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See Materials and Methods for pertinent disclosures.

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# Feasibility of US-guided High-Intensity Focused Ultrasound Treatment in Patients with Advanced Pancreatic Cancer: Initial Experience[1]

The study was approved by the university ethics committee, and informed consent was obtained from all patients. The purpose of this study was to prospectively evaluate ultrasonographically guided high-intensity focused ultrasound in the treatment of patients with advanced-stage pancreatic cancer. Eight patients underwent high-intensity focused ultrasound ablation, and laboratory and radiologic examinations were performed after intervention. Changes in symptoms and survival time were noted at follow-up. No complications were observed, and preexisting severe back pain disappeared after intervention. Follow-up images revealed an absence of tumor blood supply and shrinkage of the ablated tumor. Four patients died, and four patients were alive at the time of this writing, with a median survival time of 11.25 months. The authors conclude that high-intensity focused ultrasound ablation is safe and feasible in the treatment of advanced pancreatic cancer.


Carcinoma of the exocrine pancreas is the fourth leading cause of cancer-related death in the United States and the Western world. In 2002, 30 300 new cases were diagnosed for the United Sates, with 29 700 associated deaths (1). Because of the frequent delay in diagnosis, approximately 80% of patients have unresectable disease at presentation (2). Therefore, patients with locally advanced pancreatic cancer predominate in clinical practice. Unfortunately, until now no effective modality has been identified for the treatment of patients with locally advanced disease, although some studies have shown that chemoradiation offers a limited survival benefit (3,4). The median survival time is 6–10 months for patients with locally advanced pancreatic cancer and 3–6 months for patients with metastatic disease.

During the past decade, minimally invasive therapies have been developed as alternative modalities for unresectable tumors. These include laser therapy (5), cryotherapy (6), radiofrequency ablation (7), microwave therapy (8), and high-intensity focused ultrasound (9), all of which deliver various kinds of energy to induce coagulative necrosis of a target tumor. The clinical applications of these modalities are increasing, and they may eventually play an important role in some patients who are not candidates for surgical resection (10).

High-intensity focused ultrasound ablation is a noninvasive modality for the treatment of localized tumors. An ultrasound beam can be focused as it passes through soft tissue. This enables the use of an external ultrasound energy source to induce thermal ablation of a tumor at a depth through the intact skin. Under the guidance of real-time ultrasonographic (US) imaging, the motion of a therapeutic transducer can facilitate ablation of a three-dimensional target. The main advantages of high-intensity focused ultrasound are that it is noninvasive, it is conformal, and it enables ablation of large-volume tumors. In the past decade, this technique has been used to treat patients with benign prostatic hyperplasia (11–13) and localized prostate cancer (14–16) by using transrectal

high-intensity focused ultrasound devices. More recently, extracorporeal high-intensity focused ultrasound has been used to treat patients with various kinds of malignancies, including those of the liver, breast, kidney, bone, and soft tissue (17–19). The purpose of this study was to prospectively evaluate US-guided high-intensity focused ultrasound in the treatment of patients with advanced-stage pancreatic cancer.

## Materials and Methods

F.W. and W.Z.C. are shareholders in and consultants to Chongqing Haifu, Chongqing, China. Z.B.W. is a shareholder in and full-time employee of Chongqing Haifu. J.B. is a shareholder in Chongqing Haifu. J.Z.Z. is a consultant to Chongqing Haifu.

### Patients

From December 2000 to September 2002, eight consecutive patients were enrolled in this prospective clinical trial, which was approved by the ethics committee at our institution. Informed consent was obtained from all patients at enrollment.

All patients were initially evaluated by a team to determine suitability for surgery. This team consisted of three senior surgeons, a senior oncologist, and a senior interventional radiologist, each of whom had more than 20 years of clinical experience. They were not authors of this study, and a consensus regarding each patient's disease state was reached. Patients were judged to be unsuitable for surgery on the basis of tumor location, the tumor's proximity to major vascular structures, and the patient's inability to tolerate surgery for pancreatic disease. Patients who were not considered to be candidates for surgical resection were referred to this trial. Patients were selected for this study if they met the following selection criteria: The diagnosis of pancreatic cancer was confirmed with either biopsy during initial laparotomy or US-guided fine-needle biopsy, the patient was not considered to be a candidate for pancreaticoduodenectomy on the basis of surgical consultation, the lesion was located mainly in either the pancreatic body or the pancreatic tail (because high-intensity focused ultrasound may damage the biliary duct located in the pancreatic head), the lesion was detectable at US, the patient had a Karnofsky performance scale score of at least 70%, and no palliative antitumor treatments had been performed in the previous 3 months.

