Ultrasound–guided percutaneous laser ablation for pancreatic cancer: a new treatment option

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Research

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Abstract

Background & purpose: Most patients with pancreatic cancer (PC) suffer from an unresectable tumor at the time of diagnosis with limited treatment effectiveness. The purpose of this study is to investigate the feasibility and safety of percutaneous laser ablation (LA) for locally advanced and metastatic PC.

Methods: Between September 2016 and April 2018, nine patients (mean age, 65.2 ± 5.4 years; age range, 62–68 years) with histologically proved PC were prospectively included to undergo ultrasound-guided LA. Effect including safety, pain perception and survival were evaluated.

Results: Three patients were with locally advanced PC (stage III) and six with metastases (stage IV). All patients underwent LA in one session. The mean largest tumor diameter was 5.2±0.8 cm (range, 4.2-6.9cm). Ablation power of all patients was 5 W and the mean ablation energy was 8.3±2.4 KJ (range 4.4-12KJ). Mean ablation volume was 17.1±3.2ml (range 13.0-22.1ml), which reached 89.1±7.4% (range 80.2-98.0%) of tumor volume. After a median follow-up period of 9.7 months (range, 6-15 months), the median survival from diagnosis was 11.2 months. Four stage IV patients died during 6.5-12.5 months after LA because of one hepatic encephalopathy and three tumor progression. No major complications occurred. Pain symptom achieved significant remission ($P < 0.001$) and patients experienced ameliorative physical function after LA. Percutaneous LA for unresectable PC is generally well tolerated.

Conclusions: Preliminary results are encouraging with tumor size reducing and physical function significant improvement. US-guided percutaneous LA provides a new minimally invasive therapy modality for PC.

Introduction

Highlights

■Percutaneous laser ablation achieved 89.1±7.4% of pancreatic tumor necrosis.

■Median survival for unresectable pancreatic cancer after ablation was 10 months.

■Patients achieved significant pain and physical function amelioration after ablation.

Pancreatic cancer (PC) is the most lethal abdominal malignancy and one of leading cause of cancer-related death with a 5-year survival rate < 10% for all stages[1]. Because most patients suffer from a primarily locally unresectable tumor or with metastatic disease at the time of diagnosis, chemo- and radiotherapy so far have been as the major treatment modalities but with limited survival benefit and severe toxicity reaction. Minimally invasive ablation therapy has attracted great interest for the management of focal malignant disease during the past decade[2].Potential advantages of ablation

therapy include real-time imaging guidance, the ability to ablate tumor in patients who lose the surgical chance and reduced morbidity compared with surgery.

Several minimally invasive strategies including radiofrequency, high intensity focused ultrasound (HIFU), laser energy and cryoablation have been applied to pancreas in animal studies or limited clinical application[3–9]. Laser ablation (LA) is guided through an optic fiber and the absorption of laser energy within the tissue results in localised heating and cellular death. The main advantage of applying of neodymium-doped yttrium aluminumgarnet (Nd: YAG) LA is the less trauma with the use of fine needle guidance and more accurate thermal field control[3, 4]. LA has been used in many therapies such as retroperitoneal lymph nodes, prostate, thyroid and risky liver tumors[10–13]. However, lagging behind other ablation techniques, LA only achieved limited experimental results in porcine pancreas and few case reports on endoscopy-guided ablation of unresectable or recurrent pancreatic tumor[14–17].

The purpose of our prospective pilot study was to apply LA percutaneously under ultrasound (US) guidance to unresectable locally advanced and metastatic PC to establish the feasibility and obtain preliminary data on safety, quality of life (QOL) and pain perception.

Materials And Methods

Patients selection

The protocol was approved by our institutional review board. All participants provided written informed consent. Prospective study design and conduct were in accordance with good clinical practice and the Strengthening the Reporting of Observational Studies in Epidemiology statement for observational studies[18]. The funding organizations had no involvement in the design or conduct of this study, data management and analysis, or manuscript preparation and review or authorization for submission. The other authors declare no conflict of interest and had full control of inclusion of all study data and information. All patients were discussed and evaluated by our multidisciplinary hepato-pancreaticobiliary tumor board before inclusion. Inclusion criteria were patients with clinical unresectable locally advanced and metastatic (less than two metastatic organs occurring outside the pancreas) PC, lesions locating at the body or tail of pancreas, all the PC diagnosed based on the pathology obtained from US-guided biopsy, lesions visible on US with an acceptable and safe path between the lesion and skin, American Society of Anesthesiologists (ASA) grade of □-□. Tumor staging was defined as per the National Comprehensive Cancer Network (NCCN) staging system for PC (version1.2012)[19]. Exclusion criteria were patients who met the inclusion criteria but declined to participate in, uncontrolled or refractory ascites, ongoing obstructive jaundice, acute or active inflammatory and infectious lesions in any organ.

Between September 2016 and April 2018, nine patients (mean age, 65.2 ± 5.4 years; age range, 62–68 years) with histologically proved PC were prospectively included to undergo US-guided LA.

Preoperative preparation

Contrast-enhanced abdominal magnetic resonance imaging (MRI) and tumor marker CA 19 – 9 levels were obtained within 7 days before LA. Visual pain scores ranging from 0 to 10 were recorded. The QOL questionnaires (European Organization for Research and Treatment of Cancer QLQ-C30) at baseline were filled in by all the patients[20]. All the patients were administered somatostatin (Zhonghe, Hainan, China) at 12–24 hours before ablation to reduce the risk of pancreatitis and were administered Polyethylene Glycol Electrolytes Powder (Shutaishen, Beijing, China) at the night before LA to clean the bowel.

