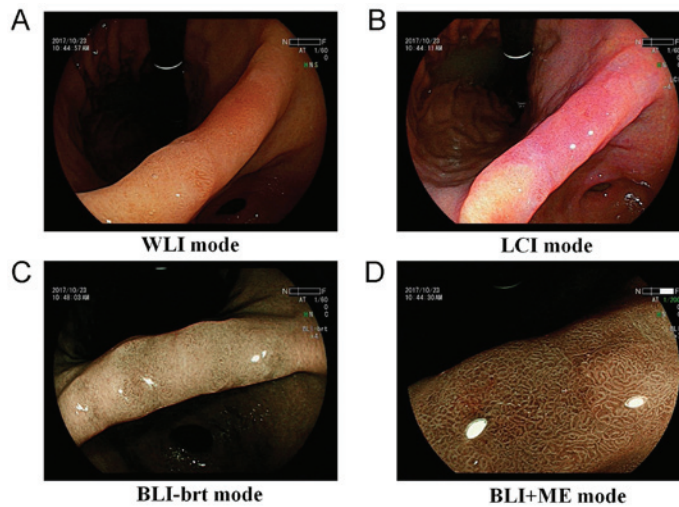


Figure 3. Chronic atrophic gastritis observation modes. Images captured of the (A) white light imaging mode, (B) linked color imaging mode used to observe the gastric mucosa. Images captured of the (C) blue laser imaging-bright mode observations of a lesion of the stomach horn. Images captured of the (D) blue laser imaging magnification mode observations of the micro surface regular pattern of the gastrointestinal angle. All images were taken from the same patient.

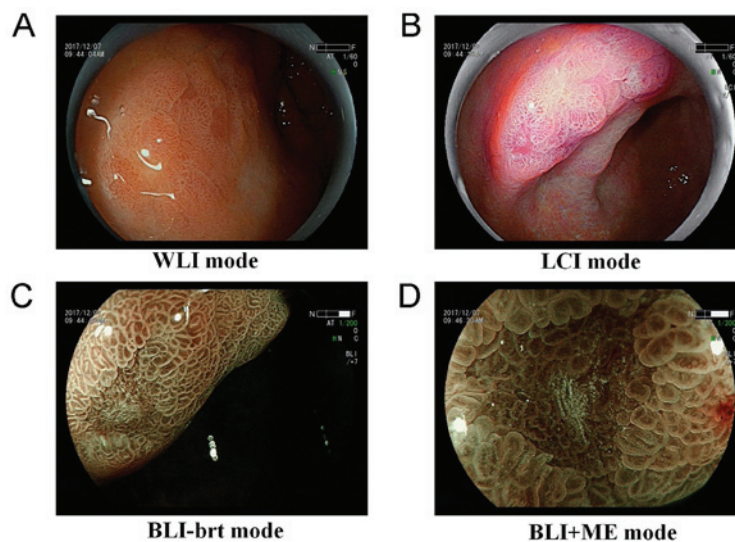


Figure 4. Various observational modes of intestinal metaplasia. Captured images of (A) the white light imaging mode, (B) linked color imaging mode, (C) blue laser imaging weak amplification mode and (D) blue laser imaging strong amplification mode observations of the gastric antrum anterior wall. All images were taken from the same patient.

HP infection, atrophic gastritis, intestinal metaplasia and intraepithelial neoplasia. The blue laser imaging technology provides clear, three-dimensional imaging compared with the traditional white light endoscopy technology. Different grades of chronic gastritis can be observed via endoscopy examinations. The current study has demonstrated that blue laser imaging can improve the screening ability of gastric mucosal diseases.

In several modes, the pathological diagnosis rate (consistency) of HP infection is the best in all pathological types of LCI group (endoscopic findings and pathological consistency). The BLI-brt mode exhibited the highest pathological diagnosis rate for atrophic gastritis. BLI/BLI + ME exhibited the highest diagnostic rate for intestinal metaplasia and low-grade intraepithelial neoplasia.

In conclusion, the present study showed that the use of blue laser endoscopy enabled doctors to diagnose observed lesions more accurately during the diagnosis of chronic gastritis. Therefore, blue laser endoscopy technology can be used in the clinical diagnosis of CG and provide accurate endoscopy classification and histological grading.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YiZ was responsible for guaranteeing integrity of the entire study, study concepts and design, definition of intellectual content, literature research, clinical studies, experimental studies, data acquisition, manuscript preparation and editing and review. FW was responsible for guaranteeing integrity of the entire study, study concepts, definition of intellectual content, experimental studies and data acquisition. YaZ was responsible for the experimental studies. GLX was responsible for the experimental studies and manuscript editing. LD was responsible for the experimental studies, manuscript editing and review. WHH was responsible for the literature research, clinical studies, experimental studies, data acquisition and analysis, statistical analysis, manuscript preparation and editing and review. BX was responsible for the entire study, study concepts and design. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Shenzhen Hospital of Southern Medical University (Shenzhen, China). Written informed consent was obtained.

Patient consent to participate

The current study is in full compliance with the ethical standards established by The Human Body Testing Committee of China.

Competing interests

The authors declare that they have no competing interests.

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