Letter to the Editor

Treatment of locally advanced pancreatic cancer with irreversible electroporation and intraoperative radiotherapy

Lingmin Jiang[1,2,3#], Xin Huang[1,2,3#], Xin Hua[4#], Qiaoqiao Li[1,2,5], Yujing Zhang[1,2,5], Jun Wang[1,2,3], Shengping Li[1,2,3]

[1]State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, China; [2]Department of Experimental Research, Sun Yat-sen University Cancer Center, Guangzhou, China; [3]Department of Pancreatobiliary Surgery, Sun Yat-sen University Cancer Center, Guangzhou, China; [4]Department of Radiation Oncology, Shanghai Jiao Tong University Medical School Affiliated Ruijin Hospital, Shanghai, China; [5]Department of Radiation Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China

[#]These authors contributed equally to this work as co-first authors.

Correspondence to: Jun Wang, MD, PhD; Shengping Li, MD, PhD. State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou 510060, China; Department of Experimental Research, Sun Yat-sen University Cancer Center, Guangzhou 510060, China; Department of Pancreatobiliary Sugery, Sun Yat-sen University Cancer, No. 651 Dongfeng Road East, Guangzhou 510060, China. Email: wangjun@sysucc.org.cn; lishp@sysucc.org.cn.

Submitted Sep 19, 2024. Accepted for publication Nov 05, 2024. Published online Nov 21, 2024.
doi: 10.21037/hbsn-24-526
View this article at: https://dx.doi.org/10.21037/hbsn-24-526

Pancreatic cancer (PC) is a highly lethal malignancy, with a 5-year survival rate of less than 8% (1). However, only 20% of patients with PC are eligible for curative resection, and their 5-year survival rate is approximately 10%.

The remaining 40% of patients who cannot undergo radical resection due to tumour invasion of local structures, such as the celiac trunk or superior mesenteric artery (SMA), are referred to as having locally advanced PC (LAPC). Irreversible electroporation (IRE) is a novel technology that uses a series of high-voltage, low-energy current electrical pulses to destroy the lipid bilayer structure of the cell membrane, producing nanopores that lead to cell death of the target cells (2). Many clinical experiences with IRE for LAPC have been published by multiple individual institutions and multicentre studies (3). However, incomplete ablation remains a continuing challenge and requires further exploration to enhance local complete cytoreduction. Intraoperative radiotherapy (IORT) has the potential to increase the chance of local tumour control by decreasing the radiation dose delivered to adjacent organs and increasing the radiation dose to the tumour bed. Thus, IORT is more widely used in LAPC. Several studies reported that patients with LAPC were much more suitable for IORT than for chemoradiation therapy and achieved a better remission rate (4).

Here, we report the case of a 50-year-old female patient with LAPC who underwent IRE and IORT and achieved a favourable response after combination therapy.

A 50-year-old Chinese woman was hospitalized and had a history of abdominal pain for 1 year. In another hospital, she was confirmed to have LAPC through imaging and pathological examination. In 2012, a thyroid cystectomy was performed because of thyroid cyst. She had never smoked or consumed alcohol, and her family history was noncontributory. Occupationally, she worked as an office manager.

A physical examination after hospitalization did not reveal any obvious abnormalities. She had a body temperature of 36.0 ℃, heart rate of 72 beats per minute, blood pressure of 114/60 mmHg, respiratory rate of 18 breaths per minute, and oxygen saturation of 100%. Her neurological status was normal.

After hospitalization, laboratory tests were performed. Blood tests revealed a high level of carbohydrate antigen 199 (CA19-9) (51.93 U/mL; normal range, 0.00–35.0 U/mL). The patient exhibited mild hepatic dysfunction characterized by slight impairment of liver function, with an alanine transaminase (ALT) level of 69.8 U/L (normal range, 7–40 U/L). In addition, the glucose concentration was 7.60 mmol/L (normal range, 3.9–6.1 mmol/L). To rule

© AME Publishing Company.

