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TITLE:

Robotic Enucleation of an Insulinoma in the Pancreatic Head

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KEYWORDS:
Robotic surgery, robotic enucleation, pancreas, insulinoma, neuroendocrine tumor, enucleation

SUMMARY
Here, we present a robotic approach to enucleate an insulinoma in the pancreatic head.

ABSTRACT
Pancreatic parenchyma sparing surgery for insulinomas avoids the risk of endocrine and exocrine insufficiency, and potential high-risk anastomoses associated with pancreatic resection. Robotic surgery may be used as an alternative for open pancreatic enucleation without compromising dexterity and 3D-vision.

We present the case of a 42-year old woman who presented with sweating, tremor and episodes of hypoglycemia. A fasting test confirmed endogenic insulin overproduction. After inconclusive CT- and MRI imaging, endoscopic ultrasonography showed a hypoechoic lesion, which was fully within the pancreatic head. Although consent was obtained for pancreatoduodenectomy, robotic enucleation seemed feasible. After mobilization, intraoperative ultrasonography was used to identify the lesion and its relation with the pancreatic duct. Dissection was performed using a traction suture, hot shears and bipolar diathermia. A sealant patch was applied for hemostasis and a drain placed. The patient developed a grade B pancreatic fistula for which endoscopic sphincterotomy was performed; the surgical drain could be removed in the outpatient clinic after 20 days. Prospective studies are needed to confirm the short- and long-term benefits of robotic enucleation of insulinomas.

INTRODUCTION

Insulinoma is the most prevalent functioning pancreatic neuroendocrine tumor (F-PNET) with an annual incidence of 1-32/100,000 patients[1]. Pancreas-sparing surgery (i.e., enucleation) is mostly indicated for single lesions as pancreatic resections could be needed in multifocal or more extensive lesions[1]. General advantages of parenchymal-sparing enucleation over pancreatoduodenectomy or distal pancreatectomy include function preservation (both exocrine and endocrine), less blood loss, shorter operative time, and the absence of high risk anastomoses as required after pancreatoduodenectomy and central pancreatectomy.

A minimally invasive surgical approach aims to shorten the time to functional recovery with comparable oncologic outcomes[1,2]. Compared to open enucleation, robotic enucleation is associated with a shorter operative time and lower blood loss with a similar risk of postoperative pancreatic fistulas and major postoperative complications[3,4]. Compared to laparoscopic enucleation, robotic enucleation seems to be associated with less intraoperative blood loss, which could be related to the additional degrees of freedom during dissection that could lead to more accurate dissection[5].

Three studies have so far addressed robotic enucleation of pancreatic neoplasms, one of which describes the technique to enucleate an insulinoma in the pediatric setting, the others describe techniques to enucleate benign pancreatic lesions[6-8]. In this study, we present a technique for robotic enucleation of an insulinoma originating from the pancreas. We fully acknowledge that many variations are possible to nearly every step. Accurate identification and meticulous dissection, especially with regards to the main pancreatic duct, are crucial.

This case shown here involves a 42-year old woman who presented with sweating, tremor and episodes of hypoglycemia. A fasting test confirmed endogenic insulin overproduction. CT and MRI were inconclusive; therefore, an endoscopic ultrasound of the pancreatic head was made. Endoscopic ultrasonography showed a non-bulging, hypoechoic lesion, which was fully embedded within the pancreatic head at 1-2 mm distance from the main pancreatic duct. The patient was consented for both a robotic pancreatoduodenectomy procedure and a robotic enucleation. Intraoperatively, the final decision was made to perform an enucleation.

PROTOCOL

The patient gave written and oral informed consent to use medical data and the operative video for education and scientific purposes. This research was performed in compliance with all institutional, national and international guidelines for human welfare. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

1. Positioning

1.1. Place the patient on a vacuum mattress in a supine French position (legs split). Lower the right arm alongside the body on an arm support and extend the left arm. Tilt the operating table

10–20° in anti-Trendelenburg and 5–10° to the left.