Equipment

All procedures were performed percutaneously with use of US scanner (Esaote, Genova, Italy) guidance with CA541 transducer with a 4-10-MHz frequency. Immediately prior to LA, contrast-enhanced US (CEUS) was used to determine the borders, locations and sizes of the PC. The contrast agent, 2.4 ml SonoVue (Bracco, Milan, Italy), was injected intravenously by bolus injection followed by a 5 ml saline flush. The relationship between PC and inferior vena cava, aorta, celiac axis, superior mesenteric vein artery and splenic artery was scanned. A Nd: YAG laser beam fiber ablation system (Echo Laser X4, Elestas.r. l. Florence, Italy) in a continuous mode was used, with a wave length of 1064 nm in which the penetration of light in the infrared spectrum is optimal. The whole equipment is shown in Fig. 1. The schematic diagram of laser ablation principle is shown in Fig. 2.

Ultrasound-guided LA procedure

The insertion route was carefully determined by US to avoid the normal pancreas, bowel, vessels, pancreatic duct and bile ducts. To reduce the repeated puncture, the route plan was inserted along the long axis of the tumor as far as possible. One or two 21G puncture needles were inserted into PC with the tip of needle 10 mm away from the distal borderline of tumor and with the shaft of needle 5–10 mm from the tumor's lateral border. Then a 300-μm diameter plane-cut quartz optical bare fiber was advanced through the sheath of the needle, and the sheath was withdrawn 10 mm to expose the 10-mm fiber. The output power of laser was set at 5W, and the energy was set for 1.5 KJ on each ablation site. If necessary, the needle and fiber were repositioned or pulled back to ablate the remaining part of the tumor. At the end of the ablations, the endoscopic ultrasound (EUS) revealed a hyperechoic area along the path of the probe surrounded by non-homogenous tissue with hyperechoic spots. The total delivered energy was automatically calculated by the equipment. Our aim was not to ablate the entire tumor but palliative tumor reduction with inactivating the tumor as much as possible, so only one or two laser fibers were used. The number was depended on the size of the PC and the relationship of lesion with adjacent tissues. If two fibers were inserted simultaneously during LA to obtain larger ablation zone, the inter-fiber distance of no more than 1.0 cm was suggested. Correct needle position and inter-fiber distance were verified by using US image. Upon completion of the ablation procedure, the CEUS scan was performed to confirm technical effect (absence of tumor enhancement). All the procedures were performed by experienced doctors under local anesthesia with good tolerance of the patients. For patients with metastases of liver and/or retroperitoneal lymph nodes, LA was also used to treat the metastatic lesion in the same session.

Assessment and follow-up

Technical success was defined as the operator was able to technically complete the ablation as planned. The main purpose of present PC treatment is to debulk the tumor rather than provide “radical treatment”, so technical efficacy namely complete ablation was not evaluated. Ablation effect evaluation was performed by three-dimensional (3D) visualization software. The MRI imaging data before and after LA were imported into the Merge eFilm Workstation (Merge Healthcare, Chicago, USA) and were analyzed by the 3D visualization software platform (Hokai, Zhuhai, China). Patient-specific anatomical information about tumors and surrounding vital structures was stereoscopically displayed. The tumor volume, stereo relationship between the tumor and surrounding organs, ablation field distribution was demonstrated precisely in the 3D visualization software before and after LA. And the volume of pancreas, tumor and ablation zone were calculated by the software. The following day, routine laboratory tests (tumor marker such as carbohydrate antigen[CA]19 – 9, amylase, and lipase levels) and contrast-enhanced MRI were performed to evaluate the ablation effect and detect potential complications. After discharge, contrast-enhanced MRI and laboratory tests were performed at 4 weeks after LA and then every 3 months. All follow-up scans were interpreted independently by two radiologists. The presence of local and distant tumor progression was ultimately determined by consensus. 3 Visual pain scores and the amount of administered pain medication were recorded. The QOL questionnaires were filled in by all the patients at 3 days,4 weeks and every 3 months after LA. One of the study coordinators noted study-related specifications before, during, and after the procedure, including the adverse events within 30 days from the procedure by using the Common Terminology Criteria of Adverse Events (version 4.0)[21].

Statistical Analysis

Continuous variables are summarized with standard descriptive statistics including means, standard deviations, medians, and ranges. Categoric variables are summarized as frequencies. The paired student t test was performed to compare the QOL and pain perception at baseline versus that at 4-week and 6-month follow-up. In addition, the Wilcoxon signed rank test was also used to compare amylase and lipase values before LA against values at 1 week after LA. Because of the small sample size, we didn't use the Kaplan-Meier method to analyze the disease-free survival and overall survival. P <.05 was considered indicative of a statistically significant difference.

Results

Baseline characteristics are summarized in Table 1. The mean largest tumor diameter was 5.2 ± 0.8 cm (range, 4.2–6.9 cm). One lesion located at the body of pancreas and three at tails and three at both bodies and tails. None of the patients had previously undergone radiation therapy and chemotherapy. The median time from diagnosis to LA was 26 days (range, 9–53 days). Three patients were with locally advanced PC (stage III), three with liver metastases (stage IV) and three with both liver and retroperitoneal lymph node metastases (stage IV). The total number of metastatic lesions for each stage IV patient were less than three and the size for each lesion was less than 2 cm. For these eight patients, the aim of LA was to decrease the tumor burden and manage the pain. No patient was lost to follow-up. Successful

fiber placement and laser delivery) were achieved in all patients. Fibers were placed ventrally in all the patients with supine position. The number of fibers used was one in two patients and two in five patients. A fiber pullback was performed in all the patients. The mean number of the applicator being inserted into the lesion independently of the pulling back maneuvers was 2.8 ± 0.9 (range 2–4). Ablation power of all patients was 5 W and the mean ablation energy was 8.3 ± 2.4 KJ (range 4.4-12KJ) with the mean ablation time of 26.9 ± 8.8 min (range 14.8–33.3 min).

