Dear Reviewer,

First of all, thank you very much for your insightful review.

Considerations regarding your inquiry about the behavior of the algorithm in relation to other lesions (e.g., esophageal cancer) were incorporated into the discussion (corresponding to the 6thand 7th paragraphs), along with possibilities for broadening the clinical scope of the proposed algorithm. Considerations regarding the applicability of the proposed model in the near future and the possibility of its use in peripheral locations were also incorporated (8th paragraph of the discussion).

Below are these additions, along with the corresponding indagations.

1) **How this Adam's optimizer detected oesophageal conditions other than esophagitis like tumor etc?**
   Concerning the predictive behavior towards other possible esophageal Z-line abnormalities, assuming that the algorithm was able to differentiate with high accuracy normal images from images with different degrees of inflammation – and consequently different mucosal lesion configurations –, it is reasonable to assume that other esophageal lesions would be differentiated from the healthy aspect, and thus categorized together with the esophagitis images. Among the possible clinical differential situations, esophageal and esophagogastric junction cancers are of particular relevance. Upper endoscopies are considered by the Society of Thoracic Surgeons and the National Comprehensive Cancer Network (NCCN) as the initial diagnostic evaluation to exclude esophageal cancer; although techniques such as chromoendoscopy and narrow band imaging are often used to increase the sensitivity of detection of lesions suggestive of malignancy, traditional endoscopic imaging still plays an important role in the investigational flowchart, and can demonstrate suspicious findings incidentally. In view of this, in order to extend the clinical utility of our proposed algorithm to the investigation of potentially malignant endoscopic findings, two main approaches are possible: (i) propose an adaptation of the model to multiclass classification and, to this end, retrain the model including endoscopic images of esophageal cancer, fine-tuning, if necessary, only the final layers, making appropriate changes in the final dense layer and in the loss function to accommodate 3 classes (thus, the final layer would now have 3 neurons with softmax activation function, and the sparse categorical crossentropy loss function would be adopted); (ii) preserve the binary classification structure, but proposing to change the labels for normal and abnormal findings (thus, the model would be used to triage any endoscopic abnormalities, ranging from inflammatory findings to lesions suggestive of malignancy) and, for this purpose, retrain the model including endoscopic images representative of other types of lesions (including neoplastic lesions). In either situation, the incorporation of images representative of lesions suspicious for malignancy would be necessary, and the weights derived from training with normal endoscopic images and with

esophagitis findings already performed would be used (same domain fine-tuning).

2) **How this will help in near future?**
   Convolutional neural networks with transfer learning for automated analysis of endoscopic images, as proposed in this study, may be incorporated into daily practice as a clinical decision support tool – screening abnormalities and indicating the need for further specialized evaluation or double checking medical reports.
3) **Can it be useful for health care workers in the peripheral locations?**
   This application would add value especially in contexts of scarce resources, in which the number of endoscopists is limited and they are often poorly trained – increasing, thus, the likelihood of diagnostic errors. Moreover, it is especially promising as an adjunct tool to telemedicine, favoring rural and remote areas.

Answering the questions you proposed has added great value to our manuscript.

Best regards.