2. Robot docking

2.1. After Verres needle insufflation on Palmers’ point, introduce four 8 mm robot trocars (R1-4) in a semi-curved line just above the umbilicus. The distance between the trocars is 6–7 cm: R1 in the right anterior axillary line, R2 in the right midclavicular line, R3 just right and above the umbilicus (camera) and R4 just medial in the left midclavicular line.

2.2. Introduce two assistant 5 mm trocars 3–4 cm below to the left (vessel sealing device) and right of the umbilicus.

3. Mobilization

3.1. Mobilize the hepatic flexure of the colon using robotic diathermia or laparoscopic sealing device.

3.2. Introduce the liver retractor from the left and retract the liver from segment III and IV. This enables optimal exposure of the surgical site. Optionally, it could suspend the stomach.

3.3. Identify the gastrocolic ligament and divide it with the vessel sealing device, hence opening the lesser sac.

3.4. Continue the mobilization from lateral to medial until the hepatic flexor of the colon is freed.

3.5. Perform Kocher’s maneuver until the left renal vein is identified. Hereafter, dissect the right gastroepiploic vein free and ligate using a vessel sealer. Both steps are optional but improve exposure and control which may be useful in case of bleeding from the pancreatic head.

3.6. Retract the pancreas and duodenum with the third robotic arm to entirely expose the abdominal aorta and inferior vena cava.

3.7. Identify the right gastroepiploic vein and divide it with the laparoscopic sealing device and clips.

3.8. Mobilize the pancreatic head using the cautery hook.

4. Intraoperative ultrasonography

4.1. Introduce the ultrasonography probe and identify the trajectory of the pancreatic duct and the intra-pancreatic lesion.

4.2. Demarcate the lesion with the cautery hook, with help of the ultrasonography probe.

5. Dissection

5.1. Place a traction suture through the lesion.

5.2. Lift the lesion up with the traction suture and enucleate the lesion circumferentially with the diathermic scissors.

5.3. Cut a finger from a sterile surgical glove and introduce it into the abdominal cavity. Put the enucleated tissue in the finger and extract the specimen. The roof of the pancreatic duct is visible at the bottom of the enucleation site.

5.4. Cut a finger from a sterile surgical glove and insert a **dry** sealant patch. Introduce the finger into the abdominal cavity. Position the sealant patch on the defect in the pancreatic parenchyma. Place two wet 10 x 10 cm gauzes on top and remove the gauzes after 3-5 minutes, the sealant patch remains on the pancreatic head.

NOTE: The sealant patch should not be made wet before positioning. Placement of a patch is optional; studies did not demonstrate its effectiveness in reducing the risk of pancreatic fistulas.

6. Drain placement

6.1. Introduce a 18-20 French drain from the right side of the patient and advance it over the pancreatic head.

6.2. Test produced drain fluids for amylase levels on the first and third postoperative day postoperatively to test for post-operative fistula. Consider placement of a stent in the pancreatic duct if the amylase level consistently exceeds 3 times the upper limit of the institutions normal serum amylase [9].

REPRESENTATIVE RESULTS:

Total operation time was 180 minutes with a blood loss of 5 mL. At the third postoperative day, drain amylase levels were still elevated. We therefore decided to attempt a stent placement in the pancreatic duct. During ERCP, this was technically not feasible, thus a pancreatic sphincterotomy was performed. This was classified as a grade B postoperative pancreatic fistula, due to the ERCP intervention[9]. The patient was discharged on postoperative day 7. After drain amylase had normalized, the drain could be removed in the outpatient clinic on postoperative day 20.

Histopathological examination revealed a grade 1 (mitotic index $<2/mm^2$ and Ki67 <3%) well-differentiated neuroendocrine tumor measuring 1.5 cm with positive insulin staining (see **Figure 1**). Tumor cells were microscopically present at the resection margin (R1).

