

December 8, 2014

Dear Editor,



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

Title: Radiofrequency ablation of pancreatic ductal adenocarcinoma - the past, the present and the future

Author: Pandya Garvi J, Shelat Vishal G

Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS Manuscript NO: 14447

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

- (1) Reviewer 02445558 - I have removed the final paragraph and the relevant reference regarding pancreatic neuroendocrine tumours as suggested. I have added and quoted Keane et al (WJG 2014) as it is more relevant to our paper. Median survival is added in the table as suggested.

This is reflected by addition of -

'Table 1 provides details of thermokinetic principles applied by various authors and Table 2 summarizes outcomes with reference to survival and morbidity/mortality.'

'Table being split into two separate tables'

'Keane M G et al conducted a systematic review on novel ablative methods in locally advanced pancreatic cancer and concluded that despite proven safety, feasibility and reproducibility; the benefit of ablative techniques on long term survival remains to be confirmed in large prospective randomized studies.³⁵

Also deleted is Ref 34 and its supporting statement from text.

- (2) Reviewer 0009064 - Many thanks for appreciating our work. On behalf of co-authors, please accept our regards.
- (3) Reviewer 02731744 - It is commented that 'rates of adverse events are not sufficiently mentioned and table is very busy' - Many thanks for this apt criticism. We have separated the data into two different tables and Table 2 does include complications of RFA encountered by various authors. Also Figure 1 does include correlation of various thermokinetic principles to complications and strategies to prevent them.

It is also commented that 'EUS guided cryoablation is reported and this method should be described'. I have added this paper as below -

"In the first in vivo study involving 22 patients with locally advanced pancreatic cancer, Arcidiacono PG et al demonstrated feasibility and safety of endoscopic ultrasound guided cryothermal ablation with technical success in 16 patients

(72.8%) and median post-ablation survival of 6 months. They described late complications of jaundice, duodenal stricture and cystic fluid collection in four patients.³⁴ Please note that due to difference in thermokinetic principles and mode of delivery, I have elected not to add this study to the existing Tables. However, I am open minded to do so if the Reviewer or Editor wishes to do so.

- (4) Reviewer 0039529 – We do agree with Dr Bradley III's comments that without a control group and quantitative compilation of complications of RFA, the current evidence remains weak. However, please note that this is a 'mini-review' of current evidence and not a meta-analysis (quantitative) paper.

3 References and typesetting were corrected

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

Sincerely yours,

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