RESPONSE TO THE REVIEWERS

3 SCIENTIFIC QUALITY

Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report, and ***highlighted the revised/added contents with yellow color in the revised manuscript****. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s); these are listed below for your convenience:*

Reviewer #1:
Scientific Quality: *Grade B (Very good)*
Language Quality: *Grade B (Minor language polishing)*
Conclusion: *Accept (General priority)*
Specific Comments to Authors:
Thanks to the authors effort in highlighting the growing role of TXI in different GI lesions and improving the quality of diagnosis

Thank you very much for reviewing our manuscript and taking your valuable time.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240.

We revised the entire manuscript for grammar using the Grammarly Editor (https://app.grammarly.com/). We have attached the paper with the revised parts highlighted in yellow at the end of the text.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

The basic rules on abbreviations are provided here:

***(1) Title:** Abbreviations are not permitted. Please spell out any abbreviation in the title.*

***(2) Running title:** Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.*

***(3) Abstract:** Abbreviations must be defined upon first appearance in the Abstract. Example 1: Hepatocellular carcinoma (HCC). Example 2:* Helicobacter pylori *(*H. pylori*).*

***(4) Key Words:** Abbreviations must be defined upon first appearance in the Key Words.*

***(5) Core Tip:** Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2:* Helicobacter pylori *(*H. pylori*)*

***(6) Main Text:** Abbreviations must be defined upon first appearance in the Main Text. Example 1: Hepatocellular carcinoma (HCC). Example 2:* Helicobacter pylori *(*H. pylori*)*

(7) ***Article Highlights:*** *Abbreviations must be defined upon first appearance in the Article Highlights. Example 1: Hepatocellular carcinoma (HCC).*

Example 2: Helicobacter pylori *(*H. pylori*)*

We confirmed that abbreviations were correctly written throughout the paper.

(8) Figures: *Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.*

We revised the Figure legends according to the comments.

(9) Tables: *Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.*

We revised the Table according to the comments.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Conflict of interest statement: *Academic Editor has no conflict of interest.*

2 Scientific quality: *The author submitted a study of topic highlight on texture and color enhancement imaging in gastrointestinal diseases. The manuscript is overall qualified.*

(1) Advantages and disadvantages: *The reviewer have given positive peer-review reports for the manuscript. Classification: Grade B; Language Quality: Grade B. The authors effort in highlighting the growing role of TXI in different GI lesions and improving the quality of diagnosis.*

(2) Main manuscript content: *The author clearly stated the purpose of the study and the research structure is complete. However, the manuscript is still required a further revision according to the detailed comments listed below.*

(3) Table(s) and figure(s): *There are 1 Figure and 1 Table should be improved. Detailed suggestions for each are listed in the specific comments section.*

(4) References: *A total of 38 references are cited, including 32 published in the last 3 years. The reviewer didn't request the authors to cite improper references published by him/herself.*

3 Language evaluation: *The English-language grammatical presentation needs to be improved to a certain extent. There are many errors in grammar and format, throughout the entire manuscript. Before final acceptance, the authors must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240.*

We revised the entire manuscript for grammar using the Grammarly Editor (https://app.grammarly.com/). We have attached the paper with the revised parts highlighted in yellow at the end of the text.

4 Specific comments: *(1) Please provide the filled conflict-of-interest disclosure form.*

We provided the COI according to the form.

(2) Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A, B, arrows, etc. All legends are incorrectly formatted and require a general title and explanation for each figure. Such as Figure 1 title. A: ; B: ; C: .

We provided the Figure in the PPT. modified the Figure legends according to the comment.

*(3) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published, and correctly indicate the reference source and copyrights. For example, "**Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×).** A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. **Citation:** Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease.* World J Gastroenterol *2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.*

We used original images in the Figure.

(4) Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

we revised the Table accordingly.