Comparable results from literature

In general, a robotic docking time of 5-10 min has been described[10] as well as an operative time of 206 ± 67 min, operative blood loss 43 ml (IQR 27-98)[11] and a median tumor size of pancreatic neuroendocrine tumours of 16 mm (IQR 11-22)[12]. The expected postoperative hospital stay is 5 days (IQR 3-12)[11], major morbidity rate 30%[11], with a very low in hospital mortality rate (0%)[12,13]. The rate of clinically relevant pancreatic fistula rate is reported to be 30-40%[11,12] and the delayed gastric emptying rate 0-26%[12,13].

FIGURE AND TABLE LEGENDS:

Figure 1: Specimen.

DISCUSSION

There are six critical steps highlighted here: positioning and robot docking, mobilization, intraoperative ultrasonography, traction suture, dissection, and drain placement. Conversion to laparotomy should be performed in case of uncontrollable intraoperative bleeding or in case the tumor is not adequately located with ultrasound.

A liver retractor is useful to expose the surgical site. Intraoperative ultrasonography plays an important role in enabling a parenchyma-sparing enucleation. Preferably, a (interventional) radiologist should identify the lesion and especially its relationship with the pancreatic duct[14]. Applying a traction suture through the lesion eases the dissection, especially in a parenchyma-sparing resection.

Besides general complications of surgery, pancreatic fistula should be closely monitored after this procedure[15]. As shown here, the lesion had a close relationship with the pancreatic duct with only 1-2 mm distance between the insulinoma and the pancreatic duct. Because of this risk, a retro pancreatic drain was positioned and monitored at least during the first postoperative days[9].

A microscopically margin-positive (R1) resection was obtained. Although microscopically margin-negative (R0) resection would be preferably, this is not deemed necessary, as this is not associated with improved long-term overall survival in pancreatic neuroendocrine tumors[16].

Limitations of robotic surgery are the availability of the robotic system, the need for specific training, lack of tactile feedback and high costs[17]. The added degrees of freedom obtained by the robotic system may be useful for enucleation of insulinomas, especially in case of a close proximity to the pancreatic duct, as in this demonstrated case.

Robotic enucleation of insulinomas seems feasible; still, future prospective studies should confirm this suggestion. We believe that the described technique, with adequate ultrasonography guided localization of the lesion, could be a valuable alternative for open enucleation as stated in guidelines[1]. Further studies are needed to compare short- and long-term outcomes after robotic, open, and laparoscopic enucleation.

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The authors have no acknowledgments.

DISCLOSURES
The authors have nothing to disclose.

