MANUSCRIPT REVISION

We would like to thank the reviewers for their comments and suggestions, which gave great contribution to improve our manuscript.

Reviewer #1:

Major Comments:

#1 As the study design, it should be stated whether all endoscopists have been blinded to previous and present H. Pylori infection.

All endoscopists who performed the exams had information about previous Hp infection. FF and BCM were blinded for previous and present Hp infection. We added this information on "Methods - Endoscopic procedures and near focus classification".

#2 In result, authors describe that upon initial examination of the gastric body with S-HD (Table 2), the finding with the best sensitivity for Hp detection was enanthema (80.9%), present in 75 patients. Exudate (99.3%), nodularity (97.1%), and atrophy (95.7%) demonstrated better specificity values, but with low sensitivity (6.4%-19.1%). The term of enanthema is not familiar as an endoscopic term. These endoscopic findings are need to be demonstrated as figures.

Thank you for this observation. The term enhantema was changed to erythema all over the document (Tytgat, GNJ. Journal of Gastroenterology and Hepatology (1991) 6, 223-234). We included the most relevant S-HD findings on Figure 1

Minor comments:

#1 The authors describe that High definition (HD) magnification endoscopy (ME) can increase the image view by more than 100 times in introduction. More specific expression is desirable.

Thank you. We added detailed information about the ME technology in introduction.

#2 Capitalize the beginning of the sentence in abstract.

We have capitalized the beginning of sentences in abstract

#3 Figures and tables are difficult to see as a whole. The fonts should be aligned.

Thank you. We made ameliorations on tables for better reading. We presume that if our article is acceptable for publication, editorial designers will format them accordingly to journal standards.

#4 About Figure 1, it is easier for the reader to understand the figure legend if it is along with the expression in the text.

We have changed the figure legend to better match the classification description. However, minor changes were made since the images on near focus examination are not as precise as those seen by magnification endoscopy (e.g. honeycomb appearance). There are also some changes seen in our figures that are not part of original description (e.g. exudate on figure 1c).

Also, the classification is by Anagnostopoulos not by Yagi.

Thank you for this observation. Yagi was the one who proposed paying particular attention to the greater curvature and anterior wall of the medium gastric body. We have moved the figure citation to the middle of the sentence to avoid mistake.

#5 The abbreviation for Helicobacter Pylori is not unified.

We unified abbreviation to Hp all over the document.

Reviewer #2:

1 Title. This study is not a diagnostic study and the aim of near-focus technology is not to detect the Helicobacter pylori infection. It would be better, like "The association between mucosal surface pattern under near-focus technology and Helicobacter pylori infection".

We agree with the reviewer's suggestion. We've changed the study title.

2 Abstract. The abstract summarized and reflect the work described in the manuscript.

Thank you for the comment

3 Key words. It is OK.

4 Background. The manuscript adequately describes the background and present status of the study. However, a diagnostic study needs to explain the clinical significance, especially under current easy-use precise detection methods, like rapid urease test and Carbon 13 breath test system.

Thank you for the thoughtful suggestion. In the end of introduction, we modified our aim according to the reviewer suggestion about the title, which we think better match our objectives. "We aimed to access the association between mucosal surface pattern under Near Focus technology and Hp infection status in a western population".

With the advent of advanced imaging technology, it comes the wish of correlating the endoscopic findings with histology, which could potentially impact the endoscopist's behavior during the endoscopic examination. We have addressed this postulation in the discussion section:
"*The awareness of these findings may lead endoscopists to change some practices during elective routine endoscopy...... This may include collecting more fragments and/or performing biopsies for histopathological analysis besides RUT.*" In addition, C13 breath test is not widely available in Brazil.

5 Methods. Why does a cross-section study consider the drop-out rate(25%) on page 8? The sample size was calculated under the sensitivity of 94% and specificity of 95%, which is far better than the current results. An association analysis, like Chi2 and logistic regression, may be reasonable for the hypothesis.

We adopted the sensitivity and specificity of 94 and 95% based on studies that have employed magnification endoscopy. This fact might explain the inferior results obtained with near focus technology.

