Response to the reviewers

Reviewer #1:

1) Firstly, the study should state clearly its aim - that the results only apply to Tubular Adenomas, as that is the only type of lesion that was evaluated by the different modalities and therefore the results of this study cannot be generalized to other colorectal lesions, such as cancer or other polyp histologies.

Response: We thank the reviewer for the careful review and insightful suggestions. We agree that our results only applied to tubular adenomas; thus, we accordingly modified the Aim of the Abstract, Introduction, and Research objectives of the Article highlights.

2) Authors state there is only one clinical study for TXI by Ishikawa et. al, however there exists another namely "Visibility of early gastric cancer in texture and color enhancement imaging" by Seiichiro Abe et al. Furthermore, a Clinical trial is currently ongoing in Adelaide, Australia for colon polyps in which WLI is compared to TXI.

Response: As suggested, Abe et al. have reported on TXI [Abe et al. *DEN Open*, 2021]. Furthermore, some clinical trials on TXI for colonoscopy are currently ongoing, such as "A randomized comparison between White Light Endoscopy (WLE) and Texture Color Enhancement Imaging (TXI) in detection of colon polyps at colonoscopy" in Adelaide, Australia; TRACK study in Rome, Italy; and COLT study in Kyoto, Japan; however, to the best of our knowledge, no published reports on colonoscopy are available in the PubMed or the Cochran Library. Thus, we changed the manuscript in the Introduction from:

Currently, the only clinical study on TXI is a report by Ishikawa et al., wherein TXI was used for imaging the stomach [27]. There are no reports on the use of TXI in the colon.

To:

Currently, the only clinical studies on TXI that have already been published are those by Ishikawa et al. and Abe et al., wherein TXI was used for imaging the stomach [27, 28]. Some clinical trials on the efficacy of TXI in colorectal polyp observation are ongoing; however, no published reports on colonoscopy are available in PubMed or the Cochrane Library.

3) The authors are advised to expand on the methods section of this paper to include more detail of the experimental process. For instances, Authors should outline more clearly the process of colonoscopy where these polyps were imaged. They state that images for different modality were taken within 15s of each other. However, when was CE done? was it the last modality? because the dye used for CE may unfairly enhace other modalities of imaging, such as NBI, if the CE was done prior to the NBI.

Response: Thank you for your suggestion. Lesions were first washed carefully with water to remove the mucus and dye from the mucosal surface; then, images were obtained through WL, TXI, and NBI. The lesions were subsequently stained for CE. Hence, CE was the last modality, as observed by the reviewer. We have included this information in the Endoscopy section of the Methods section.

4) The number of patients enrolled in the study should also be mentioned in the methods section (currently only mentioned in the results section), and it should be clearly stated that only one polyp per patient was examined.

Response: We thank the reviewer for this important observation. We have described the adenoma-based analysis in the Patients section of the Results and Table 1; however, the said expression may have been insufficient and confusing. We enrolled a total of 37 consecutive patients with 61 adenomas. We listed patients in a patient-based manner and adenomas in an adenoma-based manner. Further, we added to the Methods that multiple adenomas in one patient were individually managed. In line with these contents, we modified the Patients section of the Methods, Patients section of the Results, and Table 1 as follows:

Methods,

When the patient had multiple adenomas, they were treated individually.

Results,

The clinicopathological characteristics of the 37 consecutive patients with 61 adenomas evaluated in this study are shown in Table 1. The mean age was 59.1 years, and men accounted for 51.4%.

Table 1. Clinicopathological characteristics of patients and adenomas

Patients, n	37
Age, mean (range, SD), year	59.1 (41-79, 9.0)
Sex, male/female, n	19/18
Adenomas, n	61
Location, cecum/ascending/transverse/descending/sigmoid/rectum, n	5/8/35/3/10/0
Size, mean (range, SD), mm	4.2 (1-12, 2.3)
Morphology*, Ip/Is/IIa/IIb, n	2/6/48/5
Histological subtype, tubular/villous, n	61/0
Dysplasia, low-grade/high-grade, n	61/0

5) Authors also mention that patients who underwent polypectomy were excluded. Please elaborate on this. Are we referring to hot snare polypectomy or polyps of a particular size? and please explain the reason to exclude such patients.

Response: We apologize for this error. The description "patients who underwent polypectomy" was inadvertently incorrect. We modified the sentence form:

Patients who underwent polypectomy and those with inflammatory bowel disease were excluded.

To:

Patients with inflammatory bowel disease were excluded.