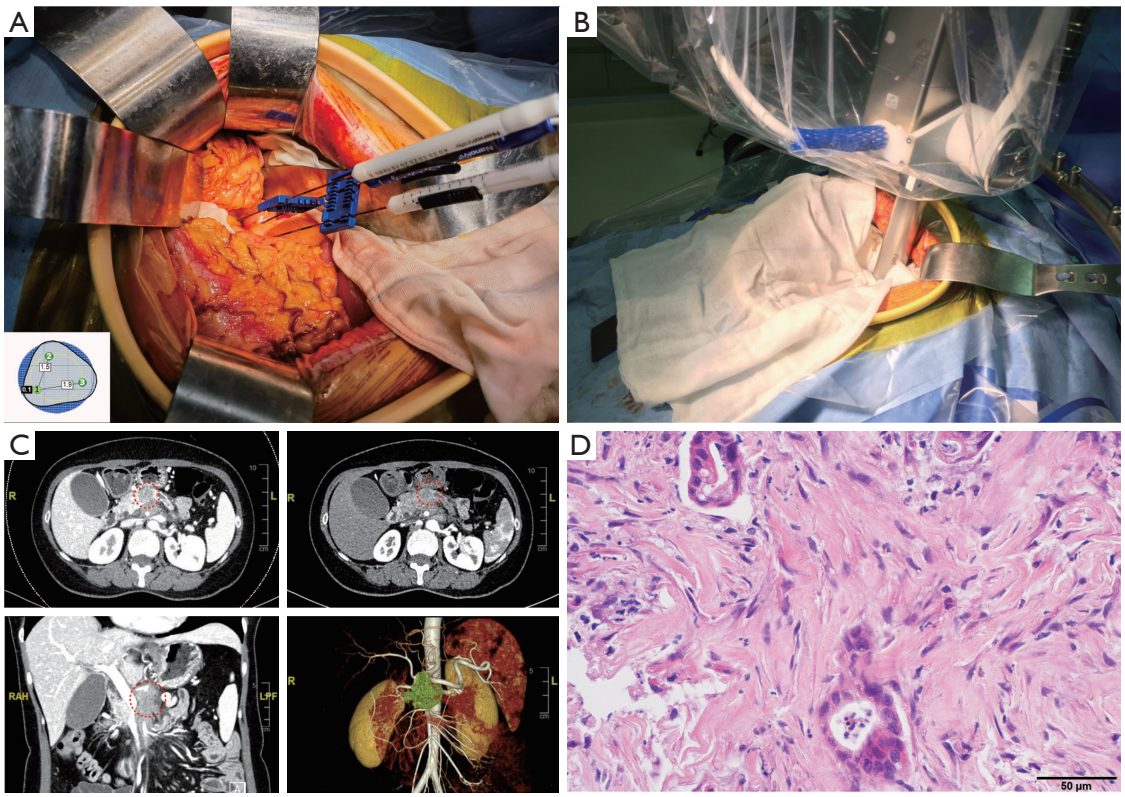

Figure 1 The intraoperative IRE and radiotherapy. (A) Intraoperative ablation needle position in the upper abdomen. IRE treatment planning screen in the bottom left. ①, ② and ③ represent the three needles, the yellow curve indicates the tumour range and the black curve represents the ablation range. (B) The intraoperative radiotherapy using INTRABEAM radiation system after IRE. (C) The computed tomography scan images before treatment. (D) Hematoxylin-eosin staining of postoperative pathological tissue. IRE, irreversible electroporation.

out immunoglobulin G4-related (IgG4-related) pancreatitis, we conducted an IgG4 test, which yielded a result of 0.609 g/L (normal range, 0.03–2.01 g/L).

An abdominal computed tomography scan with enhancement and vascular reconstruction revealed a space-occupying lesion in the pancreatic neck; the findings suggested the presence of PC with invasion of the hepatic artery, SMA, splenic artery, superior mesenteric vein (SMV), and origin of the portal vein without compression (*Figure 1*). In addition, Coeliac trunk and near artery's lymph nodes were considered as metastatic tumours. Pathological examination of a specimen from an endoscopic ultrasound puncture biopsy revealed abnormal cells, with a morphology consistent with that of adenocarcinoma. She was diagnosed with a LAPC (cT4NxM0 stage III). Following her history, imaging and examination data, IRE was selected. However, because the tumour protruding from the surface of the pancreas, it was difficult to ablate this part of the tumour by electrode needles. After discussion from multidisciplinary team, IORT was added to resolve the protrudent part of tumour on the surface of the pancreas.