Table 1
Baseline patient characteristics

Variables	Training Set (n = 1024)	Validation Set (n = 1006)	*P* Value
Mean age ± SD (years)(range)	58.3 ± 11.2 (24–91)	58.3 ± 10.9 (23–86)	0.824[a]
Sex			0.139[b]
Male	837 (78.5)	808(82.5)	
Female	187 (21.5)	198(17.5)	
Performance status			0.898[b]
0	913 (95.0)	879 (94.7)	
1	111 (5.0)	127 (5.3)	
Comorbidities			0.519[b]
Absence	410(14.6)	48(13.1)	
Presence	614(85.4)	318(86.9)	
Etiology			0.333[b]
HBV positive	645(78.3)	632(78.4)	
Other	379(11.1)	374(8.2)	
Cirrhosis			0.484[b]
Absence	94(9.3)	89(7.9)	
Presence	930(90.7)	917(92.1)	
CTP grade			0.648[b]
A	976(95.3)	967(96.1)	
B	48(4.7)	39(3.9)	
Median AFP level (ng/ml)(range)	234.6 (3.2-1381.2)	221.9 (4.8-762.8)	0.254[a]
Liver cancer			0.345[b]
HCC	1007 (98.3)	993 (98.7)	
ICC	17 (1.7)	13 (1.3)	
Median maximal tumour diameter (cm) (range)	2.8 (0.7–9.8)	2.9 (0.8–11.2)	0.188[a]

Variables	Training Set (n = 1024)	Validation Set (n = 1006)	*P* Value
No. of tumours	1670	1578	0.139[b]
Single	578(78.8)	552(58.8)	
Multiple	446(21.2)	154(41.2)	
Subcapsular			0.445[b]
Presence	177(39.6)	181(40.3)	
Absence	847(60.4)	825(59.7)	
Ablation modality			0.801[b]
RFA	162 (15.8)	167 (16.6)	
MWA	862 (84.2)	839 (83.4)	
Ablation sessions[§#]	1945	1872	0.578[b]
1	834(80.8)	801(81.6)	
> 1	190(19.2)	205(18.4)	
Median platelet counts (× 10^9)(range)	109(67–459)	110(75–751)	0.562[a]
Mean INR ± SD(range)	1.13 ± 0.21 (0.87–1.38)	1.15 ± 0.32 (0.89–1.49)	0.898[a]
Seeding[§]	15/1024 (0.9)	9/1006 (0.8)	0.867[b]
Technique effectiveness	1000/1024 (97.6)	985/1006 (97.9)	0.762[b]
Follow-up (years)			0.787[a]
Median	25.6	27.0	
Range	4.3–90.2	6.2–91.3	

Note.—Except where indicated, data are numbers of patients. Data in parentheses are percentages and were calculated by using the total number of patients in each group as the denominator. SD = standard deviation. $P < 0.05$ indicated a significant difference.

[a]Student t test

[b]Pearson χ^2 test

Data are the number of treatments.

§Data in parentheses are percentages.

HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; MWA: microwave ablation; RFA: radiofrequency ablation; HBV: hepatitis B virus; CTP:child-turcotte-pugh; AFP:α-fetoprotein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; INR: international normalized.

Progression and Survival

Progression and Survival outcomes are summarized in Table 2. Two patients received chemotherapy of eight cycles with gemcitabine after LA and three received five cycles. The neuroendocrine cancer patient and one stage IV patient refused to receive any therapy after LA. All the patients occurred local and liver tumor progression during the follow-up. The mean volume of local tumor progression was 2.7 ± 1.1 ml (range 2.5–4.2 ml). Four stage IV patients died at 6.5, 7.7, 9.4 and 12.5 months after LA because of one hepatic encephalopathy and three tumor progression, respectively. The other five patients survived during follow-up. After a median follow-up period of 9.7 months (range, 6–15 months), the median OS from diagnosis was 11.2 months (95% confidence interval [CI]: 7.2 months, 14.4 months) and the median OS from LA was 10.2 months (95% CI: 5.0 months, 13.3 months). Comparation of another ablation method in previous studies was showed in Table 3.

Table 2

Characteristics of the 15 patients who had seeding after thermal ablation

No	Age/sex	TS	Size (cm)	Number	TA	DD	SL	ST(mo)	STM	OS(mo)
1	65/M	HCC	4.5	1	B	M	AM	17.7	MWA	36.8
2	58/M	HCC	6.4	1	B	M	AM	4.2	MWA	74.2
3	67/M	HCC	3.5	1	B	M	AM	17.5	MWA	52.6
4	59/M	ICC	6.3	1	B	H	AM	6.3	RFA	14.7
5	48/M	ICC	2.7	2	B	M	AM	22.1	RFA	37.5
6	61/M	HCC	4.9	1	B	H	TM	12.0	SR	32.4
7	71/M	HCC	4.0	1	C	M	AM	30.5	MWA	54.2
8	66/M	HCC	3.7	1	B	M	AM	37.9	MWA	49.0
9	41/M	HCC	2.9	1	B	M	TM	34.3	MWA	44.7
10	47/F	HCC	3.3	2	B	H	AM	12.2	MWA	53.5
11	72/M	HCC	4.7	1	B	H	AM	15.6	SR	22.9
12	78/M	HCC	2.0	1	B	H	AM	24.0	MWA	35.6
13	51/M	ICC	2.3	1	B	H	TM	30.8	MWA	43.2
14	48/M	HCC	2.5	1	C	M	TM	17.8	MWA	67.3
15	61/M	HCC	2.5	1	B	H	TM	28.0	MWA	58.9

TS: Tumor type; TA: Type of hepatitis; B: hepatitis B virus; C: hepatitis C virus; DD: Differentiated degree; M: Middle; H:High; SL:Seeding location; ST:Seeding time; STM: Seeding treatment modality; OS:Overall survival; HCC: Hepatocellular carcinoma; ICC: Intrahepatic cholangiocarcinoma; AM: Abdominal wall; TM:Thoracic wall; MWA: Microwave ablation; RFA: Radiofrequency ablation; SR:Surgical resection.

