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Dear Editor-In-Chief, Reviewers 02505493, 00503417 and 03009411,

March 27, 2020

We greatly appreciate your careful reviews and fruitful comments for our manuscript entitled “Chronic atrophic gastritis detection with a convolutional neural network considering stomach regions”.

Please note that the title has been changed according to the suggestion from the reviewer 00503417.

We have carefully studied each Reviewer’s comments and revised our manuscript.

We submit our revised manuscript with the response sheet.

Finally, we greatly appreciate Editor-In-Chief and the Reviewers’ constructive comments again.

The responses for the comments pointed out by Reviewers marked in red in the revised manuscript.

Yours sincerely,

Manuscript NO. 54644

Misaki Kanai, Ren Togo, Takahiro Ogawa, Miki Haseyama

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Response to Reviewer 02505493's Comments

Misaki Kanai, Ren Togo, Takahiro Ogawa, Miki Haseyama

Dear Reviewer 02505493:

Thank you for your comments concerning the manuscript entitled "Chronic atrophic gastritis detection with a convolutional neural network considering stomach regions", which we submitted for publication in World Journal of Gastroenterology.

Conclusion: Accept.

Peer-review report.

The manuscript can be accepted for publication

Response.

Thank you for your review and kind comments for our manuscript.

Response to Reviewer 00503417's Comments

Misaki Kanai, Ren Togo, Takahiro Ogawa, Miki Haseyama

Dear Reviewer 00503417:

Thank you for your comments concerning the manuscript entitled "Chronic atrophic gastritis detection with a convolutional neural network considering stomach regions", which we submitted for publication in World Journal of Gastroenterology.

Conclusion: Accept.

Peer-review report.

This indeed is a useful study, especially in regions such as Japan where early detection of pre-cancerous lesions is indicated. However, I suggest the following inputs: 1. Please state in detail how the X-ray studies were performed, i.e., contrast used, amount used, technique of fluoroscopy / exposure details 2. The term 'gastritis' suggests inflammation, an entity that obviously cannot be seen on X-ray. Can the authors find a better term? For example, are they looking for stages of atrophy, as the Kimura-Takemoto classification suggests? 3. Please mention the specific features on X-ray that you looked for 4. A statement that this is a complement to endoscopy should be made. How this fits in in clinical practice can be stated

Response.

First, we appreciate Reviewer 00503417 for the precise comments.

In the above arguments, we divide the comments into the following four points.

Argument 1:

Please state in detail how the X-ray studies were performed, i.e., contrast used, amount used, technique of fluoroscopy / exposure details.

Argument 2:

The term 'gastritis' suggests inflammation, an entity that obviously cannot be seen on X-ray. Can the authors find a better term? For example, are they looking for stages of atrophy, as the Kimura-Takemoto classification suggests?

Argument 3:

Please mention the specific features on X-ray that you looked for.

Argument 4:

A statement that this is a complement to endoscopy should be made. How this fits in in clinical practice can be stated.

Response to Argument 1.

Thank you for your valuable comments for our manuscript. In this study, the double-contrast frontal view of the stomach in the supine position were used. Technique of fluoroscopy was a digital radiography (DR) system. Exposure was controlled by an automatic exposure control mechanism. These explanations were added in the revised manuscript. In addition, we added the specific condition of the X-ray examination in the revised manuscript. Please see the Sec. 2.1.

Response to Argument 2.

As the reviewer pointed out, we reconsidered the term “gastritis”. Certainly, the term “gastritis” may cause the miss-understanding since X-ray images can describe the “atrophy” of the stomach. Also, the Kimura-Takemoto classification that can evaluate the atrophy of the stomach is also employed as the ground truth of this study.

In the revised manuscript, we replace the term “gastritis” to “chronic atrophic gastritis (CAG)” to represent more specific target condition of the stomach. Due to this change, we updated our manuscript title to “Chronic atrophic gastritis detection with a convolutional neural network considering stomach regions”.

Response to Argument 3.

Thank you for your advice for our manuscript. Our model tries to recognize the features of chronic atrophic gastritis described in gastric X-ray images. We added the following explanations in the revised manuscript in Sec. 2.1.

It should be noted that the stomach with non-CAG has straight and fine fold distributions and fine mucosal surfaces, and the stomach with CAG has non-straight and snaked folds and coarse mucosal surfaces. X-ray examination can visualize these atrophic characteristics by barium contrast medium. We show that these differences can be trained on a chronic atrophic gastritis detection model with a small number of training images in this paper.

Response to Argument 4.

Thank you for your advice for our manuscript. We agree that the role of X-ray examination should be described in the paper. In the revised manuscript, we added the following explanations in Sec. 4.

In general, endoscopic examination is superior to an X-ray examination for the evaluation of CAG in imaging inspections [28]. The endoscopic examination has been recommended for gastric cancer mass screening programs in East Asian countries in recent years. For example, South Korea has started the endoscopic examination-based gastric cancer screening program since 2002, and the proportion of individuals who underwent endoscopic examination greatly increased from 31.15% in 2002 to 72.55% in 2011[28]. Also, Japan has started the endoscopic examination-based gastric cancer mass screening program in addition to an X-ray examination since 2016. However, there remains the problem that the number of individuals who can be examined in a day is limited. Hence, X-ray examination still plays an important role in gastric cancer mass screening.

To realize effective gastric cancer mass screening, it is crucial to narrow down individuals who need endoscopic examination by evaluating the condition of the stomach. Then CAD systems that can provide additional information to doctors will be helpful. Particularly, our approach presented in this paper realized the construction of machine learning-based CAG detection with a small number of training images. This suggests that the CAG detection method can be trained with data from a small-scale or medium-scale hospital without a large number of medical images for training.

[28] Lee S, Jun JK, Suh M, Park B, Noh DK, Jung K-W, et al. Gastric cancer screening uptake trends in Korea: results for the National Cancer Screening Program from 2002 to 2011: a prospective cross-sectional study. *Medicine (Baltimore)*. 2015;94(8):e533.

Response to Reviewer 03009411's Comments

Misaki Kanai, Ren Togo, Takahiro Ogawa, Miki Haseyama

Dear Reviewer 03009411:

Thank you for your comments concerning the manuscript entitled "Chronic atrophic gastritis detection with a convolutional neural network considering stomach regions", which we submitted for publication in World Journal of Gastroenterology.

Conclusion: Accept.

Peer-review report.

Helicobacter pylori associated gastritis is a common clinical disease, especially in Asia. The risk of gastric cancer is increased in patients with Helicobacter pylori associated gastritis, especially in patients with atrophic gastritis. Gastroscopy is the most direct way to find and diagnose Helicobacter pylori associated gastritis, but for patients who are not willing to accept gastroscopy or in countries and regions where gastroscopy screening has not been widely used, X-ray examination has advantages and has better clinical value to improve the accuracy of the examination. To evaluate the effectiveness of stomach regions that are automatically estimated by a deep learning-based model for gastritis detection, the authors used 815 GXIs (200 for training and 615 for evaluation) obtained from 815 subjects. By using GXIs with the stomach regions for training, the proposed method realizes accurate gastritis detection that automatically excludes the effect of regions outside the stomach. As a preliminary exploration, this study has better clinical value and application prospects, but more multi angle samples and clinical centers are needed to further explore.

Response.

Thank you for your precise review and kind comments for our manuscript. We are genuinely grateful for your understanding in regard to the advantages of our method and limitations.