***5 Recommendation:** Transfer to other BPG journals.*

Language Quality: Grade B (Minor language polishing)
Scientific Quality: Transfer to another BPG Journal

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, all of which have met the basic publishing requirements of the ***World Journal of Gastroenterology****, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.*

Hiramatsu T, Nishizawa T, Kataoka Y, Yoshida S, Matsuno T, Mizutani H, Nakagawa H, Ebinuma H, Fujishiro M, Toyoshima O. *Improved visibility of colorectal tumor by texture and color enhancement imaging with indigo carmine. World J Gastrointest Endosc 2023;**15**:690-698.*
[PMID: 38187913 PMCID: PMC10768041 DOI: 10.4253/wjge.v15.i12.690]
When revising the manuscript, it is recommended that the author supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply

PubMed, or a new tool, the Reference Citation Analysis *(*RCA*), of which data source is PubMed.* RCA *is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our* RCA *database for more information at: https://www.referencecitationanalysis.com/, or visit PubMed at: https://pubmed.ncbi.nlm.nih.gov/.*

We corrected the description of Hiramatsu et al.'s reference as instructed.

INTRODUCTION

Image-enhanced endoscopy (IEE) improves the diagnosis of gastrointestinal lesions that are challenging in conventional white-light imaging (WLI). Narrow-band imaging (NBI) developing as an IEE modality is effective in diagnosing gastrointestinal disease[1-4]. Following NBI, blue-light imaging and linked color imaging (LCI) have been developed as our new IEE modalities. The utility of BLI and LCI has also been reported extensively[5-7]. Texture and color enhancement imaging (TXI), which is a novel method to enhance images, was developed in the new endoscopy system EVIS X1 (Olympus Corporation, Tokyo, Japan) in 2020. TXI is designed to enhance three image factors, namely texture, brightness, and color, in WLI to clearly define subtle tissue differences by applying the retinex-based enhancement. TXI has two modes (i.e., modes 1 and 2). TXI mode 2 is composited with brightness adjustment in dark regions and texture enhancement for subtle contrast. Additionally, color enhancement is applied to TXI mode 1 to define the slight color contrast more clearly[8, 9]. Representative endoscopic images of colonic neoplasm are shown in **Figure 1**.

Many studies investigating the visibility and color differences of TXI have been published. For example, visibility scores and color differences of TXI for colorectal neoplasia[10–13], gastric neoplasia[14-19], gastritis[14, 20], Barrett's esophagus[21, 22], pharyngeal and esophageal cancer[23], duodenal neoplasia[24], and the papilla of Vater have been assessed[25]. However, few studies have evaluated the detection and diagnosis of lesions using TXI. Therefore, this study highlights recent reports. We selected six comparative studies that examined the effects of TXI on neoplasia detection, disease prognosis, and diagnostic accuracy (**Table 1**).

TXI FOR DETECTION OF COLORECTAL NEOPLASIA

Two randomized controlled trials (RCTs) examined the utility of TXI in colorectal neoplasia detection. Antonelli *et al.*[26] conducted an international multicenter RCT (Italy, Germany, and Japan) assessing colorectal adenoma detection using TXI compared to WLI. Patients were randomly assigned to two arms, those who underwent colonoscopy using TXI or WLI. A total of 747 patients were enrolled (mean age 62.3 years; 50.2% male). Adenoma detection rate (ADR) was higher in the TXI group compared with the WLI group (58.7% *vs*. 42.7%; adjusted relative risk 1.35, 95% confidence interval [CI] 1.17-1.56, P = 0.001). The detection rate of adenomas < 10 mm was higher with TXI than with WLI (37.1% *vs*. 24.5%). The proportion of patients with high-risk polyps was higher in the TXI group than in the WLI group (26.7% *vs*. 19.9%, 1.31, 1.01-1.71, P = 0.046). High-risk polyps were defined as at least one adenoma ≥10 mm or with high-grade dysplasia, or at least five adenomas, or any serrated polyp ≥10

mm or with dysplasia, according to the most recent European Society of Gastrointestinal Endoscopy (ESGE) guideline[27]. The mean number of adenomas per procedure (MAP) with TXI was larger than that with WLI (1.36 *vs*. 0.89; adjusted incident risk ratio 1.48, 95% CI 1.22-1.80, *P* <0.001). This is the first RCT to compare colorectal neoplasia detection using TXI and WLI. Researchers demonstrated that TXI had a higher ADR than WLI and was useful for colorectal adenoma detection. They also reported that TXI increased the detection rate of small adenomas. Furthermore, TXI provided a larger MAP and a higher high-risk polyp detection rate, indicating that a different surveillance interval after colonoscopy is recommended compared to WLI.

