

## Endoscopic ultrasound radiofrequency ablation of pancreatic insulinoma in elderly patients: Three case reports

Gemma Rossi, Maria Chiara Petrone, Gabriele Capurso, Stefano Partelli, Massimo Falconi, Paolo Giorgio Arcidiacono

**Specialty type:** Medicine, research and experimental

**Provenance and peer review:**

Unsolicited article; Externally peer reviewed

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): C, C, C  
Grade D (Fair): 0  
Grade E (Poor): 0

**P-Reviewer:** Kuraoka N, Japan;  
Rathnaswami A, India

**A-Editor:** Makker J

**Received:** August 12, 2021

**Peer-review started:** August 12, 2021

**First decision:** October 3, 2021

**Revised:** October 16, 2021

**Accepted:** May 14, 2022

**Article in press:** May 14, 2022

**Published online:** July 6, 2022



**Gemma Rossi, Maria Chiara Petrone, Gabriele Capurso, Paolo Giorgio Arcidiacono**, Division of Pancreato-Biliary Endoscopy and Endosonography, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute IRCCS, Vita-Salute San Raffaele University, Milano 20132, Italy

**Stefano Partelli, Massimo Falconi**, Department of Pancreatic Surgery, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute IRCCS, Vita-Salute San Raffaele University, Milano 20132, Italy

**Corresponding author:** Gabriele Capurso, MD, PhD, Chief Doctor, Division of Pancreato-Biliary Endoscopy and Endosonography, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute IRCCS, Vita-Salute San Raffaele University, Via Olgettina 60, Milano 20132, Italy. [capurso.gabriele@hsr.it](mailto:capurso.gabriele@hsr.it)

### Abstract

#### BACKGROUND

Endoscopic ultrasound (EUS)-guided radiofrequency ablation (RFA) has recently been proposed as a local treatment for functional pancreatic neuroendocrine neoplasms in patients unfit for surgery, in order to obtain clinical syndrome regression. Data on the safety and long-term effectiveness of this approach are scarce, and EUS-RFA procedures are not standardized.

#### CASE SUMMARY

The present case series reports 3 elderly patients with a pancreatic insulinoma and comorbidities, locally treated by EUS-guided RFA with clinical success in terms of hypoglycemic symptoms. RFA procedures were performed during deep sedation, under EUS control with a 19 G needle, an electrode 5-mm in size at a power of 30 W and multiple RFA applications during the same session in order to treat the whole area of the lesions. Immediate relief of symptoms was evident in 2 patients after the first EUS-RFA, while in the third patient a second endoscopic treatment was needed. All 3 patients are symptom-free without need of medications after 24 mo of follow-up with imaging follow-up showing no disease recurrence. A single adverse event of intraprocedural bleeding occurred, which was successfully treated endoscopically.

#### CONCLUSION

EUS-RFA represents an effective and safe alternative to surgery for the treatment

of insulinomas in elderly patients at high surgical risk. However, larger multicenter studies with longer follow-up are needed in order to better assess its safety and clinical success.

**Key Words:** Endoscopic ultrasound; Radiofrequency ablation; Insulinomas; Neuroendocrine neoplasms; Ablative therapies; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Endoscopic ultrasound (EUS)-guided radiofrequency ablation (RFA) has been proposed as a local treatment for functional pancreatic neuroendocrine neoplasms in patients unfit for surgery. However, data on safety and long-term effectiveness are scarce and procedures are not standardized. The present case series reports 3 elderly patients with comorbidities diagnosed with a pancreatic insulinoma who received local treatment by EUS-guided RFA with a standardized protocol, with clinical success in terms of hypoglycemic symptoms over a relatively long follow-up. Effective EUS-RFA represents an alternative to surgery for the treatment of insulinoma in elderly patients at high surgical risk. However, larger multicenter studies with longer follow-up are needed in order to assess the safety and clinical success of this treatment.