Table 3
Univariate analysis for seeding after thermal ablation for liver malignancy

Factors	No. of Patients	Univariate Analysis	
		HR (95% CI)	*P* value*
Age (years)		1.908 (0.948, 3.838)	0.270
< 65	412		
≥ 65	612		
Gender		0.839 (0.462, 1.524)	0.565
Male	837		
Female	187		
Comorbidities		2.129 (0.651, 6.961)	0.211
Absence	410		
Presence	614		
Etiology			
HBV	645	3.782 (0.703, 5.141)	0.516
Other	379		
Cirrhosis		1.404 (0.508, 3.875)	0.513
Absence	94		
Presence	930		
Tumor size(cm)		2.072 (1.250, 3.436)	0.005
< 5	478		
5–12	546		
No. of tumours		5.627 (2.992, 10.581)	0.043
Single	578		
Multiple	446		
Subcapsular		3.110 (1.097, 8.817)	0.003
Absence	177		
Presence	847		
Ablation modality		1.227 (0.907, 1.661)	0.185

Factors	No. of Patients	Univariate Analysis	
		HR (95% CI)	*P* value*
RFA	373		
MWA	167		
AFP		1.428 (0.732, 2.788)	0.026
≤ 20	285		
> 20	255		
INR		2.012 (1.582, 5.760)	0.007
≤ 1.1	316		
> 1.1	708		
CTP grade		1.110 (0.497, 3.817)	0.233
A	976		
B	48		
Ablation sessions		3.245(1.432, 5.212)	0.033
1	823		
> 1	201		

Note.—Data in parentheses are 95% confidence intervals.**P* values were determined with Cox proportional hazards regression models. *P* < 0.05 indicated a significant difference.HR: hazard ratio;CI: confidence intervals□HBV: hepatitis B virus; CTP:child-turcotte-pugh; AFP:α-fetoprotein; INR: international normalized ratio.

Table 4

Multivariate analysis of seeding after thermal abaltion with Cox proportional hazards model

Variable	β Level	SE	Wald	*P* Value	HR	95% CI	
						Upper	Lower
Tumor diameter	1.568	0.537	10.850	0.005	5.087	1.964	17.226
Subcapsular	1.854	0.483	13.590	< 0.001	6.520	2.188	14.437
AFP	1.308	0.575	3.940	0.017	2.977	1.757	4.262
INR	-1.113	0.489	3.357	0.023	0.329	0.126	0.856

MWA: microwave ablation; HR: hazard ratio; CI: confidence intervals; AFP:α-fetoprotein; INR: international normalized ratio.

Ablation effect evaluation

The metastases of liver and retroperitoneal lymph nodes were treated by LA during the PC ablation procedure. The detailed methods were described as that in the literatures[10, 22]. The median postprocedural hospital stay was 5 days (range 4–9 days). Mean pancreas volume was 93.2 ± 20.4 ml (range 71.1-123.2 ml). Mean tumor volume was 18.1 ± 4.6 ml (range 14.5–23.1 ml) and ablation volume was 16.0 ± 4.4 ml (range 13.0-22.1 ml), which reached 89.1 ± 7.4% (range 80.2–98.0%) of tumor volume. All the volumes were evaluated by 3D visualisation software. Figures 3 and 4 shows two cases of typical imaging characteristics of the tumor in pancreatic body and tail respectively before, during and after LA.

Post procedural pain and QOL

All the patients completed the QOL and pain questionnaires before LA, and all completed the questionnaires at 4 weeks and every 3 months after LA. One week after LA, the reported pain was moderate, with a median visual analog scale score of 3 ± 1.2 (range, 2–5) compared with baseline of 7.2 ± 0.8 (range, 6–8) ($P < 0.001$). Pain control was managed with acetaminophen combined with a nonsteroidal anti-inflammatory drug if needed. During the follow-up, no patients reported the deterioration for the pain compared with one week after LA. The QOL questionnaires revealed that after LA, and showed in Supplement Table 1.

Complications

No patients died within 90 days after LA. No grade III, IV or V complications including pancreatitis, bile leakage and biliary obstruction occurred. Gastrointestinal complications such as nausea, abdominal pain, loss of appetite was observed in all the patients within 3 days after LA. Two patients developed localized pancreatic juice effusion (2.4 × 2.3 cm and 2.0 × 1.8 cm, respectively) 3 days after LA with the symptom of mild pain, and the cysts were absorbed or decreased in 3 months after LA without any treatment.

Discussion

PC is a dismal disease associated with a very poor prognosis especially for late stages, despite multimodal therapy. In the current study, we treated local advanced and metastatic PC by a Nd:YAG laser-beam fiber ablation and found good local response of the malignancies at the median 9.7-month follow-up. LA is a novel technique to manage PC. In 2010, the first LA of pancreas study on 8 healthy pigs was performed by means of endoscopic US guidance[14]. Currently there are four clinical case report papers that reported the initial results of the method with the enrolled patient number of 1, 1, 3 and 9. [14–17] They all showed the technique was safe and useful for unresectable or recurrent PC patients under endoscopic US or per-oral pancreatoscopy guidance. For the study with 9 patients by Di Matteo FM[14], the median lesion size was 35.4 mm (range 21–45 mm). The patients were performed endoscopic US guided LA with the median OS of 7.4 months. To the best of our knowledge, this is the first report in the treatment of PC patients by percutaneous LA.