Patients with unstable hematogenic parameters and active infection were excluded from this study. In addition, patients were excluded if the lesion was undetectable at US, the lesion was located in the pancreatic head, the tumor invaded the duodenal wall, or the patient had jaundice owing to biliary obstruction. Twenty-three patients were initially judged to have met the inclusion criteria; eight patients (35%) were enrolled in this study. The remaining 15 patients (65%) were excluded from the study because the lesion was located in the pancreatic head ($n = 8$), the patient had obstructive jaundice ($n = 4$), the tumor invaded the duodenal wall ($n = 2$), or the patient had severe lung infection ($n = 1$).

Patients were enrolled consecutively at clinical presentation and ranged in age from 48 to 86 years (mean, 62 years). The diagnosis of pancreatic cancer was confirmed with either biopsy performed during initial laparotomy ($n = 2$) or US-guided fine-needle biopsy ($n = 6$) before high-intensity focused ultrasound. Seven patients had ductal adenocarcinoma, and one patient had mucinous adenocarcinoma. In the two patients, a planned surgical resection was not performed during laparotomy because the tumor was close to major vascular vessels. On the basis of findings of either computed tomography (CT) or magnetic resonance (MR) imaging, three patients had stage III disease and five had stage IV disease according to the TNM staging system. Before entry into the study, three patients had undergone no previous intervention and five had undergone conventional treatments, which included nontherapeutic laparotomy (2 and 4 months before high-intensity focused ultrasound) in two patients, transcatheter arterial chemotherapy (4 and 5 months before high-intensity focused ultrasound) in two patients, and local radiation therapy (4 months before high-intensity focused ultrasound) in one patient. There were no positive responses from the previous treatments—in particular, there was no relief of cancer-related pain. Five patients had metastasis to the liver, and one patient had metastasis to the bone. All patients had constant pain of visceral origin localized to the region of the middle and upper back and required appropriate pain medications before high-intensity focused ultrasound. The diameter of the primary tumor ranged from 4.5–8.0 × 4.0–7.5 cm (mean, 5.89 × 5.40 cm). The characteristics of each patient and tumor are summarized in Table 1.

### High-Intensity Focused Ultrasound System and Treatment

The same therapeutic high-intensity focused ultrasound system (Chongqing Haifu HIFU; Chongqing Haifu, Chongqing, China) was used to treat all patients under the guidance of real-time US. The treatment procedure has been described in detail previously (17,19–22). Briefly, therapeutic ultrasound energy is produced by a 12-cm-diameter transducer with a focal length of 135 mm operating at a frequency of 0.8 MHz. The focal region is 9.8 mm along the beam axis and 1.3 mm in the transverse direction. In the center of the high-intensity focused ultrasound transducer, a 3.5–5.0-MHz diagnostic US probe is used as the real-time imaging unit of the system for targeting the tumor to be treated, guiding ultrasound energy deposition, and assessing coagulation necrosis during the high-intensity focused ultrasound procedure. The integrated transducer is mounted in a water bag filled with degassed water. With use of computer control, the integrated transducer can be moved smoothly in six directions, including three orthogonal directions (x, y, z), rotation along the ultrasound beam axis (θ), and rotation along the long (γ) or short (φ) axis of the bed.

High-intensity focused ultrasound treatment was performed with patients under anesthesia by two doctors together (F.W., H.Z.). Five patients received general anesthesia, and three received epidural anesthesia. After suitable anesthesia was achieved, the patients were carefully positioned prone. The abdominal skin overlying the lesion was in contact with degassed water. Real-time US was used to target the tumor by moving the integrated probe, and the tumor was divided into sections with 5-mm separation. By means of scanning the high-intensity focused ultrasound beam, the targeted regions in each section were completely ablated. This process was repeated on a section-by-section basis to achieve complete ablation of the tumor volume in a manner similar to cutting away slices of bread. During high-intensity focused ultrasound ablation, the real-time US scans obtained immediately before and after individual exposures were compared to determine whether the echogenic changes of the high-intensity focused ultrasound–treated region, which are indicative of the extent of coagulation necrosis, had cov-