We realize that a drop out rate of 25% is high for a cross-sectional study. Our study protocol depended on the adherence of 10 endoscopists to fill out the form with detailed information after the procedures. We hypothesized that, in a busy agenda, not all endoscopists would adhere to the study protocol. Surprisingly, that was not the case. In the end, 187 patients were included, a sample size that could be smaller. However, we believe this fact does not invalidate our findings.

6 Results. If the hypothesis and statistical methods changed, the results need to be revised.

We fully agree that this is more of an association study than a diagnostic study. However, we felt that calculating the sensitivity, specificity, NPV and PPV for near focus findings is more useful to express the results for the reader and in clinical practice. E.g., the presence of RAC indicates that Hp infection is absent in more than 90% of the cases. In Table 3, we have also demonstrated the association of near focus findings and Hp infection status using chi-square test. In addition, the studies that dealt with the association of endoscopic mucosal pattern with Hp infection status have calculated sensitivity, specificity, NPV and PPV to express their results (Table 6).

7 Discussion. The lower efficiency of current results than previous results needs to be discussed. The clinical significance needs to be further illustrated.

Thank you for this observation.

We found wide variability of sensitivity and specificity among studies. Among the studies summarized on Table 6, six had better sensitivity and 5 had lower sensitivity than ours. Jang et al, who also studied near focus imaging, present similar sensitivity (86.5% vs 87%) and slightly higher specificity (84.1% vs 70.7%). Our specificity was superior to four other studies - Glover (2021), Ebigbo (2020), Yagi (2013) and Garcez (2019). Our study presented the second higher NPV (94%).

We added a paragraph to discuss the difference of statistical results among studies:

"Taken together, sensitivity of "loss of RAC" to predict Hp infection varied from 66% to 100% and specificity varied from 48% to 100%. Excluding the studies that used ME, the one with higher sensitivity was also the one with lower specificity (Garcez et al.). The wide variability of sensitivity and specificity of RAC identification and Hp status among studies might be explained by different technology applied and different endoscopists' expertise. Apparently, there is lower variability of NPV among studies, meaning that the presence of RAC is a good indicator of Hp negative status."

8 Illustrations and tables. The statistical test in Table 1 needs to be supplied because this study is not RCT.

Thank you. We included statistical test in table 1.

9 Biostatistics. The statistical test in Table 1 needs to be supplied.

Thank you. We included statistical test in table 1.

10 Units. It is OK.

11 References. Some new references need to be updated.

We included new references from 2020 and 2021.

12 Quality of manuscript organization and presentation. It is OK.

13 Research methods and reporting. Authors prepared their manuscripts according to manuscript type and the appropriate categories, STROBE Statement.

14 Ethics statements. The manuscript meets the requirements of ethics.

Reviewer #3:

1. The title reflect the main subject about endoscopy for the detection for Helicobacter pylori, title was clear and easy to understand but in the text "Near focus high-definition" I suggest add the word "technique" or "technology" after that to promote interested article for reader.

We have changed the study title according to reviewer's #2 suggestion and included the word "technology" according to reviewer's #3 suggestion.

2. The abstract summarize and reflect the work described in the manuscript.

Thank you for the comment

3. The key words reflect the focus of the manuscript.

Thank you for the comment

4. The manuscript adequately describe the background, present status, and significance of the study. The authors explain progression of Near Focus technology which new use in Western countries.

Thank you for the comment

5. The manuscript describe methods in adequate detail, study subjects were clear, with demonstrate IRB number or text to human ethics consideration. I suggest the authors explain about "examinations were performed by nine senior endoscopists" in the context of research involvement, methods to validate all comments and information bias.

We have added "over 10 years experience" to explain the senior endoscopists.

6. The research objectives achieved by the experiments used in this study. I suggest the authors revise Figure 2: Study flowchart, size of text.

We have improved the Figure 2, increasing the font size. We also provided a separate editable word document in case the editors accept our paper for publication.

7. The manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly, and logically.

We thank the reviewer for the comment

8. Tables and figures sufficient, good quality and appropriately illustrative of the paper contents.

9. The manuscript meet the requirements of biostatistics.

10. The manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections.

We thank the reviewer for the comment