The American Joint Committee on Cancer (AJCC) staging system is the most widely used system to stage pancreatic cancer, which provides the basis for evaluating the resectability of the cancer and

stratifying survival by stage[23]. The unresectable categories include the subset of stage III that is defined as locally advanced and Stage IV as metastatic PC. According to the National Comprehensive Cancer Network guideline, the recommended treatment for unresectable PC were chemotherapy or chemoradiotherapy. Ablation technique was not recommended in the NCCN guideline for PC treatment, though it has achieved a vital role in the management of several malignancies such as hepatocellular carcinoma, hepatic metastatic lesions, and renal cell carcinoma for the advantage of minimally invasion and effectiveness. PC therapy is an arduous challenge for thermal ablation from anatomical consideration. Only limited studies have reported the application of ablation in experimental and clinical setting in the management of solid and cystic PC, including radiofrequency, microwave, ethanol ablation, high-intensity focused US, cryoablation and irreversible electroporation technique[5, 6, 9, 24–27]. Among them, radiofrequency, cryoablation and ethanol ablation were most commonly used methods for unresectable PC[25].

LA as one of the thermal therapies, it induces tumor cellular necrosis due to a localized high temperature increase by the absorption of laser energy within the tissue. Theoretically, LA shares some advantages for PC therapy. PC is physically diffuse and extends retroperitoneally. It can be traversed by the pancreatic duct and is closely related to the distal common bile duct, duodenum, stomach, transverse colon and abdominal blood vessels. The major difficulty of PC ablation in the risks of inadvertent thermal injury for adjacent tissues and almost impossibility of complete ablation of all tumor bulk. Laser can create accurate, predictable, and reproducible ablation zones that induce minimal changes outside the targeted ablation zone[10, 28]. It uses a 21-Gauge guidance needle as the ethanol ablation, which avoids the larger diameter of the radiofrequency or cryoablation needle puncture and reduces potential injury to gastrointestinal tract. And different from ethanol ablation that produces liquid distribution non-uniformly in the tumor and the limited ablation area, LA can induce a form of controlled, well-defined ablation area by fine optical fibers. These characteristics may offer potential advantages over other ablative techniques for PC treatment.

Majority of literatures reported the guidance approach of PC ablation were intra-operation and endosonography[25], which allowed a safer approach to target pancreatic lesions that located at deep retroperitoneal cavity. It is extremely difficult to reach PC clearly by a percutaneous approach by obtaining real-time imaging. In the current study, we tried to use US to percutaneously guide the insertion of Nd: YAG laser fibers. Results verified that percutaneous ablation under US guidance is possible to choose a safe route, and real-time US imaging can track the needle and thermal field. No significant puncture and ablation-related major complications occurred. Moreover, CEUS was used to evaluate ablation effect immediately and decisions on whether additional LA is required can be made immediately. This provided a potential of more minimal invasive technique for PC therapy.

We sum up our initial experience of percutaneous LA of PC as follows. (1) We choose lesions at body and tail of pancreas as indication in this pilot study. Such tumors had less encasement of abdominal blood vessel and were far from bile duct and duodenum, which may be safer for percutaneous ablation. (2) Gastrointestinal tract shielding is a major difficulty for percutaneous ablation. Therefore, we cleaned the

intestines by using laxative at the night before LA and performed local anesthesia to relieve flatulence induced by sedation anesthesia. That may provide a clear puncture route on US imaging. (3) According to reported results of ablation of PC in recent 5 years, the ablation related mortality was 0–3% and morbidity was 3.5–28%[25]. All of our patients achieved safe therapies without any major complication even if by percutaneous approach, which may be attribute to careful indication selection, precise US guidance and fiber placement. (4) For patients with locally advanced and metastatic PC, the median survival in most historical studies ranges from 8–12 and 5–7 months, respectively[23]. Our study showed comparable results, but the patients shared a relatively good performance status and quality of life from LA, which avoid the ethanol ablation of celiac plexus to control pain.

Our study had several limitations. First, our population size was small, which was compatible with a pilot study. Second, we only selected tumors at body and tail of pancreas as indication. Future plans will enroll the tumors at head of pancreas. Third, we used the 3D visualization software only to calculate the ablation volume ratio and observe residual tumor stereoscopically. The technique can also be applied in planning and navigating of LA to achieve better PC therapy results in the future. A larger trial is planned to more rigorously investigate cancer-related outcomes.

Conclusions

In conclusion, percutaneous LA for locally advanced and metastatic PC appears to be a safe and feasible focal therapy option with minimal invasion. The technique shows an encouraging pain control effect and the results support the setup of clinical trials with large sample to assess the efficacy of LA for unresectable PC patients.

Declarations

Ethics approval and consent to participate

The ethics committee board of the Chinese PLA General Hospital, approved the use of patients with pancreatic cancer after LA for this study.

Availability of data and materials

Please contact the corresponding author for all data requests.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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Authors' contribution

Dr Yu and Dr Liang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Liang, Yu Jie.

Acquisition of data: Liang, Yu, Han, An, Dong.

Analysis and interpretation of data: Yu, An, Feng, Xu.

Drafting of the manuscript: Yu.

Critical revision of the manuscript for important intellectual content: Liang.

