

## ANSWERING REVIEWERS



January , 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: EPSP Manuscript 7799-Review highlight ver.doc).

**Title:** Chromoendoscopy of gastric adenoma using an acetic acid indigocarmine mixture

**Author:** Yoshiyasu Kono, Ryuta Takenaka, Yoshiro Kawahara, Hiroyuki Okada, Keisuke Hori, Seiji Kawano, Yasushi Yamasaki, Koji Takemoto, Takayoshi Miyake, Shigeatsu Fujiki, Kazuhide Yamamoto.

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 7799

The manuscript has been improved according to the suggestions of reviewer:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer. Below are the editor's and our corrections.

### **Point-by-point responses to the reviewer**

**1. About the unclear sentences (in the section Introduction - the first sentence, in the second paragraph second and fourth sentences).**

As pointed by the reviewer, we revised unclear sentences as bellows.

Original (Page 5, Line 2):

Esophagogastroduodenoscopy (EGD) accompanied by forceps biopsy is thought to be the most reliable modality for diagnosing gastric cancer [1] and endoscopic treatment, such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), is performed on the basis of the findings of forceps biopsy.

Revised:

Histological diagnosis by forceps biopsy before endoscopic resection (ER), such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), is important to determine whether ER should be performed [1].

Original (Page 5, Line 16):

We reported a novel chromoendoscopy procedure using an acetic acid indigocarmine mixture (AIM) was effective for recognizing the margins of early gastric cancer (EGC) [11], and in some cases,

the color of the EGC area appeared reddish by degrees after instillation of the AIM solution [12].

Revised:

We previously reported that a novel chromoendoscopy procedure using an acetic acid indigocarmine mixture (AIM) was effective for recognizing the margins of early gastric cancer (EGC) [13], and that the color of the EGC sometimes turned reddish by degrees after instillation of the AIM solution [14].

Original (Page 5, Line 22):

However, there have been no reports of AIM-chromoendoscopy (AIM-CE) in borderline lesions.

Revised:

However, there have been no reports of AIM-chromoendoscopy (AIM-CE) for diagnosing a coexisting gastric cancer component in gastric adenomas.

## 2. About the endoscopic procedure

As the reviewer suggested, we cited our papers in the section Material.

Original (Page 7, Line 16):

After washing away the IC solution, 40 mL AIM solution (0.6% acetic acid with 0.4% IC) was sprinkled onto the lesions and images were recorded again every 30 seconds for 3 minutes.

Revised:

After washing away the IC solution, 40 mL AIM solution (0.6% acetic acid with 0.4% IC) was sprinkled onto the lesions and images were recorded again every 30 seconds for 3 minutes [14].

## 3. About the figure 1 and figure 2

As suggested by the reviewer, we placed the figure 1 and figure 2 in the section Results.

Deleted sentence

Original (Page 7, Line 18):

When the surface color was judged to have turned reddish, compared to the surrounding mucosa, the reddish color change was recorded as positive (Figure 1, 2).

Added sentence

Revised: in the Result section

In AIM-CE, the reddish color change was recorded as positive when the surface color was judged to have turned reddish compared to the surrounding mucosa. Figure 1 and 2 show the typical cases of no change and reddish color change in AIM-CE, respectively.

## 4. About the statistical analysis

As suggested by the reviewer, we showed the respective analysis which of the data are used.

Original (Page 8, Line 20):

Statistical differences were calculated by the Fisher's exact test, Mann-Whitney *U* test, McNemar's test, and the logistic regression test. P values < 0.05 were considered to be statistically significant.

Revised:

Fisher's exact test or  $\chi^2$  test was used for all categorical variables, and the Mann - Whitney *U* test was used for continuous variables. McNemar's test was used for comparison of diagnostic ability between WLE and AIM - CE. Univariate and multivariate logistic regression analyses were used to

determine the significant factors contributing to diagnosis of EGC. Variables found in the univariate analysis to be significantly associated with diagnosis of EGC were included in a multivariable logistic regression analysis. All statistical calculations were carried out using JMP software (for Windows, version 10).  $P$  values  $< 0.05$  were considered to be statistically significant in all tests.

## 5. About the Results

As suggested by the reviewer, we revised the sentences as bellows in section Results.

