## Reviewer 1.

ESD has a bilateral character, including a minimally invasive therapy to maintain ga stric function and a maximally accurate approach for investigating T-1 stage. Therefore, ESD is carried out unless there is a contraindication of massive in vasion: rupturing of the SM layer.

However, EUS scanning of the stomach layer invasion is very difficult even for the expert because of the bursiform stomach shape, tumor location, infiltrative growth, air bubble interference, and muscle shrinking effect. This paper's result is only by trainee hands. So, the author should disclose the result of the <u>interobserver agreement</u> (trainee vs. supervisor) with kappa coefficient.

With your data, the diagnostic yields of EUS-SSI for SM invasion (T1b) are as follows: **Sn=60%**, Sp=92.3%, PPV=85.7%, NPV=75%, and AC=78.2%. **I never perform this EUS-SSI with this low sensitivity.** I definitely chose ESD unless contraindication under endoscopic findings.

Major comments: #1 Please state the aim and outcome of this study in the method section with a heading.

- -> We do not think it is appropriate to include the aim and outcome of this study in a method session. The aim of the study was revealed in the introduction session and the outcome was shown in the results session.
- > OK. Please refer to the author's guidelines.

Major comments: #2 About the following sentence, "Subsequently, they underwent endoscopic or surgical resection within 7 days". Why did you carry out EUS just before ESD? Is there a risk of submucosal fibrosis caused by submucosal saline injection?

It seems like this study is in a retrospective fashion (recruitment in 2019, approval number SGPAIK"2021"-10-019). The results of EUS-SSI did not influence on treatment (Case 6, 7, 23, 24). Should be clarified. Also, treatment flow and decision making flow for your institute should be shown.

-> Our hospital conducts EUS before deciding how to treat stomach cancer. EUS was performed during the diagnosis process, and surgery or ESD is usually performed within one week of diagnosis.

Submucosal fibrosis due to submucosal saline injection was not identified as the final pathological finding in all patients.

> OK. I understand it.

In this study, the results of EUS-SSI were not directly applied in the treatment method decision. It was just a study to compare diagnostic accuracy of EUS and EUS-SSI. I think that more research is needed to apply the results of EUS-SSI to clinical practice.

- > Did the 24 patients be recruited consecutively?
- -> Yes. We enrolled patients diagnosed with early gastric cancer during the study period in the order of diagnosis. However, the order of participation in the study and the order of receiving treatment do not necessarily match.
- > The aim of this paper is to investigate the effectiveness of EUS-SSI. Why didn't the author disclose accuracy, sensitivity, specificity, NPV, and PPV? With your data (table 1,2), the diagnostic yields of EUS-SSI for SM invasion (T1b) are as follows: Sn=60%(6/10), Sp=92.3%(12/13), PPV=85.7%(6/7), NPV=75%(12/16), and AC=78.3%(18/23). Those of EUS-only are follows: Sn=30%(3/7), Sp=46.2%(6/13), PPV=30.0%(3/10), NPV=46.2%(6/13), and AC=39.1%(9/23). I never perform this EUS-SSI because the sensitivity is 60%.

By the way, why are there only 22 cases in "EUS only" group in Table 2.?\_

-> We do not believe that the results of this study can be directly applied to clinical practice. It would not be possible to make important treatment decisions based on the results of only 24 patients. Larger clinical studies will have to prove this result.

In "EUS-only" group, one patient diagnosed with T2 in the preoperative exam was excluded, and one patient diagnosed with T2 at the postoperative patholo gic stage was excluded.

