

## **ESPS PEER-REVIEW REPORT & Authors Response**

**Name of journal:** World Journal of Gastrointestinal Endoscopy

**ESPS manuscript NO:** 32309

**Title:** Terahertz Endoscopic Imaging for Colorectal Cancer Detection: Current Status

**Reviewer's code:** 00031150

### **COMMENTS TO AUTHORS**

This is a comprehensive review of the THZ technology. However in clinical medicine there exist some caveats before publishing:

**Author's Response:** We thank the reviewer for the positive review. We really appreciate their valuable time. We are delighted to hear that our work is very good and qualifies for priority publishing. We address his/her comments below.

1) P5, L10: "time consuming and painful process" This is not true in the age of moderate sedation with propofol, well accepted by the patients.

**Response:** We thank the reviewer for thorough review of our manuscript. As per your suggestion, we retracted the words 'time consuming and painful process' from the manuscript and please see the revised manuscript.

2) P8, table 1 : DBCE can be omitted from the table as it is not more used in screening for CRC.

**Response:** We completely agree with the reviewer about the use of double contrast barium enema method. We deleted the entire row that corresponds to DCBE from the table. Please see the revised manuscript.

3) P11, line 14 "... typically fiberoptic" Those tools are not anymore used in clinical medicine. The entire manuscript is wrote for the difference between normal tissue and cancer. This is not affordable for clinical medicine. Here we wait for methods to discover hyperplastic from adenomatous polyps. A CRC can also be detected by a beginner of colonoscopy.

**Response:** We once again thank the reviewer for stating the potential need remove the information related to the past technology and include the missing details related to the early stage abnormality detection. Terahertz frequency has the potential to differentiate normal, dysplastic, from cancerous colon and can detect abnormalities in the early stage.

We certainly agree with the reviewer and revised our manuscript accordingly. Please refer to the highlighted (in blue) Section 2B of the manuscript. 1) We added a figure showing the data from dysplastic colonic tissues collected from 30 patients. 2) We also added the text 'Reid et. al. have

imaged excised cancerous, dysplastic and healthy colonic tissues obtained from 30 patients in reflection modality[38]. They used a stand-alone portable terahertz imaging system TIP imaga1000. The frequency of the imaging system was 0.03 - 1 THz. An image is shown in figure 5, from which it can be seen that the cancerous and dysplastic tissue regions show contrast relative to the normal tissue, indicating differences in the reflected waveforms. Figure 5a shows an example THz image of tissue containing healthy regions, dysplasia and cancerous tissue, and 5b depicts the histology results (drawn onto a photographic image of the tissue samples) and in 5c the histology results are overlaid on the THz image. Impulse functions for the respective tissue types are extracted. In this example, regions a and b are normal tissue, c is dysplastic tissue and d is cancerous tissue[38]. (Printed with permission)'.

In addition, we are currently in the process of testing the current technology identify the stages of colon cancer and other abnormalities. Therefore, we added the text to the summary highlighted in blue font as, 'A lot of the technological barriers have been overcome and the next step for the field is the development and testing of an in vivo terahertz endoscopy system capable of providing sensitivity and specificity numbers for the technique in identifying multiple stages of colon cancer.'

**Reviewer's code:** 03036231

## COMMENTS TO AUTHORS

In this review, authors summarized the steps required for clinical application of terahertz imaging of CRC and provided an update on the current status of terahertz imaging. The imaging system represents a significant step towards clinical endoscopic application for in-vivo colon cancer screening. This paper was written clearly, however I want to know some points of this imaging system as follows as a clinical colorectal cancer surgeon. In the clinical field, early stage cancer (ex, cancer in adenoma, LST) is difficult to diagnose by endoscopy. Figures of this paper looked like advanced cancers, so can the system identify early stage cancers?

**Author's Response:** We really thank the reviewer for the thorough and positive review. We really appreciate your time. We are delighted to hear that our work is very interesting, written clearly, and has useful applications in clinical perspective. We address your comments below. Thank you for stating the potential need to include the missing details related to the early stage colon abnormality detection. Terahertz frequency has the potential to differentiate normal, dysplastic, from cancerous colon and can detect abnormalities in the early stage.

We certainly agree with the reviewer and revised our manuscript accordingly. Please refer to the highlighted (in blue) Section 2B of the manuscript. 1) We added a figure showing the data from dysplastic colonic tissues collected from 30 patients. 2) We also added the text 'Reid et. al. have imaged excised cancerous, dysplastic and healthy colonic tissues obtained from 30 patients in reflection modality[38]. They used a stand-alone portable terahertz imaging system TIP imaga1000. The frequency of the imaging system was 0.03 - 1 THz. An image is shown in figure 5, from which it can be seen that the cancerous and dysplastic tissue regions show contrast relative to the normal tissue, indicating differences in the reflected waveforms. Figure 5a shows an example THz image of tissue containing healthy regions, dysplasia and cancerous tissue, and 5b depicts the histology results (drawn onto a photographic image of the tissue samples) and in 5c the histology results are overlaid on the THz image. Impulse functions for the respective tissue types are extracted. In this example, regions a and b are normal tissue, c is dysplastic tissue and d is cancerous tissue[38]. (Printed with permission)'.

This manuscript presents the current state-of-art terahertz technology and the potential applications. We are currently in the process of testing the prototype endoscope in identifying different stages of colon cancer and other abnormalities. Therefore, we added the text to the summary highlighted in blue font as, 'A lot of the technological barriers have been overcome and the next step for the field is the development and testing of an in vivo terahertz endoscopy system capable of providing sensitivity and specificity numbers for the technique in identifying multiple stages of colon cancer.'