

## **Implementation of a Polling Protocol for Predicting Celiac Disease in Videocapsule Analysis**

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We would like to thank the reviewers and editors for their kind assistance in improving the quality of the manuscript. All changes in the manuscript text will be shown in blue.

Reviewer # 1

This manuscript outlines an approach to the interpretation of data from videocapsule endoscopy in the assessment of a small number of patients with Coeliac disease. Comments: 1. This assessment draws on a small group of patients. Is this sufficient to be able to draw conclusions? Further, were sufficient patients within each grouping (of Marsh criteria) included?

We agree that the small N reduces the potential impact and revised the text accordingly in the conclusions of the Abstract:

Automata-based polling may be useful to indicate presence of mucosal atrophy, indicative of celiac disease, across the entire small bowel, though this must be confirmed in a larger patient set.

And in the Conclusion section of the Discussion:

The findings of this study suggest that the technique may be useful for discerning images of celiac patients with villous atrophy from images of control patients lacking atrophy, though this must be confirmed with a larger data set that includes different Marsh grades of intestinal damage.

2. One assumes that all patients had previously undergone standard upper gastrointestinal endoscopy with multiple biopsies from the duodenum for the confirmation of the diagnosis. This is not clearly stated. How many biopsies were included?

We now state in the Methods:

In all except one patient, six biopsy specimens were obtained during endoscopy and then analyzed using light microscopy. In one hemophiliac patient, biopsies were not obtained.

3. Further, the authors looked at more distal intestinal sites (beyond D3/4). How was the gold standard able to be considered in this context? (Images were from sections of the small bowel that were not assessed histologically).

The reviewer is correct that there was no gold standard of biopsy specimen for levels 3 and 4. In the Limitations we now mention:

Since there was no gold standard of biopsy specimen for levels 3 and 4 analysis, villous atrophy may have been absent from these regions in celiac patients, which would result in classification error.

4. The Introduction could be shortened.

We appreciate the reviewer's comment and have significantly shortened the Introduction.

5. Table Headings could be enhanced 6. Figures 2, 3, 4 and 5 could have correct and enhanced legends in standard fashion

We thank the reviewer and have improved Table and Figure legends and headings..

Reviewer # 2

Ciaccio and co-authors investigate the benefit of automated analysis of video capsule imaging in celiac disease. The authors conclude from their data that the method is useful in detection of villous atrophy, especially in proximal locations of the small intestine. Comments The study is limited by the small number of patients included.

We agree that this point should be emphasized and have changed the text accordingly, also in response to Reviewer #1:

In the Conclusions of the Abstract:

Automata-based polling may be useful to indicate presence of mucosal atrophy, indicative of celiac disease, across the entire small bowel, though this must be confirmed in a larger patient set.

And in the Conclusion section of the Discussion:

The findings of this study suggest that the technique may be useful for discerning images of celiac patients with villous atrophy from images of control patients lacking atrophy, though this must be confirmed with a larger data set

The finding that the procedure is more efficacious in the proximal small intestine should be discussed in more detail; what could be of relevance?

We appreciate this comment from the reviewer and now state in the Results:

For two of the marsh Marsh type IIIA celiac patients, and for the patient lacking biopsy, no prediction was also made at location 4, suggesting that images acquired from this location (ileum) are more difficult to evaluate, or that there is a lesser degree of villous atrophy, as compared with more proximal small intestinal locations.

Some text errors throughout the manuscript should be cleaned.

We apologize to the reviewer and have corrected a number of typos in the manuscript.