- > As the author described in the introduction, **assessing SM1 or SM2 is critical for d ecision-**
- making: ESD or surgery. The cutoff point of T1a/T1b is not so crucial for decision-making. Although this study aim was to "confirm whether SSI could be a method to improve the accuracy of EUS in distinguishing T1a and T1b lesions", it should be r efocused on distinguishing T1b1 (SM1) and T1b2 (SM2).
- -> I agree with you. In a better designed study, this should be studied.
- > In addition, the number of T1b (EUS only Dx)-T1b (pathological Dx) **should be 4**, **not 3. Please confirm the data analysis with your supervisor.**
- -> According to Table 3, three are correct
- > What is the <u>terminology of accuracy</u>? For example, in table 2, the accuracy of EUS-SSI for SM invasion is calculated as follows: (12+6)/23\*100=78.3%.
- -> Accuracy refers to the concordance between T stage in preoperative EUS and T stage in postoperative patologic finding.
- > Treatment / decision making flow for your institute should be shown.
- -> Our hospital determines the treatment policy in accordance with the Korean Practice Guideline for Gastric Cancer 2018 for the absolute and expanded indications

for ESD in EGC. However, in actual clinical practice, it is not possible to treat all patients according to the guidelines because the patient's age, underlying disease, and socioeconomic factors are considered a lot.

Major comments: #3 About the following sentence, "All recruited patients agreed to be enrolled in this clinical trial patients and provided informed consent." Please revise this manuscript under a native speaker of English.

Also, should be thoroughly checked again for abbreviations including table and figure legends.

- -> We re-examined these parts and made appropriate corrections. Modified parts are marked in bold.
- > OK. I understand it.

Major comments: #4 About the following sentence, "...by one endoscopist with only 6 months' experience with EUS." Was this study conducted by only a 'trainee'? Please disclose those data under an 'expert'. In addition, please show the concordance rate between both endoscopists.

- -> This study was conducted only by beginners who had been in EUS for 6 months.
- > EUS scanning of the stomach layer invasion is very difficult even for the expert because of the bursiform stomach shape, tumor location, infiltrative growth, air bubble interference, and muscle shrinking effect. This paper's result is only by trainee hands. So, the author should disclose the result of the <u>interobserver agreement</u> (trainee vs. supervisor) with kappa coefficient.
- -> When designing this study, we did not take this aspect into consideration as we did not intend to see the agreement or difference in the results between the researchers.

Major comments: #5 About the following sentence, "The puncture points were located 0.5 cm beyond the edge of the lesion, and saline injection was stopped once the gastric mucosa had been elevated by approximately 1 cm." With this injection around the lesion, is it impossible to inject the submucosal saline under the SM invasion at the central site appropriately, especially for a widely spread or fibrotic lesion? How did you measure this 1 cm mucosal elevation?

-> We did not inject the needle directly at the center site of the the lesion because we were concerned about tumor spreading by the needle.

We injected saline so that it swells by about 1 cm compared to the surrounding mucosa visually, and this was confirmed through EUS.

> It is impossible to lift the central lesion enough when in a widely spread lesion. The author should discuss this point as limitation.

-> In the case of a widely spread lesion, it may be difficult to lift the central lesion, but there was no lesion in which cental lifting was impossible in our observed lesion. In the case of patient 7, the gross endoscopy revealed that the lesion was huge, 65 mm in size, but the size of the lesion observed in EUS was as small as 20 mm, and was confirmed to be 18 x 15 mm in postoperative pathologic finding.

Major comments: #6 In the result, the author should exclude the patient with T2 cancer before analysis. Please describe the inclusion/exclusion criteria in the method session. "endoscopically diagnosed EGC lesions" is unclear. Does this mean EGC diagnosed by white light or combined with NBI (and magnifying)? Were there any cases of endoscopically diagnosed T2 or more lesions turned out to be T1 by surgical exploration? Please draw the flow chart of the included patients.

- -> The patients enroled in this study were "EGC diagnosed by endoscopic gross findings". EUS findings are not included in the criteria for selecting or excluding patients. The macroscopic findings of the endoscopy were judged in combination with the NBI image. Patients diagnosed with gastric cancer with T2 or higher endoscopically were not included in this study.
- > Treatment / decision making flow for your institute should be shown.
- -> We mentioned this part before.
- > If "EGC diagnosed by endoscopic gross findings" were enrolled, Case 18 (T2 case9 should be enrolled in calculating and else, nevertheless it may lower each variable.
- -> In this study, the results were analyzed only with EUS findings.