A series of IRE and IORT procedures were performed with institutional ethics approval and informed consent from the patient. Six days after admission, she underwent IRE under general anaesthesia with tracheal intubation. A subcostal incision was made to expose her abdominal cavity, and the Kocher manoeuvre was subsequently performed to dissect the gastrocolic ligament and duodenal lateral peritoneum, which exposed the pancreatic tumour. Intraoperative ultrasound demonstrated that the lesion was approximately 3.2 cm × 3.0 cm × 2.5 cm in size. Dissection and pancreatic isolation (starting from the tail and moving to the right) revealed that the tumour had invaded the SMV, SMA, and common hepatic artery. In short, examination data were imported the into the system (Angiodynamics, Inc., Latham, NY, USA). The system calculated the

© AME Publishing Company.

ablation range and simulated the arrangement of ablation needles to make the ablation range completely. According to simulated needle diagram, three 19G needles were inserted under ultrasound guidance (*Figure 1A*) and the distance was 1.5–2.0 cm with electroporation defect of 1,500 volts/cm and 90 μsec wavelength. Needles were then withdrawn for stepwise ablation. For areas of the tumour that were not covered by the first ablation, needles could be reinserted to achieve total ablation. Since the tumour protruded from the surface of the pancreas, IORT was performed under the guidance of experts in the Department of Radiotherapy. The INTRABEAM system was applied into the surgical field, and a 6-cm flatbed source applicator was selected based on the appearance of the tumour bed (*Figure 1B*). After applying an aseptic protective cover, the source applicator was placed close to the tumour bed, and the patient's surrounding bowel and organs were protected using two layers of surgical gauze (approximately 2 cm thick). Radiotherapy was started using the following parameters: a radiotherapy dose of 5.48 Gy, an irradiation time of 17 minutes 49 seconds, an acceleration voltage of 50 kV, and an acceleration current of 40 μA. One drainage tube was placed at the treatment edge of pancreatic surface. Her abdominal cavity was closed after confirming that there was no bleeding or pancreatic leakage. The total intraoperative blood loss was 10 mL. The postoperative biopsy pathology diagnosed with moderately to poorly differentiated adenocarcinoma of the pancreas (*Figure 1D*).

The gastrointestinal function was recovered on postoperative day 3, and the gastric feeding tube was subsequently removed. On postoperative day 4, <30 mL of fluid (amylase 14 U/L) was drained via the abdominal drainage tube, which was removed before our patient was discharged on postoperative day 8. No surgery-related complications were observed, her postoperative CA19-9 level was 22.65 U/mL, and her abdominal pain based on the numerical rating scale for cancer pain had completely disappeared. Follow-up imaging was performed at the time of one month and then at 6-month intervals. S-1 was administered orally twice daily at a dose of 80–100 mg/day for 14 days, followed by 7 days without treatment. The pain was significantly relieved, sleep quality and self-care ability were improved after a series of treatments. She was followed up regularly. Unfortunately, the patient died 47 months after initial treatment due to a tumour recurrence, which resulted in intestinal obstruction. The recurrence occurred at the local site, with suspicious peritoneal metastases also noted.

Here, we present a case with PC who underwent IRE combined with IORT. The treatment effectively relieved the abdominal pain and did not cause postoperative complications. She exhibited prolonged survival and good health after leaving the hospital.

Compared with other conventional local thermal ablative techniques, IRE lacks a heat sink and can cause less injury to adjacent vital structures. It has also become increasingly popular for the treatment of multiple solid organ malignancies, such as liver and prostate malignancies. This strategy could improve the poor survival of patients with LAPC or local postresection recurrence of PC. Ruarus *et al.* suggested that the median survival in patients with primary LAPC after IRE exceeded the target median survival in those who received chemotherapy alone (5).

IORT techniques allow radiation therapy to be delivered at a dose while excluding part or all of the nearby dose-limiting sensitive structures. The effective radiation dose was increased, and the local tumour control was potentially improved. Many authors have studied the effects of IORT on advanced tumours and residual tumour sections after surgical resection. They concluded that it had an effect on residual tumour cells after incomplete resection and reduced the incidence of recurrence (6). The use of IORT has been offered for unresectable tumours to provide local tumour control and an effort to improve survival (7). Unlike external radiation therapy, IORT acts directly on the treatment site and can deliver a large radiation dose that provides ≥2 times the biological effect of separate doses and protects the surrounding organs and tissues (8). For LAPC, Nishimura *et al.* reported that the addition of IORT led to a significant improvement in pain relief compared to that in a control group (9). The INTRABEAM system for IORT produces softer, shallower, and lower-energy X-rays than does the Mobetron system. It has rapidly been adopted in surgery for breast cancer, vertebral metastasis and colorectal cancer because of its accuracy, minimal invasiveness and low depth of penetration.