### i. About Age and gender, Tumor size, and the other data

Original (Page 10, Line 2):

#### *Age and gender*

The difference of median ages between the adenocarcinoma group and the adenoma group was not significant. There were significantly fewer females in the adenocarcinoma group than in the adenoma group (Table 1).

#### *Tumor size*

The adenocarcinoma lesions were significantly larger in diameter than the adenoma lesions ( $P = 0.019$ ). All adenocarcinoma lesions were well-differentiated tubular adenocarcinomas and were restricted within the mucosal layer (Table 1).

Revised:

#### *Clinical parameters in all cases*

Table 1 shows the clinical characteristics of the 54 cases. The difference of median ages between the adenocarcinoma group and the adenoma group was not significant ( $P = 0.85$ ). The gender ratio differed significantly different between the adenocarcinoma group and the adenoma group ( $P = 0.047$ )

All adenocarcinoma lesions were well-differentiated tubular adenocarcinomas and were restricted within the mucosal layer. The adenocarcinoma lesions were significantly larger in diameter than the adenoma lesions ( $Z = 2.3$ ,  $P = 0.019$ , Man-Whitney  $U$  test). There were no significant differences between the adenocarcinoma group and the adenoma group in tumor location and macroscopic type ( $P = 0.33$  and  $P = 0.84$ , respectively).

### ii. About the Table 2

As suggested by the reviewer, we omitted Table 2 from the text because its content is explained in the text.

### iii. About the text missing the p values for significant differences

As suggested by the reviewer, we placed p values for significant differences as bellows.

Original (Page 11, Line 8):

Table 3 shows the diagnostic ability of WLE and AIM - CE. The sensitivity of AIM - CE is significantly higher than that of WLE.

Revised:

Table 2 shows the diagnostic ability of WLE and AIM-CE. The sensitivity of reddish color change in AIM-CE is significantly higher than that of WLE (*vs* tumor size  $\geq 2$ cm;  $P = 0.016$ , *vs* normochromic or reddish surface color;  $P = 0.046$ , depressed macroscopic type;  $P = 0.0030$ ).

## 6. About the captions of the tables

As suggested by the reviewer, we revised as follows.

Original (Page 24, Line 1):

Table 1 Clinical characteristics of 54 cases.

Revised:

Table 1 - Data from the clinical characteristics of 54 cases.

Original (Page 26, Line 1):

Table 3 Diagnostic ability of WLE and AIM-CE

Revised:

Table 2 - Data from the diagnostic ability of WLE and AIM-CE

Original (Page 27, Line 1):

Table 4 Logistic regression analysis of factors contributing to diagnosis of EGC

Revised:

Table 3 - Data from the logistic regression analysis of factors contributing to diagnosis of EGC

## 7. About Discussion

As suggested by the reviewer, we revised the sentences as follows.

Original (Page 12, Line 18):

In this study, the concordance rate was 57.4%, which was slightly lower than previously reported. A possible reason is that, usually, only one sample was taken by forceps biopsy in this study. Because the sample number was lower, the concordance rate could be lower.

Revised:

In this study, lesions were resected in en bloc fashion by ESD and, because the sample number was lower and the en bloc resection rate was higher, the concordance rate could be lower.

Original (Page 13, Line 4):

Kitoh et al. reported two endoscopic findings, focal redness and lack of glossiness, were significant factors associated with gastric cancer<sup>[31]</sup>.

Revised:

In 2005, Kitoh et al. reported that two endoscopic findings, focal redness and lack of glossiness, were significant factors associated with gastric cancer<sup>[26]</sup>.

Original (Page 14, Line 10):

When the surface color of the lesions changes reddish after applying the AIM solution, endoscopic treatment such as EMR or ESD may be recommended.

Revised:

If the surface color of the lesions changes to reddish after applying the AIM solution, we should consider an endoscopic treatment such as EMR or ESD.

## 8. About the figures

As suggested by the reviewer, we place yellow arrows around the lesions in Figure 1 and Figure 2.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Yoshiyasu Kono, M.D.

Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine,  
Dentistry and Pharmaceutical Sciences

2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan.

Fax: +81-86-225-5991

E-mail: [hxnwq178@yahoo.co.jp](mailto:hxnwq178@yahoo.co.jp)