RESPONSE TO REVIEWERS

OCTOBER 11, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5010-REVISED.doc).

Title: Does Training and Experience influence the Accuracy of CT Colonography Interpretation?

Author: Greg Rosenfeld, Yi Tzu Nancy Fu, Brendan Quiney, Hong Qian, Darin Krygier, Jacquie Brown, Patrick Vos, Pari Tiwari, Jennifer Telford, Brian Bressler and Robert Enns

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5010

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
Please see individual responses in the reviewers comments document
3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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Jin-Lei Wang, Director, Editorial Office

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Dear Dr. Wang,

Thank you for considering our manuscript for publication in your journal. We thank the reviewers for their comments which we believe have improved the manuscript. I have summarized the Reviewers comments in this document and attached notes to identify the changes that were made in order to incorporate the reviewers suggestions.

I am sorry for the delay in responding to your revision request. I have completed the necessary documents that you have requested except for the copyright document which requires a few more signatures. In the interest of returning the revisions as soon as possible, I have returned the revised document without the copyright transfer form.

Thank you for taking the time to review these changes and please do not hesitate to contact me if there are further questions or concerns.

Sincerely,

Greg Rosenfeld

Reviewer #1 (4187)

The manuscript is interesting - Change the conclusions. Short phrases. Do not speculate. Points minor - What is NPO?Changed accordingly - What was the time of withdrawal of colonoscopies? The withdrawal time was not recorded for this study. The reason for this is that it was not felt to be relevant given the technique of segmental unblinding. The withdrawal times were all substantially longer than the recommended 6 mins. In many cases, times were over 30 mins. This is because each segment was examined in a standard fashion and then re-exmined after the results of the CTC were made known - What was the level of cleanliness for colonoscopies? In the interest of brevity, this was omitted. Scopes were cleaned as per the usual hospital protocol.
- The definition of "polyps present" remove from data analysis Done- How do you explain the presence of extra-luminal air Following the CTC?Information added to the manuscript - Results (False positives) How many patients had no polyps? 70 patients or 60 patients (30 had polyps)Manuscript revised for clarity - How much time it took to perform a CTC? We did not record the time for completion of CTC only the reading times for the individual readers. We did not feel that this added very much to the manuscript and therefore, we have not added this.
Discuss whether there are papers that use sedation for CTC - Add the % of extracolonic findings. What explains the great variability of extracolonic findings? Extra colonic findings were recorded out of interest sake and because it is part of the standard of care when performing a CTC in our institution. The "novice readers were not trained and therefore could not be expected to adequately interpret extra colonic findings. The main issue here is that colonoscopy is UNABLE to detect them, where most radiologists would be able to detect them. Therefore this is one potential benefit of CTC in the Screening situation.
Are these findings important or unimportant?Manuscript revised accordingly Description - Flat polyps had as ranked Paris type 0-II? Does CTC saw We did not do any subset analysis of flat versus polypoid lesions and did not record the Paris classification. Therefore, we are unable to do it post hoc and the small sample size would make any analysis dubious? - Check the references, eg 21.Corrections made.

Reviewer #2

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These are comments to the editor:

The authors performed a prospective study to assess the effect of experience on the accuracy of CTC and the preference of patients comparing CTC and colonoscopy. Overall, the study was well designed and variables were well controlled (the colonoscopy was carried on the same day of CTC, four readers were representative, and interpretation was blinded). However, it added relatively limited information to current literature body. Lacking of learning curve of CTC was meaningful, but not directly linked to training requirements, and preference of colonoscopy over CTC was concluded from a relatively small group of patients (n=20).

Here listed some unclarities:

1. The authors seemed to have used only polyp as the end point, while both CTC and colonoscopy can offer clinicians far more information, some of which can be assessed in both exams and potentially comparable. As per the original landmark trial by Pickhardt, et al., we chose to evaluate CTC as a screening test for diagnosing adenomatous polyps and colon cancer in average risk. As we were interesting in evaluating a learning curve in CTC interpretation, we did not look at other endpoints.

2. Some questions about the methods:
The patient selection process could be listed, like how many patients, if any, were initially enrolled but excluded according to the criteria. Manuscript Changed. There were no patients who were enrolled but subsequently excluded. However, as mentioned in the manuscript for one patient the protocol had to be modified and the colonscopy delayed because of the presence of extra luminal air. We did not keep track of those who were approached but decided not to participate.
One patient with extra luminal air was reported. It could be summarized how many patients overally reported kinds of complications. Changed
Only 20 patients out of the 90 participated in the prefenrence questionnaires, therefore the results could be easily influenced by kinds of bias. The manuscript was changed to more clearly show that ALL of the patients completed the survey. Only 20 patients received the mail out survey which was only to demonstrate sufficient test/retest reliability of the survey.

Overall, this is an useful paper. Organizing such study was not easy in clinics. The authors could have more discussion from their results to the general training requirments of clinical procedures as CTC.

Reviewer #3:

Results and Discussion: -The author showed the result of false negative and false positive. However, what cause false negative and false positive of CTC should be shown in detail and discussed. Do they differ among 4 observers? For example, why did GI Fellow #1 detected more polyps than the radiologist and the Radiology resident? This should be discussed. -Not so sure that 90 cases are enough to demonstrate the learning curve. -Discussion section is too short. Many aspects are not discussed in details such as false negative and false positive cases, interpretation time, extracolonic findings. -The author should discuss more on the accuracy among 4 observers, particular why the experience GI Radiologist had the lower accuracy rate than Radiology resident. -The high accuracy rate of polyp detection can be achieved by 30-cases training set. However, the accuracy rates decreased over period of time in 3 observers. This point should be discussed why the accuracy decreased. -Even though, the author stated that the extracolonic finding is not the end point of this study, but the author presented the result on the extracolonic finding, which differed among observers. This issue might affect on CTC interpretation. Need discussion. Conclusion: -A bit long As per the Reviewer's suggestion, the discussion has been expanded to include these suggestions and the conclusion shortened

Reviewer #4:

Design "…but were maintained NPO thereafter until completion of both procedures"Changes Made: this sentence needs clarification. Results "the false positive rates were 3.8% for the Radiologist, 0% for the Radiology resident' This seems somehow difficult to explain. The authors should discuss on it. "the readers overall accuracy rates stayed stable throughout the study period". It is not clear enough how long the study period was. In fact learning curves usually are estimated in long time periods. It is not clear why the extracolonic findings were recorded, while there were not

analyzed. Discussion' "the accuracy rates for three of the readers declined slightly with increasing experience…" This seems rather paradoxical and the authors need to discuss more on it. "The sensitivity rates ranging from 54% to 84% for the detection of polyps > 6mm were lower in our study than seen previously in some studies". It would be beneficial to explain this fact, if the authors could also refer to the quality of CTC examinations using a scale. Manuscript has been changed to reflect these suggestions. Unfortunately, We have not rated the quality of CTscans and are unable to do so retrospectively