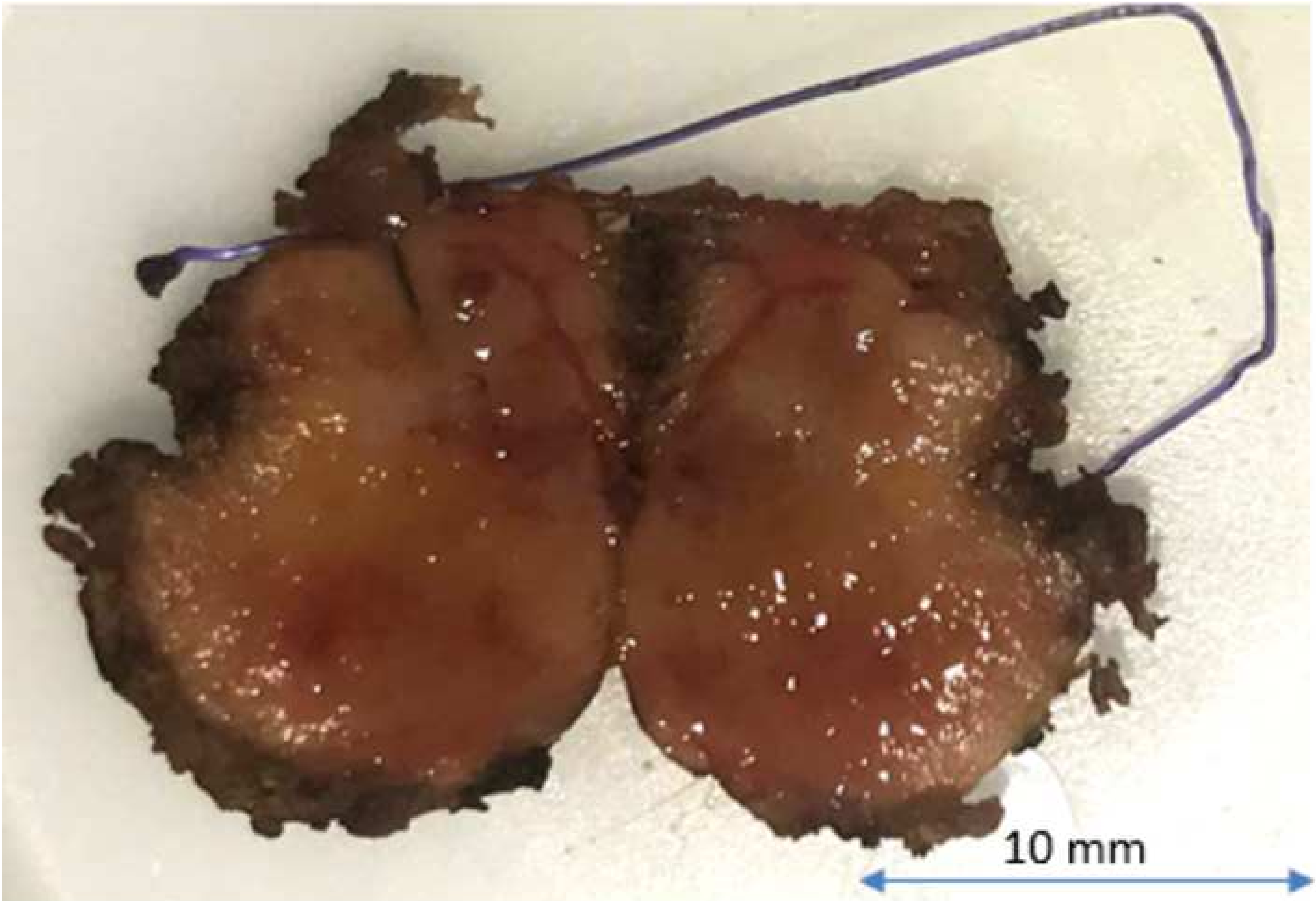
REFERENCES:
1 Falconi, M. et al. ENETS Consensus Guidelines Update for the Management of Patients with Functional Pancreatic Neuroendocrine Tumors and Non-Functional Pancreatic Neuroendocrine Tumors. *Neuroendocrinology.* **103** (2), 153-171 (2016).
2 Su, A. P. et al. Is laparoscopic approach for pancreatic insulinomas safe? Results of a systematic review and meta-analysis. *Journal of Surgical Research.* **186** (1), 126-134 (2014).
3 Shi, Y. et al. Pancreatic enucleation using the da Vinci robotic surgical system: a report of 26 cases. *The International Journal of Medical Robotics.* **12** (4), 751-757 (2016).
4 Tian, F. et al. Propensity score-matched analysis of robotic versus open surgical enucleation for small pancreatic neuroendocrine tumours. *British Journal of Surgery.* **103** (10), 1358-1364 (2016).
5 Zhang, T. et al. Enucleation of pancreatic lesions: indications, outcomes, and risk factors for clinical pancreatic fistula. *Journal of Gastrointestinal Surgery.* **17** (12), 2099-2104 (2013).
6 Liang, M. et al. Robotic enucleation for pediatric insulinoma with MEN1 syndrome: a case report and literature review. **18** (1), 44 (2018).
7 Ore, A. S., Barrows, C. E., Solis-Velasco, M., Shaker, J., Moser, A. J. Robotic enucleation of benign pancreatic tumors. *Journal of Visualized Surgery.* **3** (10) (2017).
8 Jin, J. B. et al. Robotic Enucleation for Benign or Borderline Tumours of the Pancreas: A Retrospective Analysis and Comparison from a High-Volume Centre in Asia. *World Journal of Surgery.* **40** (12), 3009-3020 (2016).
9 Bassi, C. et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery.* **161** (3), 584-591 (2017).
10 Boone, B. A. et al. Assessment of quality outcomes for robotic pancreaticoduodenectomy: identification of the learning curve. *JAMA Surgery.* **150** (5), 416-422 (2015).
11 Zureikat, A. H. et al. 250 robotic pancreatic resections: safety and feasibility. *Annals of Surgery.* **258** (4), 554-559; 559-562 (2013).
12 Jilesen, A. P. J. et al. Postoperative Outcomes of Enucleation and Standard Resections in Patients with a Pancreatic Neuroendocrine Tumor. *World Journal of Surgery.* **40** (3), 715-728 (2016).
13 Crippa, S. et al. Surgical Management of Insulinomas: Short- and Long-term Outcomes After Enucleations and Pancreatic Resections. *JAMA Surgeryery.* **147** (3), 261-266 (2012).
14 Li, W. et al. Laparoscopic ultrasound enhances diagnosis and localization of insulinoma in pancreatic head and neck for laparoscopic surgery with satisfactory postsurgical outcomes. *Ultrasound in Medicine and Biology.* **37** (7), 1017-1023 (2011).
15 Lu, W. J. et al. Enucleation of benign or borderline pancreatic head tumors adjacent to