Major comments: #7 In the third paragraph in the result session. The EUS feature with and without SM invasion should be defined in the methods session.

- -> We added this to the method session.
- >Well-described.

Major comments: #8 All EUS figures are poor. What do those markers indicate? Please explain them in the figure legends. Please magnify them and indicate the first, second, third, fourth, and injected saline layers with arrowheads for readers. Figures should be composed of endoscopic, EUS, and pathological images.

-> As pointed out, markers are indicated by arrows in the figure. We thought that the pathologic findings were in agreement with the EUS findings, so it was not meaningful to include a pathological images.

- > I can not find the revised figure because the revised figure is not attached.
- -> We attach figures 1-3 again here.

## Figure 1.

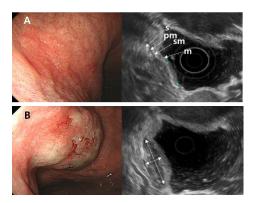


Figure 2.

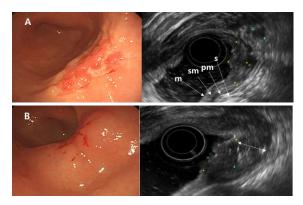
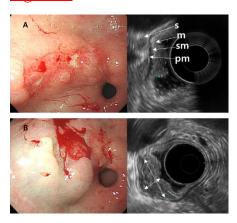


Figure 3.



- > Comparison of EUS vs. pathology is critical. The author should show the represent ative pairs.
- -> The pathology results were not controversial and there was no bias according to the gross findings of the lesion.

Major comments: #9 To my knowledge, maximum Hz available for UE-260 is 12MHz. Is 20MHz correct? Also, I do not know any injection needle applicable for UE-260

(with instrumental channel 2.2mm). What did the authors use? Or did they used other scopes prior to EUS for injection?

-> You are right. We fixed it to 12 MHz. Saline injection was performed through a gastroscope (Olympus GIF-HQ290 Endoscopic System, Olympus Co. Tokyo. Japan).

>Well-responded.

Major comments: #10 Usually, the problem with EUS for diagnosing tumor depth is underdiagnosing due to the difficulty of visualizing the pin-pointed (may be larger in cases) SM invasion (T1b) of tumor. Why are there so many cases of overdiagnosis (33.3%). Should be discussed or noted in limitation.

-> This study was conducted by a endoscopist with only 6 months experience with EUS. Therefore, it is considered that there is a difference between the results of the examination by an experienced inspector.

This study is not to investigate the accuracy of EUS EGC diagnosis, but to compare the diagnostic accuracy of EUS and EUS-SSI for EGC.

- > The author should disclose the result of the <u>interobserver agreement (trainee vs.</u> <u>supervisor) with kappa coefficient</u>.
- -> This part has been mentioned previously.
- > What in the world do you think is the clinical impact of a EUS study performed by only trainee? None. At least the result of expert (in your institute) is necessary.
- -> The purpose of our study is not to apply the EUS results performed by trainees to clinical practice. The purpose of this study is to find a way to further improve the accuracy of diagnosis for lesions where it is difficult for beginners to learn EUS to judge the outcome.

Minor comments: #1 About the disclosure of the equipment. Please add the city and country.

- -> Yes, we added this.
- >Well-responded.

Minor comments: #2 Introduction "with metastasis" not necessary in the 1st sentence.

- -> We deleted this.
- >Well-responded.

Minor comments: #3 SM1 refers to submucosal invasion to  $<500 \mu m$ .

- -> We corrected this part as pointed out.
- >Well-responded.

Minor comments: #4 SM3 should be defined.

-> It seems unnatural to mention the definition of SM3 in terms of the flow of content. SM3 was defined as an invasion depth of  $\geq 1,000~\mu m$ .

SI lowered the rate of overstaging.

>Well-responded.