Yoshida *et al*.[28] performed a multicenter RCT evaluating the efficacy of an additional 30-second (Add-30-s) observation of the right-sided colon (i.e., cecum to ascending colon) using TXI compared with NBI observation. Patients were assigned to either the TXI or NBI group. The right colon was first observed with WLI in both groups; then, the right colon was examined with Add-30-s observations using either TXI or NBI. Three-hundred fifty-eight patients were enrolled (mean age 68.3 years, 63.4% male). This study showed the non-inferiorities of TXI to NBI (0.29 *vs*. 0.30, difference for non-inferiority -0.01, 95% CI -0.10 to 0.08, *P* = 0.02) in the mean number of adenomas and sessile serrated lesions (SSLs) per procedure (MASP). The difference in MAP between TXI and NBI groups was also significant for non-inferiority (0.23 *vs*. 0.24, -0.01, -0.09 to 0.007, *P* = 0.01). Multivariable analyses showed no significant differences in MASPs and MAPs between the TXI and NBI groups, regardless of bowel preparation, endoscopes, and endoscopist level. Increases in the ADR, adenoma

and SSL detection rate, and polyp detection rate for the right colon from WLI to TXI were 10.2%, 13.0%, and 15.3%, respectively, and from WLI to NBI were 10.5%, 12.7%, and 13.8%, respectively. The increases in the TXI and NBI groups were not significantly different. This is the first non-inferiority RCT comparing TXI and NBI for colorectal neoplasia detection. The authors recommend that either TXI or NBI be used for Ad-30-s observation.

Sakamoto *et al*.[29] conducted a retrospective crossover study that compared colorectal neoplasia detection using TXI and WLI. They repeated the right colon observation twice with WLI or TXI as the first observation in the WLI and TXI groups, respectively. Then, the right-sided colon was re-examined as a second look using TXI or WLI, whichever was not used for the first observation. The remaining colorectal mucosa was examined using the first observation method. This study included 470 patients (mean age 64.0 years, 64.0% male). Multivariable analyses showed that the MAP and ADR in the TXI group were higher than those in the WLI group (1.5 *vs*. 1.0, adjusted odds ratio 1.4, 95% CI 1.2-1.6, P <0.001; 58.2% *vs*. 46.8%, 1.5, 1.0-2.3, P = 0.044), regardless of patient demographic characteristics, withdrawal time, bowel preparation, and endoscopes. TXI detected more adenomas in the ascending colon with a non-polypoid morphology and a size of 6-9 mm. Fewer non-polypoid lesions were missed in the TXI group than in the WLI group (16.6% *vs*. 30.6%). This cross-over study indicated that TXI was more suitable than WLI for the detection of adenomas, especially small non-polypoid adenomas, in the ascending colon.

TXI FOR ULCERATIVE COLITIS

A cohort study established a score using the TXI as a predictor of ulcerative colitis (UC) relapse and investigated its usefulness. Hayashi *et al.*[30] did a prospective single-center, single-arm cohort study. They developed the TXI scores as follows: score 0 = no accentuated redness; score 1 = accentuated redness; and score 2 = accentuated redness and poor visibility of deep vessels. The endoscopic images of 146 patients with UC in remission were reviewed. Patients with a TXI score of 2 had lower UC relapse-free rates than those with TXI scores of 0 and 1 (log-rank test, P <0.01). When pathologic remission was defined as Matts grade ≤2, the rate of pathologic remission decreased with higher TXI scores (TXI score 0, 95.2%; TXI score 1, 67.8%; TXI score 2, 40.0%, respectively, P = 0.01). In multivariate analysis, TXI score 2 was associated with UC relapse (hazard ratio 4.16, 95% CI 1.72-10.04, P <0.01), whereas the Mayo endoscopic subscore (MES) was not. Furthermore, the relapse-free rate was lower in MES 1 with a TXI score of 2 than in MES 0 or MES 1 with a TXI score of 0 or 1. The authors concluded that TXI could identify populations with poor prognosis in MES 1, for whom treatment intensification has been controversial.