In the present case, we used IRE combined with IORT for LAPC protruding from the surface of the pancreas. IRE can kill almost all tumour cells, and IORT can help to treat residual tumours. It is a valuable treatment option for patients with LAPC, and it is possible to combine these procedures with IRE ablation and the delivery of an IORT dose, which provides immediate stability, pain relief and sterilization of PCs. This application also broadens the potential applications of the INTRABEAM system. Song *et al.* reported a case report on the use of surgery with IORT and reported that it was safe to apply IORT using

© AME Publishing Company.

INTRABEAM radiation in LAPC patients (10). It has been reported that IORT after resection results in a median survival time of 19.1 months and 2-year local control of 83.7%, which was better than historical controls. However, since long-term experiences with IRE and IORT are not available at present, more cases and experimental evidence are needed to explore the underlying mechanisms involved.

The combination of IRE and IORT require further investigation through relevant fundamental research, and further validation with large sample data is still needed.

Acknowledgments

Funding: This work was supported by the Cancer Innovative Research Program of Sun Yat-sen University Cancer Center and 308-Program for Clinical Research of Sun Yat-sen University Cancer Center.

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article has undergone external peer review.

Peer Review File: Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-24-526/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-24-526/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the institutional board of Sun Yat-sen University Cancer Center (Approval No. SL-B2024-534-01) and informed consent was obtained from the guardian.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. CA Cancer J Clin 2022;72:7-33.
2. Kos B, Voigt P, Miklavcic D, et al. Careful treatment planning enables safe ablation of liver tumors adjacent to major blood vessels by percutaneous irreversible electroporation (IRE). Radiol Oncol 2015;49:234-41.
3. He C, Wang J, Zhang Y, et al. Comparison of combination therapies in the management of locally advanced pancreatic cancer: Induction chemotherapy followed by irreversible electroporation vs radiofrequency ablation. Cancer Med 2020;9:4699-710.
4. Ogawa K, Karasawa K, Ito Y, et al. Intraoperative radiotherapy for resected pancreatic cancer: a multi-institutional retrospective analysis of 210 patients. Int J Radiat Oncol Biol Phys 2010;77:734-42.
5. Ruarus AH, Vroomen LGPH, Geboers B, et al. Percutaneous Irreversible Electroporation in Locally Advanced and Recurrent Pancreatic Cancer (PANFIRE-2): A Multicenter, Prospective, Single-Arm, Phase II Study. Radiology 2020;294:212-20.
6. Calvo FA, Serrano J, Cambeiro M, et al. Intra-Operative Electron Radiation Therapy: An Update of the Evidence Collected in 40 Years to Search for Models for Electron-FLASH Studies. Cancers (Basel) 2022;14:3693.
7. Palta M, Willett C, Czito B. The role of intraoperative radiation therapy in patients with pancreatic cancer. Semin Radiat Oncol 2014;24:126-31.
8. Calvo FA, Meirino RM, Orecchia R. Intraoperative radiation therapy first part: rationale and techniques. Crit Rev Oncol Hematol 2006;59:106-15.
9. Nishimura Y, Hosotani R, Shibamoto Y, et al. External and intraoperative radiotherapy for resectable and unresectable pancreatic cancer: analysis of survival rates and complications. Int J Radiat Oncol Biol Phys 1997;39:39-49.
10. Song X, Shao Z, Liang H. Using the new INTRABEAM mobile intraoperative radiotherapy system during surgery for pancreatic cancer: a case report. J Med Case Rep 2019;13:23.

Cite this article as: Jiang L, Huang X, Hua X, Li Q, Zhang Y, Wang J, Li S. Treatment of locally advanced pancreatic cancer with irreversible electroporation and intraoperative radiotherapy. HepatoBiliary Surg Nutr 2024;13(6):1087-1090. doi: 10.21037/hbsn-24-526