6) The authors define the size, morphology and location of the adenomas - were these consistent with and representative of the general population? If not, then these results cannot be generalized to the entire population. It is recommended to add the statistics of the polyp characteristics of japan in order to compare with your center.

Response: We thank the reviewer for this pertinent suggestion. In Japan, Kobayashi et al. previously studied 1402 polyps with a median size of 6 mm. Fifty-eight percent of the polyps were located in the proximal colon. Type II (flat) morphology accounted for 47% of the samples. All adenomas were tubular. The study included 14% of the serrated polyps [Kobayashi et al. *United European Gastroenterol J*, 2019]. Another Japanese study by Ito et al. also investigated 1958 polyps with an average size of 7.9–10.2 mm. The proximal colon accounted for 55.9%–57.8% of these polyps. Of the total, 35.5%–42.2% polyps accounted for type II shapes. Further, of the total, 76.1%–78.9%, 4.1%–6.2%, and 7.1%–13.0% polyps accounted for low-grade dysplasia, high-grade dysplasia, and serrated polyps [Ito et al. *Endosc Int Open*, 2021]. However, the colorectal adenomas that we investigated were as small as 4.2 mm, and most of them were morphologically flat (86.9%) and located in the proximal colon (78.7%), compared with the adenomas in these previous studies. Our previous study showed that an expert endoscopist with a high adenoma detection rate frequently detected diminutive and flat adenomas in the proximal colon [Toyoshima et al. *Endosc Int Open* 2020). In the present study, one expert endoscopist conducted all colonoscopies; hence, the adenomas investigated cannot be generalized. In the future, studies with a larger number of cases evaluated by non-expert endoscopists are warranted.

We inserted the above contents to the limitations of the Discussion.

7) What is aspirational endoscopist in the introduction section?

Response: In a Canadian study, Hilsden et al. defined three benchmarks for assessment (i.e., minimally acceptable, standard of care, and aspirational) based on the average adenoma detection rate of performance groups defined by baseline year adenoma detection rate quartiles [Hilsden et al. *Am J Gastroenterol*. 2019]. The calculated benchmarks were as follows: minimally acceptable 25%, standard of care 30%, and aspirational 39%. We cited the concept of an aspirational endoscopist, which was the benchmark for their study. We would like to describe here that adenomas are common findings currently. This is because endoscopists with a high adenoma detection rate, referred to as aspirational endoscopists, detect adenomas in more than 40% of endoscopies. We agree that our expression was insufficient and confusing; thus, we have modified the manuscript as follows:

Currently, adenomas are a common finding. Previous studies have mentioned endoscopists with high adenoma detection rates, especially aspirational endoscopists who detected adenomas in more than 40% of patients [3, 4].

To:

Hilsden et al. reported the following benchmarks of adenoma detection rates: minimally acceptable, 25%; standard of care, 30%; and aspirational, 39%. It is recommended that the endoscopists overcome the "minimally acceptable" threshold [3, 4].

8) What is the retinex theory? please define this in layman's term for the intended audience of the paper

Response: Retinex is a theory of human color vision proposed by Land and McCann to account for color sensations in real scenes. Retinex is a coined word that combines the retina and cortex (cerebral cortex). Retinex is based on the theory of "color constancy" and "brightness constancy," according to which the human eye can perceive color and brightness regardless of the illumination light. The Retinex theory has been applied to technologies, such as for improving image quality.

We inserted the contents to the manuscript in the Introduction.

9) "A8 was used for WLI for enhanced structure level" - please elaborate further on what "A8" is, and what is being conveyed here to the non-technical audience of the journal

Response: Structural enhancement increases the sharpness of endoscopic images using processing algorithms for noise reduction. It highlights subtle tissue textures and slight color variations in the mucosa. Two modes are provided: Type A and Type B. Endoscopists can choose a level from one to eight. Type A is ideal for the observation of larger mucosal tissues with high contrast, while Type B is suitable for observation of vascular tissues.

As suggested, we inserted the following sentences in the Endoscopy section of the Methods section:

The type A mode is ideal for observation of larger mucosal tissues with high contrast, whereas the type B mode is suitable for observation of vascular tissues. There are eight levels among the type A mode, of which A8 is the most emphasized, and A1 is the least emphasized mode.

10) Add Olympus, JNET and NBI to key words I am unable to see the reference list in this manuscript.

Response: We thank the reviewer for their valuable comments. As per the reviewer's suggestion, we added Olympus, JNET, and NBI to the keywords and deleted texture and color enhancement imaging, LCI, and linked color imaging.