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Figures

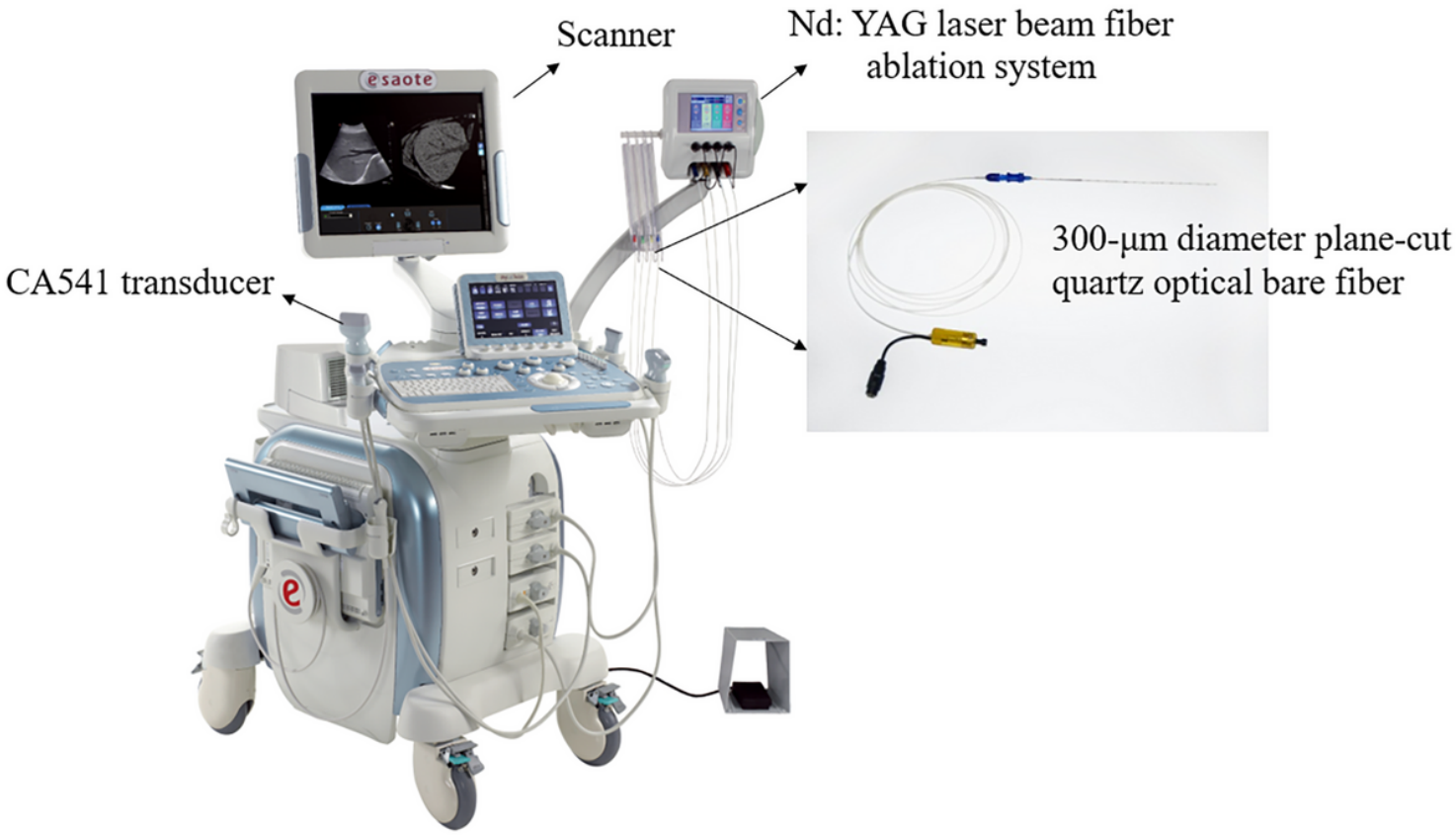

Figure 1

Introduction to the composition of the ultrasonic integrated laser system.