**Citation:** Rossi G, Petrone MC, Capurso G, Partelli S, Falconi M, Arcidiacono PG. Endoscopic ultrasound radiofrequency ablation of pancreatic insulinoma in elderly patients: Three case reports. *World J Clin Cases* 2022; 10(19): 6514-6519

**URL:** <https://www.wjgnet.com/2307-8960/full/v10/i19/6514.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v10.i19.6514>

## INTRODUCTION

The incidence of pancreatic neuroendocrine neoplasms (p-NENs) has increased over the last decades due to advances in imaging methods[1]. Non-functional p-NENs that were typically diagnosed at advanced stages when the volume of the lesions determined symptoms, are now often incidentally diagnosed as small (< 2 cm) lesions and whether any treatment should be pursued is debatable[2].

Functional p-NENs (F-pNENs) are usually recognized at early stages, due to the presence of a specific syndrome[3]. Surgery is always indicated in symptomatic cases as the gold standard. However, given the high morbidity and mortality of pancreatic surgery, alternative treatments such as endoscopic ultrasound (EUS)-guided radiofrequency ablation (RFA) can be considered in order to obtain resolution of the syndrome in elderly patients with comorbidities and high surgical risks. The current literature[4] is scarce regarding data on EUS-RFA treatment of F-pNENs. Therefore, safety concerns remain and long-term data on the efficacy of this treatment are needed[5]. Moreover, specific RFA settings (particularly in terms of ablation power) are not standardized.

## CASE PRESENTATION

### Chief complaints

This is a case series presenting data on the feasibility, safety and clinical efficacy of EUS-guided RFA to induce relief of the clinical syndrome in 3 elderly patients with symptomatic pancreatic insulinomas at high surgical risk.

### History of present illness

Three elderly patients with symptomatic pancreatic insulinomas underwent a total of 4 EUS-RFA procedures performed after failure or limited control with medical treatments.

**Case 1:** An 84-year-old male patient had repeated episodes of syncope for 3 years, associated with blood glucose < 20 mg/dL and neuroglycopenic symptoms with prompt relief of symptoms following the administration of glucose. The diagnosis of insulinoma was supported by a preoperative fasting test.

**Case 2:** An 82-year-old male patient, with 2 previous episodes of syncope and marked hypoglycemia (glucose = 38 and 32 mg/dL) was referred to our center. A fasting test confirmed the diagnosis of insulinoma with glucose and C-peptide levels (glucose 40 mg/dL, C-peptide 0.7 ng/mL).

**Case 3:** An 84-year-old female patient was referred to our center after two years of symptomatic hypoglycemic episodes (glucose < 30 mg/dL). A fasting test was suggestive of pancreatic insulinoma, with neuroglycopenic symptoms after fasting associated with levels of glucose 30 mg/dL and C-peptide 0.9 ng/mL (normal values: 1.1-4.4 ng/mL).

### **History of past illness**

**Case 1:** The patient had chronic renal failure and severe ischemic heart disease.

**Case 2 and case 3:** These 2 patients were affected by severe chronic obstructive pneumopathy disease.

### **Personal and family history**

No family history of NENs was present in these cases.

### **Physical examination**

Case 1 had moderate obesity. The other two patients did not present specific signs at physical examination.

### **Laboratory examinations**

All three patients had consistent and constant neuroglycopenic symptoms and diagnosis was supported by elevated insulin, C-peptide and proinsulin blood levels at the preoperative fasting test. The same plasma markers were monitored after EUS-guided RFA to support the relief of hypoglycemic symptoms and clinical syndrome.

### **Imaging examinations**

All the patients underwent magnetic resonance imaging (MRI) with administration of contrast medium and the lesions were diagnosed as likely p-NENs ranging in size from 9 to 14 mm.

---

## **MULTIDISCIPLINARY EXPERT CONSULTATION**

The patients were referred to our multidisciplinary neuroendocrine tumor board, and due to their age and comorbidities it was decided to treat the lesions with EUS-RFA at the Hospital's Endosonography Unit.

---

## **FINAL DIAGNOSIS**

A cytological diagnosis of insulinoma was obtained with EUS-FNA in case 2. In case 1 and case 3 the clinical, biochemical and radiological findings were considered typical for insulinoma and multidisciplinary evaluation considered biopsies unnecessary as cited in international guidelines[2,6].