the common pancreatic duct. *Pancreas.* **41** (2), 336-337 (2012).

16 Zhang, X. F. et al. Margin status and long-term prognosis of primary pancreatic neuroendocrine tumor after curative resection: Results from the US Neuroendocrine Tumor Study Group. *Surgery.* **165** (3), 548-556 (2019).

17 Gkegkes, I. D., Mamais, I. A., Iavazzo, C. Robotics in general surgery: A systematic cost assessment. *Journal of Minimal Access Surgery.* **13** (4), 243-255 (2017).

Figure 1



Name of Material/Equipment	Company	Catalog Number
Arietta V70 Ultrasound	Hitachi	-
Cobra Liver Retractor Diamond-Flex	CareFusion	89-6216
da Vinci Surgeon Console	Intuitive Surgical	SS999
da Vinci Vision Cart	Intuitive Surgical	VS999
da Vinci Xi	Intuitive Surgical	K131861
da Vinci Xi Endoscope with Camera, 8 mm, 30˚	Intuitive Surgical	470027
ENDOEYE Rigid Video Laparoscope, 10 mm, 30°	Olympus	WA50042A
ENDOWRIST Fenestrated Bipolar Forceps	Intuitive Surgical	470205
ENDOWRIST HOT SHEARS	Intuitive Surgical	470179
ENDOWRIST Mega SutureCut Needle Driver	Intuitive Surgical	470309
ENDOWRIST Permanent Cautery Hook	Intuitive Surgical	470183
ENDOWRIST PROGrasp Forceps	Intuitive Surgical	470093
LigaSure Dolphin Tip 37cm	Medtronic	LS1500
Robotic ultrasonography transducer	Hitachi	L43K
TachoSil 4.8 cm x 4.8 cm	Baxter Healthcare Corporation	1144923

Comments/Description

The ultrasound system.

Retracting the liver for optimal exposure of the surgical site.

Used to control the surgical robot.

The vision cart houses advanced vision and energy technologies and provides communications across da Vinci system components.

The surgical robot: ’patient side-cart’.

The camera of the da Vinci robot.

To see within the intra-abdominal cavity.

Used for dissection and coagulation.

Used for cutting and coagulation.

Used as a needle driver.

Used for coagulation.

Used for dissection.

Used for vessel sealing and dividing.

Used for intraoperative laparoscopic ultrasonography.

Used for coagulation.

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Dear Mr. Steindel,

We are pleased with the comments from the reviewers and editors on our manuscript 'Robotic Enucleation of an Insulinoma in the Pancreatic Head'. We thank the editors and reviewers for their efforts and have considered the comments and revised both the manuscript and video accordingly. We addressed the review comments individually below:

General:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.
    - The manuscript was thoroughly proofread for spelling or grammar issues.
2. For in-text formatting, corresponding reference numbers should appear as numbered superscripts (without parentheses) after the appropriate statement(s).
    - We have changed the reference style accordingly.
3. "A Video Vignette" is not necessary for the title.
    - We have removed 'A Video Vignette' from the title.