TXI FOR GASTRIC CANCER AND GASTRITIS

Two studies have investigated the efficacy of TXI in treating gastric lesions. Kemmoto *et al.*[31] performed a cross-sectional study analyzing gastric cancer (GC) detection during gastroscopic screening. They compared the GC detection rate in TXI mode 2 with that of the WLI observations. A total of 13440 patients (median age 57 years; 60.6% male) were included in this study. The GC

detection rate was higher in the TXI group than in the WLI group (0.71% *vs*. 0.29%), especially among patients who had undergone *Helicobacter pylori* eradication (1.36% *vs*. 0.43%). The positive predictive value of GC on biopsy was higher in the TXI group than in the WLI group (11.0% *vs*. 4.9%). Furthermore, the Expert-WLI group, which was limited to patients who underwent WLI by three endoscopists with the highest GC detection rates, was compared with the TXI group. The detection rates of GC after *H. pylori* eradication in the lower stomach, with 0-IIc endoscopic morphology according to the Paris classification, and with the histologically differentiated type were higher in the TXI group than in the Expert-WLI group (0.87% *vs*. 0.17%, 1.36% *vs*. 0.43%, and 1.36% *vs*. 0.52%, respectively). The authors concluded that TXI mode 2 improved the detection of GC after *H. pylori* eradication in the L-region with superficially depressed and differentiated types. This study demonstrated the usefulness of TXI observation in GC screening.

Kitagawa *et al*.[32] examined the diagnostic accuracy of *H. pylori* infections in the stomach. The patients were divided into three groups based on *H. pylori* infection status: current, past, and non-infection. The diagnostic accuracy for *H. pylori* infection status was compared in TXI with WLI observation. Endoscopic images of 60 patients (median age 73 years; 68.3% male) were reviewed. The sensitivity and accuracy for current *H. pylori* infection in TXI were higher than those of WLI (69.2% *vs*. 52.5%, $P = 0.012$; 85.3% *vs*. 78.7%, $P = 0.034$). The diagnostic odds ratio of diffuse redness for current infection, map-like redness for past infection, and regular arrangement of collecting venules (RAC) for non-infection in TXI observation were higher than

those in WLI observation (56.21 *vs*. 22.00, 10.97 *vs*. 6.29, and 42.25 *vs*. 25.24, respectively). TXI may be useful for diagnosing *H. pylori* infection during gastroscopy.

CONCLUSION AND PERSPECTIVES

We have highlighted recent reports examining the usefulness of TXI for gastrointestinal diseases in clinical practice (**Table 1**). For colorectal neoplasia, an RCT and a crossover study demonstrated that TXI had a higher ADR and MAP than WLI, and an RCT showed that TXI had non-inferiority to NBI in terms of MASP and MAP. A scoring system using the TXI was shown to be useful in predicting UC relapse in a cohort study. For the stomach, TXI was reported to improve GC detection and diagnostic accuracy of active *H. pylori* gastritis compared to WLI. TXI can selectively enhance brightness in dark areas of an endoscopic image and can enhance subtle tissue differences, such as slight morphological or color changes, while simultaneously preventing over-enhancement[8]. These characteristics of TXI may aid in making more accurate diagnoses.

Further validation of the detection of neoplastic and inflammatory lesions using TXI is required. Furthermore, investigations on whether the use of TXI endoscopy is associated with better patient prognosis are desirable. Studies have shown that endoscopy with magnification, dye spraying[10, 11, 33, 34], and artificial intelligence[35-37] is useful for diagnosing neoplasia and inflammation, and validation of these modalities in combination with TXI is expected. Therapeutic applications of TXI are expected in the future[38]. The two modes of

TXI have different features, so they should be separately described in future studies. There have been many reports from Japan, and further international research is required. In conclusion, TXI can improve the detection and qualitative diagnosis of gastrointestinal lesions.

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