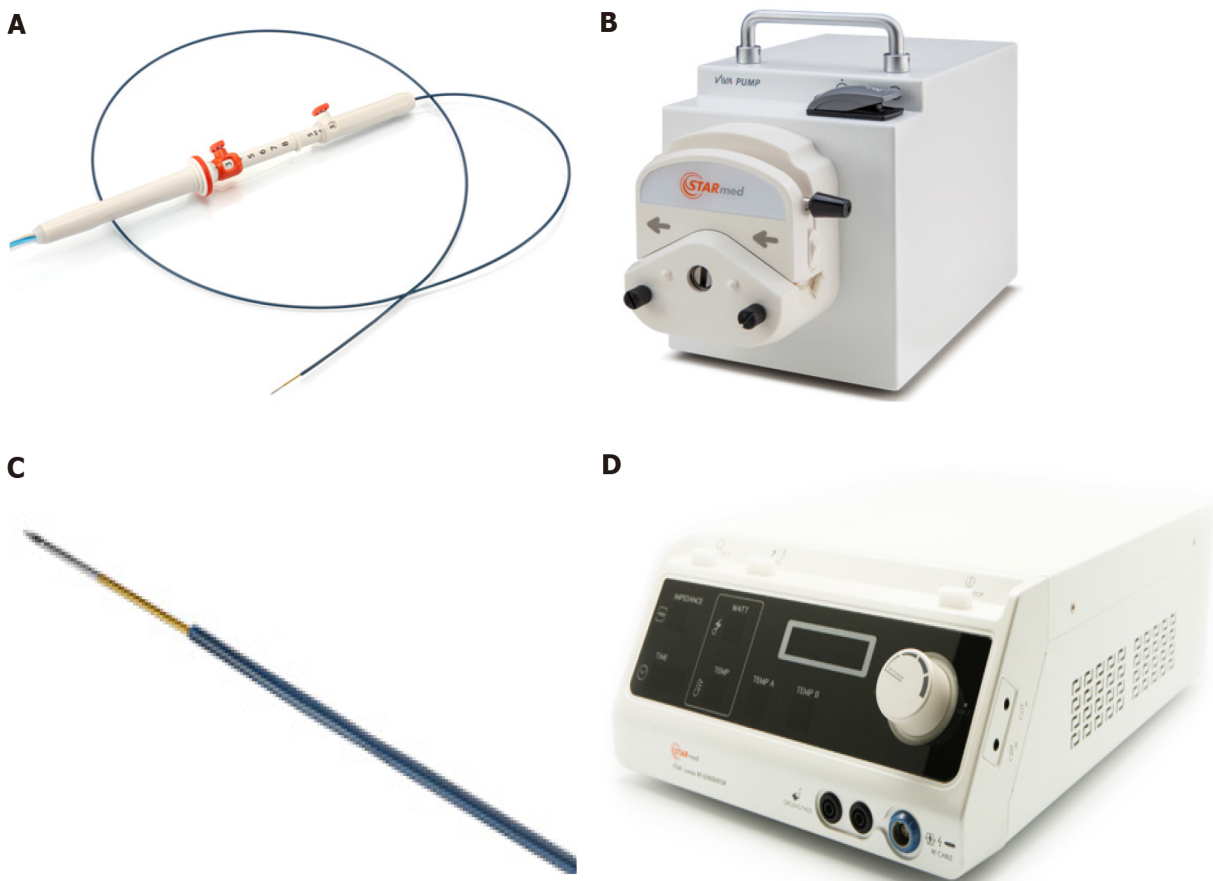
---

## **TREATMENT**

During the endoscopic procedure the patients underwent deep sedation and were placed in the left lateral position. In each case, RFA was delivered by a 19-gauge needle (EUSRA; STARmed Co., Ltd., Goyang, Korea), with a 5 mm-active monopolar electrode on the distal part of the probe (delivering the ablation). The needle was inserted in the operative channel of a therapeutic EUS-scope (Pentax EG-3870UTK or Pentax 38J10UT), connected to an ultrasound platform (Hitachi Arietta 750 or Hitachi Arietta 850). The needle was also connected to a RFA generator (VIVA; STARmed Co., Ltd., Goyang, Korea) delivering the thermal energy to ablate the lesions and was also connected to a peristaltic pump infusing cold saline solution (at 0 °C, to avoid tissue charring around the probe, maximizing the lesion ablation volume). **Figure 1** describes the RFA system. The generator was set at 30 W of power in all procedures and treatment was applied for different times depending on tissue impedance (system was stopped at impedance > 500 Ω, resulting in an ineffective treatment), until a complete "cloud effect" was obtained in the lesion area (multiple RFA applications were performed during the same endoscopic session). Each patient underwent a computed tomography (CT) scan 24-72 h after the RFA procedure, in order to assess the size of the necrotic area inside the lesions and exclude complications.

