

Dr. Fang-Fang Ji
Science Editor
World Journal of Gastrointestinal Oncology

September 5, 2018

Dear Dr. Ji,

We would like to thank the reviewers for their useful comments. We describe our opinion on the review as bellow.

Reviewer 1 (Code: 03018297)

- Comments; 1

1. The manuscript is about " Raman spectroscopy for the diagnosis of unlabeled and unstained histopathological tissue specimens". The experiment results suggest the feasibility of the spectroscopic method as a diagnostic tool for gastric cancer using unstained pathological specimens. How about the disadvantages for this spectroscopic method compared with the stained pathological method?

- We appreciate the reviewer who questioned the fundamental and important thing. We believe that the most important factor in histopathological diagnosis is to observe cell morphology in detail. Raman spectroscopy is capable of imaging pathological specimens and can show cell and tissue morphology. However, at present, general stained pathological method can show more detailed forms than images by Raman spectroscopy. Therefore, we currently think that Raman spectroscopy is an auxiliary technique that can add qualitative information to histopathological diagnosis by stained pathological method. We added the sentence "Currently, Raman spectroscopy is an ancillary technique for adding qualitative information to histopathological morphological diagnosis" on page 13, lines 14–15 (marked with yellow line).

Reviewer 2 (Code: 03478911)

- Comments; 1

1. A new methodology that suggested by the authors is considered to provide crucial information that can improve compliance of the patients through noninvasive methods. This reviewer has no specific concerns to raise. Although there are some limitations to the analysis due to unexpected conditions, such as thickness of specimens, the limitations of the new methodology will be overcome through further research.

- We appreciate the reviewer who gave a positive and constructive evaluation. We currently evaluate that Raman spectroscopy is an auxiliary technique to add qualitative information to pathological tissue diagnosis. However, we are eager to raise the accuracy of estimation by Raman spectroscopy and to complete it as a technology that can obtain both high-precision morphological information and qualitative information.

Other revision

1. We added "ORCID number" on page 2, lines 5–10 (marked with yellow line).

2. We modified authors abbreviation names on page 2, lines 12–17 (marked with yellow line).
3. We added “Institutional review board statement” on page 2, lines 20–21 (marked with yellow line).
4. We moved “Clinical trial registration statement” to page 2, lines 23–24 (marked with yellow line).
5. We added “Informed consent statement” on page 2, lines 26–27 (marked with yellow line).
6. We added “Biostatistics statement” on page 2, line 29– page 3, line 6 (marked with yellow line).
7. We moved “Conflict-of-interest statement” to page 3, lines 8– 9 (marked with yellow line).
8. We added “Data sharing statement” on page 3, line 11 (marked with yellow line).
9. We added “CONSORT 2010 statement” on page 3, lines 13–14 (marked with yellow line).
10. We modified “Abstract” section on page 4, lines 1– 21 (marked with yellow line) along the guideline.
11. We added all authors abbreviation names and manuscript title after “Core tip” section on page 5, lines 8– 10 (marked with yellow line).
12. We modified the letters of “INTRODUCTION” to bold and capital on page 6, line 1 (marked with yellow line).
13. We modified the letters of “MATERIALS AND METHODS” to bold and capital on page 7, line 6 (marked with yellow line).
14. We moved the words of “of the mid-stomach” to page 7, lines 13–14 (marked with yellow line).
15. We modified the letters of “RESULTS” to bold and capital on page 10, line 6 (marked with yellow line).
16. We modified the letters of “DISCUSSION” to bold and capital on page 11, line 5 (marked with yellow line).
17. We made “Limitation” independent as a paragraph on page 12, line 19– page 13, line 8 (marked with yellow line).
18. We added “ARTICLE HIGHLIGHTS” section on page 13, line 30– page 17, line 9 (marked with yellow line).

19. We modified the letters of “ACKNOWLEDGEMENTS” to bold and capital on page 17, lines 11 (marked with yellow line).

20. We modified the p values symbol as ^aP < 0.05, ^bP < 0.01 on page 25, line 2 (marked with yellow line) and Figure 3.

21. We modified the p values symbol as ^cP < 0.05, ^dP < 0.01 on page 27, line 2 (marked with yellow line) and Figure 5.

We believe that our prospective translational research will be of great interest to oncologists, pathologists, molecular biologists and gastroenterologists. As a journal covering international issues relevant to gastroenterological and oncological specialists, and one of the leading journals worldwide for original research with a focus on gastrointestinal oncology, *World Journal of Gastrointestinal Oncology* represents the perfect platform for us to share these results with the international research community.

We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the manuscript and agree with submission to *World Journal of Gastrointestinal Oncology*. The authors have no conflicts of interest to declare.

Please address all correspondence to:

Hiroaki Ito, MD
Department of Surgery,
Digestive Disease Center,
Showa University Koto Toyosu Hospital,
5-1-38 Toyosu
Koto-ku
Tokyo 135-8577, Japan
Tel: +81- 3-6204-6000; Fax: +81- 3-6204-6396; E-mail: h.ito@med.showa-u.ac.jp

We look forward to hearing from you at your earliest convenience.

Yours sincerely,

Hiroaki Ito, MD