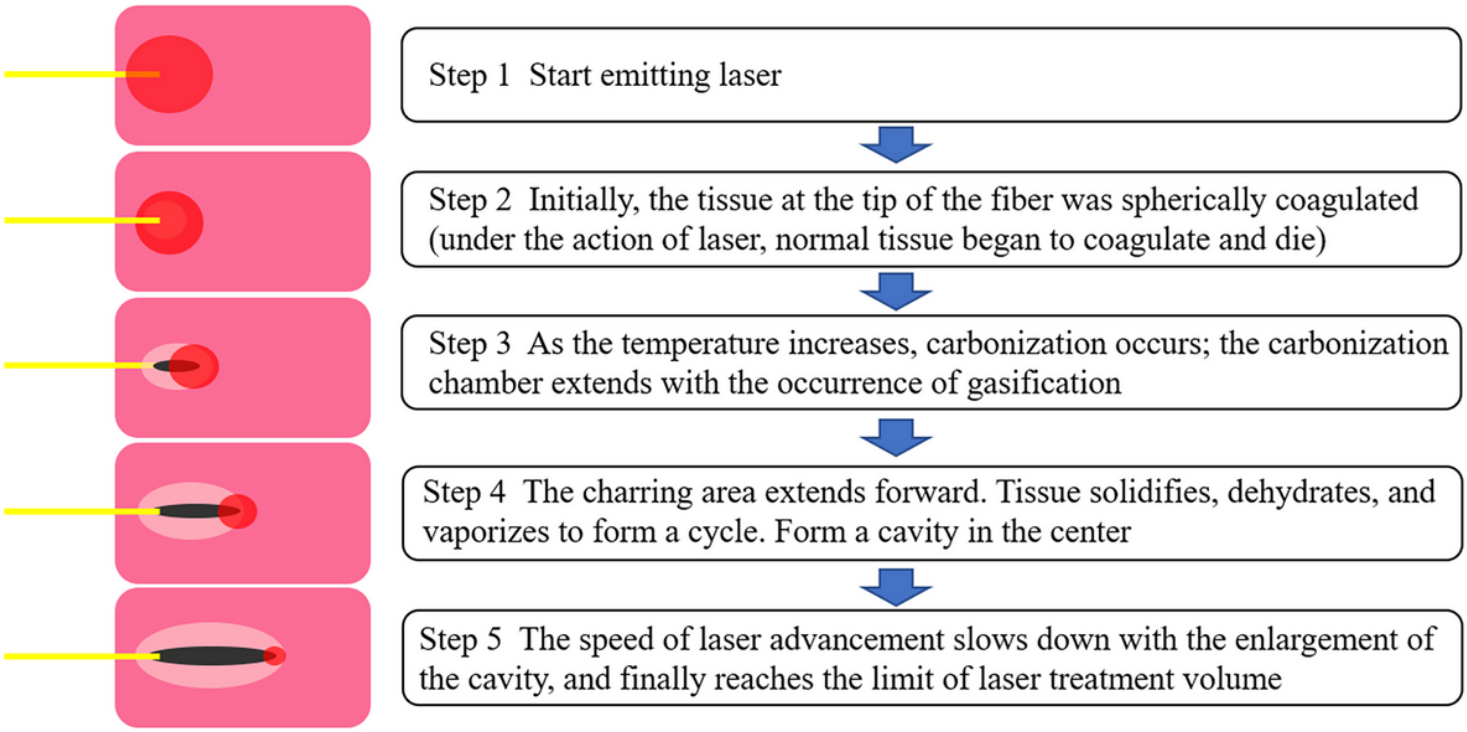

Figure 2

Laser ablation principle diagram.

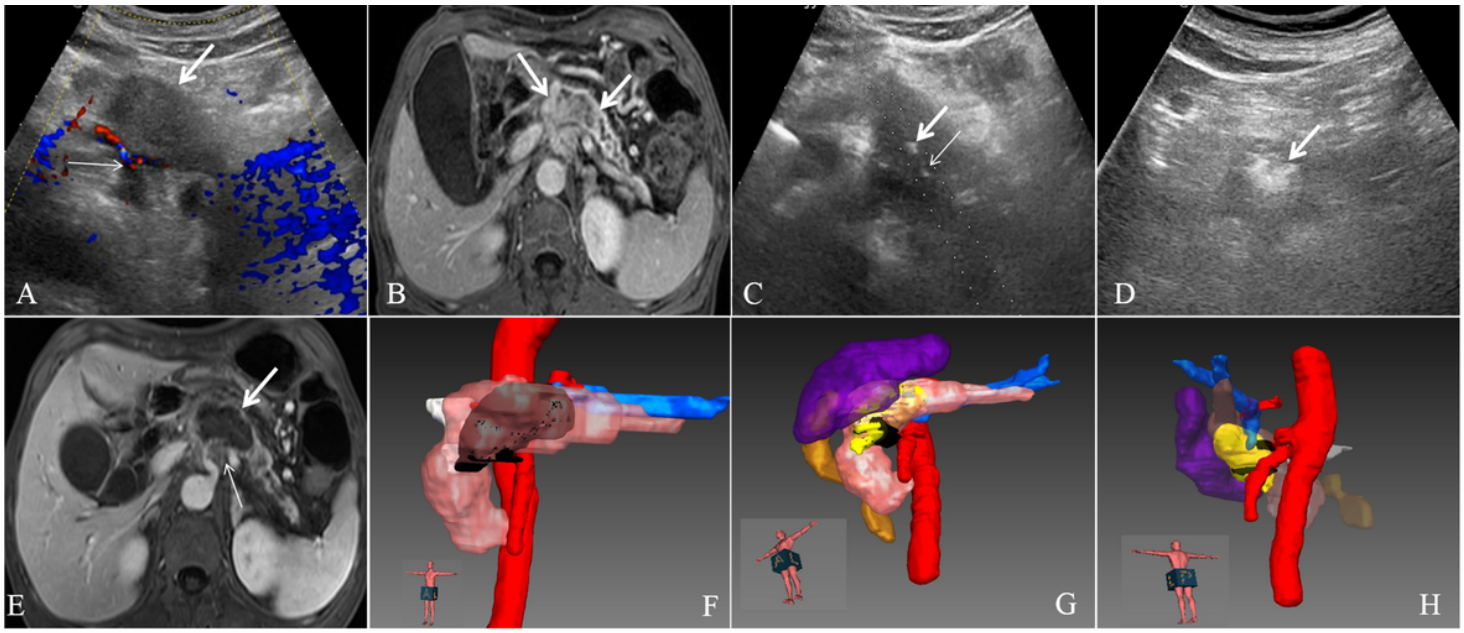

Figure 3

Transverse images in a 64-year-old man with a 4.9×3.2 cm cancer in pancreatic neck treated with laser ablation. A, Pre-ablation ultrasound (US) scan shows one hypoechoic lesion (arrows) extends into the celiac axis (fine arrows) on color doppler flow imaging. B, Pre-ablation contrast enhanced magnetic resonance imaging (MRI) scan shows the lesion is heterogeneous hyperintense (arrow). C, During the ablation procedure with the patient in a supine position, the tips of guidance needle (arrow) and the fiber (fine arrows) can be seen in the tumor on US scan. D, US scan shows the hyperechoic zone (arrow) produced by laser ablation. E, On contrast-enhanced MRI scan obtained 3 days after ablation, no enhancement is seen in the ablation zone (arrows) and a little residual tumor with hypointense is seen adjacent to celiac axis(fine arrows).F, The pre-treatment three dimentional visualization ablation treatment planning (3DVATP) software stereo display of the relationship between the tumor (black) and surrounding organs (red, abdominal aorta and celiac axis; pink, pancreas; blue, splenic vein; white, superior mesenteric vein). G, After rotating 90 degrees, the (3DVATP) software stereo display of the ablation zone (yellow) overlapping the majority of the tumor volume. The dorsal residual tumor is black; (purple, stomach; brown, duodenum). H, After rotating 180 degrees, the dorsal residual tumor was seen clearly adjacent to celiac axis (red). The system calculates the volumes of the tumor and ablation zone are 23.1ml and 22.1ml, respectively.