### **Case 1**

One single endoscopic session was conducted with 4 subsequent EUS-RFA applications at 3 W for 12-16-12-10 s each and stopped when the impedance increased.



**Figure 1 Radiofrequency ablation system.** A: Needle, similar to an endoscopic ultrasound fine needle aspiration or biopsy needle; B: Peristaltic pump which can infuse during the ablation, the electrode with chilled solution, maximizing volume ablation; C: Electrode on the distal needle tip, delivering radiofrequency ablation; D: Radiofrequency generator, with the possibility to monitor ablation parameters: Power, time, impedance. Citation: Rossi G, Petrone MC; Capurso G, Albarello L, Testoni SGG, Archibugi L, Lena MS, Doglioni C, Arcidiacono PG. Standardization of a Radiofrequency Ablation Tool in an Ex-Vivo Porcine Liver Model. *Gastrointest Disord* 2020; 2: 300-309. Copyright© The Authors 2020. Published by MDPI. No special permission is required to reuse all or part of article published by MDPI, including figures and tables, see <https://www.mdpi.com/openaccess#Permissions>. The authors have obtained the permission for figure using from Rossi G (Supplementary material).

### Case 2

A first RFA procedure was performed with 3 applications lasting 20, 15 and 15 s each at a power of 30 W. Complete relief of symptoms was not obtained, while a 72-h CT scan showed a 7 mm hypodense necrotic area. Blood tests were consistent with ablation failure. A second EUS-RFA session was performed after 1 mo. Four RFA applications were carried out for 10, 8, 6, and 8 s, respectively, until complete covering of the pancreatic insulinoma by a hyperechoic cloud was observed. Possibly due to the proximity between the lesion and gastroduodenal artery (Figure 2A), immediate post-procedural bleeding was endoscopically evidenced with a submucosal hematoma located at the superior duodenal genu, due to a side-branch artery injury. Bleeding was immediately treated by mechanical (metallic clip) and injective (adrenalin dilution: 1:10000) hemostatic therapy with success (Figure 2B).

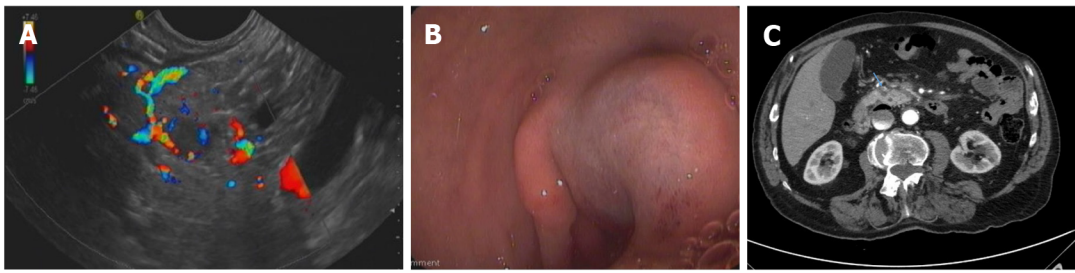
### Case 3

The procedure was performed by 3 applications lasting 6 s each at the standard power of 30 W.

## OUTCOME AND FOLLOW-UP

### Case 1

No immediate or late complications occurred and immediate clinical success with syndrome relief was obtained. A CT scan performed 48-h after the procedure showed a 14 mm hypodense necrotic area in the pancreatic tail, as the outcome of the procedure. A subsequent diagnostic EUS performed after 3 mo, showed a total non-vascularized 12 mm area on contrast enhancement (Sonovue®, Bracco) at the site of the previous RFA (Video). The patient is still asymptomatic (with mild hyperglycemia), after 27-mo of clinical follow-up. No further radiological examinations were performed due to chronic renal failure and related-risks of CT or MRI-contrast medium administration.