Protocol:

1. We will likely not be able to hold a copy of the written consent-can the statement to that effect be removed?
    - We have removed the sentence 'A copy of the written consent is available for review by the Editor-in-Chief of this journal'.
2. For each protocol step, please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. If revisions cause a step to have more than 2-3 actions and 4 sentences per step, please split into separate steps or substeps.
    - We have added some details to the protocol.

Results:

1. Would it be possible to include more 'visual' summation of results; e.g., a table outlining efficacy for this procedure? This could be both here and the video.
    - We have not made an additional table, as there is not a lot of data to tabulate.
2. The 'Comparable results from literature' section in the Discussion should be moved here.
    - We have moved the 'Comparable results from literature' section here.

References:

1. Please ensure that the references appear as the following: [Lastname, F.I., LastName, F.I., LastName, F.I. Article Title. *Source*. **Volume** (Issue), FirstPage – LastPage (YEAR).] For more than 6 authors, list only the first author then et al.
    - We have changed the reference style accordingly.

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Table of Materials:

1. Please ensure the Table of Materials has information on all materials and equipment used, especially those mentioned in the Protocol.
    - We have checked the Table of Materials. All used materials and equipment mentioned in the protocol is stated in the Table of Materials.
2. Please remove trademark (™) and registered (®) symbols from the Table and Materials.
    - We have removed trademark (™) and registered (®) symbols from the Table and Materials.

Video:

1. Please ensure the written protocol and video narration agree as much as possible; e.g., there is more information regarding steps 3.4, 3.5, and 5.2 in the narration than the text.
    - We have tried to agree the written protocol and video narration as much as possible.
2. 0:00-0:42, 0:57-1:07, 1:18-1:20, 3:19-3:21, 3:42-3:45, 4:05-4:09, 5:13-5:15, 5:30-5:32, 5:37-6:06 - The Amsterdam UMC logo should be removed at the listed times. The animated splash at 6:06 can remain in the video.
    - The Amsterdam UMC logo is removed at the specified times. We have not removed the animated splash of the logo at the end.
3. The narration audio should be peaking between -6 and -12 dB. The volume of the audio will need to be raised a bit to achieve this.
    - We have raised the overall volume of the video.
4. 1:00- The brand name "Da Vinci" is mentioned in the narration here. The brand names "Da Vinci®", "HOT SHEARS™", and "PROGRASP™" are written on screen. All references to brand names need to be removed and replaced with generic terms.
    - The brand name 'Da Vinci Xi' is now removed from the narration. The brand names 'Da Vinci', 'HOT SHEARS', 'PROGRASP' and 'Ligasure' are now removed from the video.
5. 1:40-2:12, 2:27-2:53, 4:09-4:40, 5:15-5:30 - This is too long a span of time and too many different shots for the video to be silent. Either narration needs to be added to offer some explanation of what is being shown, or the video needs to be edited down for length.
    - We have moved some narration in the video, have added additional narration and shortened the video where deemed necessary.
6. 5:00 - TACHOSIL® is spoken in the narration and written on screen here. The brand name references should be removed.
    - The brand name 'TACHOSIL' is now removed from the video.
7. The video needs to have Results and Conclusions sections, identified by title cards.
    - We have changed the 'Specimen' section and title card to 'Results'. A new 'Conclusion' section was added.

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Reviewer 1:
We thank the reviewer for the compliment and agree that insights into operative techniques are very useful for the readers.

Reviewer 2:
We thank the reviewer for addressing the small clerical errors. These are now taken care of. A pre-operatively placed stent in the pancreatic duct would indeed aid in identification of the pancreatic duct and help preventing a postoperative pancreatic fistula. However, in this case, the patient was counselled for a pancreatoduodenectomy, in which pre-operative stenting would not be necessary.

Sincerely,
On behalf of all co-authors,
Enes Kaçmaz

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