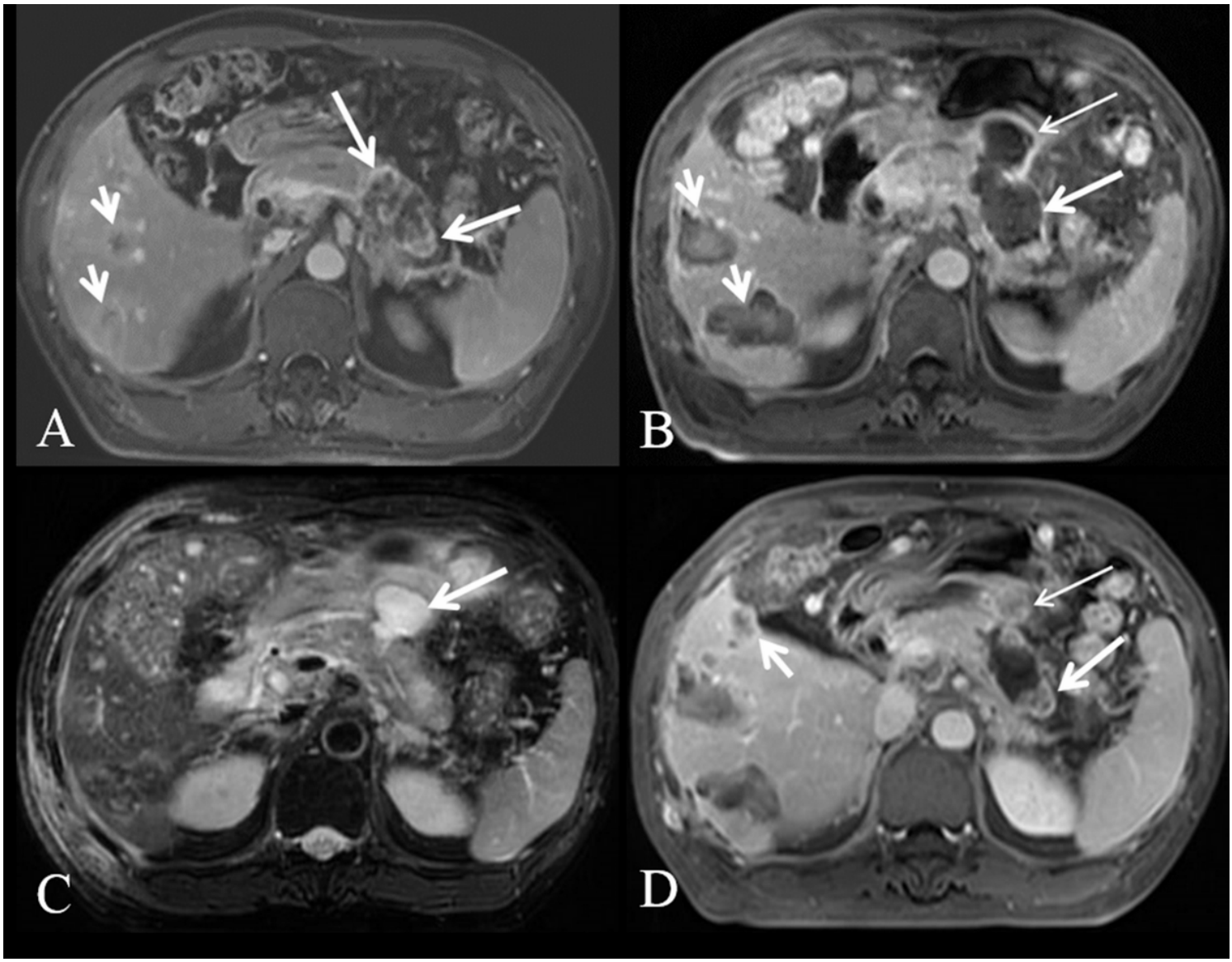

Figure 4

Transverse images in a 68-year-old man with a 4.2×2.5 cm cancer in pancreatic tail and two liver metastases (<2.0 cm in largest size) treated with laser ablation. A, Preablation contrast enhanced MRI scan shows one heterogeneous hypointense lesion (big arrows) in the pancreas and two in the liver (small arrows).B, On contrast-enhanced MRI scan obtained 7 days after ablation, no enhancement is seen in the ablation zone (big arrow) of pancreas and before the ablation zone(fine arrow). The liver ablation also shows no enhancement (small arrows). C, T2-weighted MRI reveals hyperintense lesion (arrow), which is typical for fluid collection and no enhancement on contrast enhanced MRI. It is diagnosed as localized pancreatic juice effusion. D, On contrast-enhanced MRI scan obtained 3months after ablation, small hypointense lesion is seen in the pancreatic tail (big arrow) and liver (small arrows), which present tumor progression. The localized pancreatic juice effusion (fine arrow) shows hypointense and shrinking. According to the calculation by the three dimentional visualization software, the volumes of the pancreatic tumor and ablation zone are 14.5 ml and 14.2ml, and the volume of progressed tumor is 1.1ml.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryData.pdf