DOI: 10.12998/wjcc.v10.i19.6514 Copyright ©The Author(s) 2022.

**Figure 2 Case 2 imaging.** A: A hyper-vascularized lesion compatible with an insulinoma, extremely close to the gastroduodenal artery is visible; B: Submucosal bleeding after radiofrequency ablation, treated by endoscopic hemostasis; C: Computed tomography scan 72 h after radiofrequency ablation: An 8 mm hypodense necrotic area at the previous lesion location, without signs of bleeding.

### Case 2

The patient showed relief of hypoglycemic symptoms immediately after the second procedure with normalization of glucose blood levels. A CT scan performed 72 h after RFA revealed an 8-mm hypodense necrotic area at the site of the lesion, without evidence of bleeding (Figure 2C). The patient refused further radiological follow-up and complete symptom relief persists at 24 mo with normalization of biochemical tests.

### Case 3

A CT scan with contrast enhancement was performed 72 h after RFA and confirmed the presence of a 13-mm necrotic area inside the lesion, and complete relief from hypoglycemic symptoms was obtained. After 15 mo the patient remains asymptomatic without the need for treatment. A contrast-enhanced MRI performed 14 mo after the procedure confirmed the complete disappearance of the treated lesion in the pancreatic body.

## DISCUSSION

EUS-RFA represents a potentially useful and safe option to treat insulinomas and related symptoms in patients at high surgical risk, especially in cases of pancreatic head/neck lesions, requiring a Whipple resection. EUS-RFA is relatively safe, although specific care needs to be paid to the bleeding risk of such hypervascularized lesions. Usually RFA-related complications can be endoscopically treated by a highly experienced endoscopist. In the present series, EUS-RFA led to symptom relief during a relatively long follow-up, with a single endoscopic session in 2 patients and 2 endoscopic sessions in the remaining patient. Notably, while most of the published case series on this topic did not present specific and standardized ablation settings[7-10], in the present study we standardized the setting of the ablation power in line with previous *ex-vivo* animal[11] and human studies (unpublished data), with the application of 30 W and stopping energy delivery when tissue impedance increased. All 3 patients are symptom-free after more than 12 mo of clinical and biochemical follow-up and the lesion is no longer visible after 14 mo in one of the patients who underwent radiological examination.

## CONCLUSION

Larger multicenter studies with a longer and standardized follow-up are needed in order to confirm the safety and long-term clinical success of EUS-RFA in patients with p-NENs. The results of a large ongoing multicenter study endorsed by the European Neuroendocrine Tumour Society are eagerly awaited (ClinicalTrials.gov Identifier: NCT03834701).

## FOOTNOTES

**Author contributions:** Rossi G, Petrone MC, Capurso G, Arcidiacono PG made substantial contributions to conception and design of the study, acquisition of data, or analysis and interpretation of data; Rossi G, Petrone MC, Capurso G, Partelli S, Falconi M, Arcidiacono PG drafted the article or made critical revisions related to important intellectual content of the manuscript; and all authors provided final approval of the version of the article to be published.

**Informed consent statement:** All three patients included in the present case series gave their consent prior to study



inclusion.

**Conflict-of-interest statement:** The authors have note conflicts of interest to declare.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** Italy

**ORCID number:** Gemma Rossi 0000-0003-4071-8247; Maria Chiara Petrone 0000-0002-1045-209X; Gabriele Capurso 0000-0002-0019-8753; Stefano Partelli 0000-0001-8938-6170; Massimo Falconi 0000-0001-9654-7243; Paolo Giorgio Arcidiacono 0000-0001-6692-7720.

