



August 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12122-edited.docx)

Title: Role of preoperative Endoscopic ultrasound-guided fine-needle tattooing of a pancreatic head insulinoma

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Name of Journal: *World Journal of Gastrointestinal Endoscopy*

ESPS Manuscript NO: 12122

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) Spell out the title
- (2) Provide the short running title
- (3) Delete the reference in the abstract part
- (4) Add the comments part.

3 References and typesetting were corrected

4 Answering the reviewer comments

4.1 Reviewer #1(00057400)

Comments: Interesting case worthy of publication→accepted

4.2 Reviewer #2(00070143)

Comments: Dear Editor, In fact, tattoo is the known method for detecting the pancreatic lesions. However, insulinoma is rare and it is difficult to see during the operation. Even this is only one case it can be publish. → accepted

4.3 Reviewer #3(00730463)

Comments: no comments → accepted

4.4 Reviewer #4(00057400)

Comments and answers: → rejected

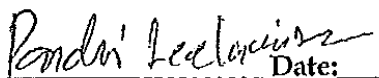
1. The tattooing of a pancreatic lesion has been previously employed for localizing pancreatic insulinomas well as other neuroendocrinetumors or benign or malignant pancreatic neoplasms with the aim of helping the surgeon during a laparoscopic approach to the pancreas. Endoscopic ultrasound-guided tattooing is safe and is associated with a decreased operative time for laparoscopic distal pancreatectomy compared with nontattooed patients. However, this method has not been employed for a laparoscopic or open enucleation of a neuroendocrine tumor. EUS and IOUS are the best methods for detecting the insulinomas with a sensitivity that approach the 100% in several surgical series. Why the tattoo of the lesion could increase the accuracy of these methods?
 - Difficulty of preoperative and intraoperative localization of the insulinoma are different. Most of the time there is no problem to detect or locate the insulinoma preoperatively, since CT, MRI and EUS, has a very high sensitivity 98-100% especially after the widespread use of EUS. However, intraoperative localization of the insulinoma in the pancreatic could become problematic even insulinoma that was detected clearly in the preoperative imaging. As mention in the manuscript, the rate of intraoperative detection, including intraoperative palpation and intraoperative ultrasound (IOUS) varies between studies, ranging from 83-98%.[3] According to previous case report and series also support that surgeons could be possibly unable to localize the insulinoma intraoperatively in the pancreas and patients required unnecessary or extended blind resections.[1-3] Tattooing will facilitate the surgeon to detect intraoperatively the nonpalpable insulinoma especially deep in parenchyma of pancreatic head area and avoid the risk of unnecessary surgery as a compliment to the IOUS.
2. How the tattooing of the lesion could mark with a greatest accuracy the margins of the insulinoma and guide the surgeon during the enucleation really avoiding the lesion of the surrounding pancreatic duct and vessels? It is not probable that the ink injected during the procedure spreads around the pancreatic parenchyma surrounding the insulinoma and masks its margins?
 - Tattooing is not to mark the margins but rather assist in identification of lesion is deep in parenchyma of pancreas. This will help surgeon to localize the non-palpable insulinoma and know exactly where the tumor is with trace color of the carbon particle especially if a lesion is deep in parenchyma. Surgeon can pay more attention and perform meticulous dissection to the area of insulinoma. Apparently, the sterile carbon particle does not obscure the tumor and cause difficulty dissecting insulinoma in our case scenario. But of course, it depends on expertise of endoscopist, the amount of carbon particle and accuracy of the injection. This method was also reported in a previous case report but use different dye which was methylene-blue to identified pancreatic body insulinoma after failure of first attempt resecting operation. [3]

References

- 1 Newman NA, Lennon AM, Edil BH, Gilson MM, Giday SA, Canto MI, Schulick RD, Makary MA. Preoperative endoscopic tattooing of pancreatic body and tail lesions decreases operative time for laparoscopic distal pancreatectomy. *Surgery* 2010; **148**(2): 371-377 [PMID: 20554299 DOI: 10.1016/j.surg.2010.04.008]
- 2 Nikfarjam M, Warshaw AL, Axelrod L, Deshpande V, Thayer SP, Ferrone CR, Fernández-del Castillo C. Improved contemporary surgical management of insulinomas: a 25-year experience at the Massachusetts General Hospital. *Annals of surgery* 2008; **247**(1): 165 [PMID: 18156937 DOI: 10.1097/SLA.0b013e31815792ed]
- 3 Zografos G. N, Stathopoulou A, Mitropapas G, Karoubalis J, Kontogeorgos G, Kaltsas G, ... & Papastratis G. I Preoperative imaging and localization of small sized insulinoma with EUS-guided fine needle tattooing: a case report. *Hormones (Athens)* 4, no. 2 (2005): 111-116. [PMID:16613814]

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

Sincerely yours,

 Date: 7/31/14

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