

Format for ANSWERING REVIEWERS

January 11th, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS 13846-review.doc).

Title: Feasibility and safety of endoscopic cryoablation at the duodenal papilla: porcine model

Authors: Dennis Yang, Mary K. Reinhard, Mihir S. Wagh

Name of Journal: World Journal of Gastrointestinal Endoscopy

ESPS Manuscript NO: 13846

- The manuscript has been improved according to the suggestions of the editor and reviewers. We appreciate their comments and have included the appropriate changes in our revised manuscript and response as detailed below.

Editor:

- 1) **COMMENT#1:** "IRB statement. Sample wording: The study was reviewed and approved by the Institutional Review Board".

RESPONSE: As outlined in my email to Mr. Yue-Li Tian, animal studies in our institution are approved by IACUC. The IRB committee does not oversee or is involved in any animal studies. We have provided the IACUC statement in this submission.

- 2) **COMMENT#2** "Please add your cited references to 36".

RESPONSE: This is a very subspecialized topic. There are only a few studies that have looked at cryotherapy in the GI tract. Most studies have focused specifically in the esophagus. This is the first study evaluating cryotherapy at the duodenal papilla. We have referenced (21 citations) all pertinent studies related to this manuscript.

Reviewer 00073423

- 1) COMMENT #1: "Well designed, elegant animal study. The primary aim of the study was to assess the safety of a new therapeutic modality. The first acquired data proved the feasibility and safety during the short term follow-up period. The data are important and could be used in human studies. I just have some items to be discussed. There were 4 survival animals. Why other 2 pigs did not survive?"

RESPONSE: We appreciate the reviewer's comment. This was designed as a pilot study with the primary aim of assessing the feasibility and safety of liquid nitrogen spray cryoablation at the duodenal papilla in a porcine model. The first two animals in this study were used exclusively to evaluate the feasibility (i.e. technical success) of cryoablation at the duodenal papilla and thus; they were not survived. We survived the next 4 experiments in order to assess both endoscopic and histologic changes following cryotherapy, in addition to the feasibility and safety of the technique. We have made the appropriate change in the manuscript (page 9) to clarify why the first two animals were not survived.

- 2) COMMENT #2: "I could suggest if it could be worth to follow-up the animals for the longer period 4-12 weeks? Or until the lesions heal. The occurrence of distal biliary duct structuring could be evaluated?"

RESPONSE: As a pilot study, the aim of this study was primarily to assess the feasibility and safety of this novel technique. The survival animals were followed for 7 days (similar follow up period to prior animal studies on cryotherapy – Johnston et al 1999) to evaluate the immediate gross and histologic effects of cryoablation at the duodenal papilla. We agree with the reviewer that future studies with lengthier follow-up can determine the potential long-term effects of this modality on the papilla and biliary system. We have stated in the discussion section (page 15) of the manuscript that short-term follow up is a potential limitation of a pilot study of this nature.

Reviewer 00034616 recommended the manuscript to be accepted for publication without additional comments to the authors.

- Typesetting was corrected
- Format has been updated

- Supporting documents have been included with the manuscript.

Thank you again for considering our manuscript for publication in the *World Journal of Gastrointestinal Endoscopy*.

Sincerely yours,

Dennis Yang, MD

Mihir S. Wagh, MD

Divisions of Gastroenterology, University of Florida, Gainesville, FL, USA

Telephone: 1-352-27309474 Fax: 1-352-6279002.