**S-Editor:** Wang JJ

**L-Editor:** Webster JR

**P-Editor:** Wang JJ

## REFERENCES

- 1 **Fitzgerald TL**, Hickner ZJ, Schmitz M, Kort EJ. Changing incidence of pancreatic neoplasms: a 16-year review of statewide tumor registry. *Pancreas* 2008; **37**: 134-138 [PMID: 18665072 DOI: 10.1097/MPA.0b013e318163a329]
- 2 **Falconi M**, Eriksson B, Kaltsas G, Bartsch DK, Capdevila J, Caplin M, Kos-Kudla B, Kwekkeboom D, Rindi G, Klöppel G, Reed N, Kianmanesh R, Jensen RT; Vienna Consensus Conference participants. ENETS Consensus Guidelines Update for the Management of Patients with Functional Pancreatic Neuroendocrine Tumors and Non-Functional Pancreatic Neuroendocrine Tumors. *Neuroendocrinology* 2016; **103**: 153-171 [PMID: 26742109 DOI: 10.1159/000443171]
- 3 **Lee DW**, Kim MK, Kim HG. Diagnosis of Pancreatic Neuroendocrine Tumors. *Clin Endosc* 2017; **50**: 537-545 [PMID: 29207856 DOI: 10.5946/ce.2017.131]
- 4 **Imperatore N**, de Nucci G, Mandelli ED, de Leone A, Zito FP, Lombardi G, Manes G. Endoscopic ultrasound-guided radiofrequency ablation of pancreatic neuroendocrine tumors: a systematic review of the literature. *Endosc Int Open* 2020; **8**: E1759-E1764 [PMID: 33269308 DOI: 10.1055/a-1261-9605]
- 5 **Larghi A**, Rizzatti G, Rımbaş M, Crino SF, Gasbarrini A, Costamagna G. EUS-guided radiofrequency ablation as an alternative to surgery for pancreatic neuroendocrine neoplasms: Who should we treat? *Endosc Ultrasound* 2019; **8**: 220-226 [PMID: 31249164 DOI: 10.4103/eus.eus\_28\_19]
- 6 **Jensen RT**, Cadiot G, Brandi ML, de Herder WW, Kaltsas G, Komminoth P, Scoazec JY, Salazar R, Sauvanet A, Kianmanesh R; Barcelona Consensus Conference participants. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms: functional pancreatic endocrine tumor syndromes. *Neuroendocrinology* 2012; **95**: 98-119 [PMID: 22261919 DOI: 10.1159/000335591]
- 7 **Lakhtakia S**, Ramchandani M, Galasso D, Gupta R, Venugopal S, Kalpala R, Reddy DN. EUS-guided radiofrequency ablation for management of pancreatic insulinoma by using a novel needle electrode (with videos). *Gastrointest Endosc* 2016; **83**: 234-239 [PMID: 26394384 DOI: 10.1016/j.gie.2015.08.085]
- 8 **Choi JH**, Seo DW, Song TJ, Park DH, Lee SS, Lee SK, Kim MH. Endoscopic ultrasound-guided radiofrequency ablation for management of benign solid pancreatic tumors. *Endoscopy* 2018; **50**: 1099-1104 [PMID: 29727904 DOI: 10.1055/a-0583-8387]
- 9 **Oleinikov K**, Dancour A, Epshtein J, Benson A, Mazeh H, Tal I, Matalon S, Benbassat CA, Livovsky DM, Goldin E, Gross DJ, Jacob H, Grozinsky-Glasberg S. Endoscopic Ultrasound-Guided Radiofrequency Ablation: A New Therapeutic Approach for Pancreatic Neuroendocrine Tumors. *J Clin Endocrinol Metab* 2019; **104**: 2637-2647 [PMID: 31102458 DOI: 10.1210/jc.2019-00282]
- 10 **Furnica RM**, Deprez P, Maiter D, Vandeleene B, Borbath I. Endoscopic ultrasound-guided radiofrequency ablation: An effective and safe alternative for the treatment of benign insulinoma. *Ann Endocrinol (Paris)* 2020; **81**: 567-571 [PMID: 33285105 DOI: 10.1016/j.ando.2020.11.009]
- 11 **Rossi G**, Petrone MC; Capurso G, Albarello L, Testoni SGG, Archibugi L, Lena MS, Doglioni C, Arcidiacono PG. Standardization of a Radiofrequency Ablation Tool in an Ex-Vivo Porcine Liver Model. *Gastrointest Disord* 2020; **2**: 300-309 [DOI: 10.3390/gidisord2030027]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