**TABLE 1**
**Summary of Patient and Tumor Characteristics**

| Patient No./Age (y)/Sex | Tumor Location | Diameter of Primary Tumor (cm) | Symptoms at Presentation* | TNM Stage | Metastasis | Prior Therapy |
|---|---|---|---|---|---|---|
| 1/78/M | Body and head | 7.5 × 6.5 | Severe pain, weight loss | III | None | None |
| 2/86/M | Body and tail | 5.0 × 4.5 | Severe pain, weight loss, abdominal mass | IV | Extensive liver and bone metastases | None |
| 3/54/M | Body and head | 8.0 × 7.5 | Severe pain | IV | Three liver metastases | Exploratory surgery |
| 4/58/M | Body and tail | 6.6 × 6.0 | Moderate pain | III | None | Transcatheter arterial chemotherapy† |
| 5/56/F | Body and tail | 6.0 × 5.0 | Moderate pain | IV | Multiple liver metastases | Local radiation therapy |
| 6/48/M | Body | 4.5 × 4.5 | Moderate pain | IV | Single liver metastasis | Exploratory surgery |
| 7/54/M | Body and tail | 5.0 × 5.0 | Moderate pain | IV | Multiple liver metastases | Transcatheter arterial chemotherapy† |
| 8/62/F | Body | 4.5 × 4.0 | Moderate pain | III | None | None |

* Moderate pain necessitated ibuprofen analgesia, and severe pain necessitated oral opiate analgesia.
† Two grams of 5-fluorouracil was infused via the celiac artery and the superior mesenteric artery.

ered the desired treatment area. The patient was monitored to track blood pressure, pulse, respiration rate, temperature, and peripheral oxygenation during the high-intensity focused ultrasound procedure.

### Pretreatment Preparation

Preoperative clinical assessments included obtaining the patient's medical history, physical examination, hematologic evaluation, routine determination of serum electrolyte levels, liver and renal function tests, serum bilirubin and amylase measurements, chest radiography, electrocardiography, and bone scanning. Color Doppler US and either CT or MR imaging were performed in all patients before high-intensity focused ultrasound treatment.

In a previous study (J. Bai, MD, unpublished data, 1999), no pancreatitis occurred after high-intensity focused ultrasound ablation of the normal pancreas tissue in cats. It is still possible, however, that the thermal ablation of pancreatic cancer in humans could cause traumatic pancreatitis—particularly necrotic pancreatitis. To reduce the likelihood of this serious side effect, 14-peptide somatostatin, a strong inhibitor of pancreas exocrine secretion, was used in all patients before the procedure. At the beginning of high-intensity focused ultrasound treatment, 3 mg of 14-peptide somatostatin (Serono Biotech & Beyond, Geneva, Switzerland) was intravenously injected in each patient.

### Assessment of Safety

After high-intensity focused ultrasound treatment, the serum amylase and bilirubin levels were monitored daily for 1 week. Complications that may have been related to high-intensity focused ultrasound, including abdominal pain, pancreatitis, peritonitis, jaundice, skin burn, tumor bleeding, large vessel rupture, and gastrointestinal perforation, were recorded in each patient by three observers together (K.Q.L., C.B.J., F.L.X.).

### Follow-up

Vital signs were monitored for 24 hours after the patient recovered from anesthesia. Any changes from the symptoms seen at presentation were recorded. No food was given within 5 days after high-intensity focused ultrasound, and intravenous infusion, including 9 mg of 14-peptide somatostatin daily, was introduced. All patients stayed in the hospital for at least 1 week. During the hospital stay, complete blood counts and electrolyte levels were monitored and liver function tests were performed twice a week.

Follow-up imaging examinations were performed to evaluate the therapeutic effectiveness of high-intensity focused ultrasound. All patients underwent pre- and posttreatment color Doppler US with a 3.5-MHz convex-array probe (Q-2000; Siemens, Erlangen, Germany). Color Doppler US was performed jointly by two radiologists (J.Z.Z., H.B.S.), and the measurements were interpreted by means of consensus between three observers (J.Z.Z., H.B.S., and H.Z., with 20, 7, and 8 years experience with color Doppler US, respectively). With the pulsed Doppler method, tumor vascularity was evaluated as intratumoral flow signals. We noted only whether pulsatile color flow was present or absent within tumor.

Three patients underwent transverse conventional CT (Sytec 4000; GE Medical Systems, Milwaukee, Wis) at follow-up. Initial unenhanced imaging was performed with 7-mm-thick sections at 10-mm intervals through the abdomen. The liver, pancreas, and kidney were included because most of the patients in the study population had liver metastasis when they underwent high-intensity focused ultrasound ablation. For contrast material–enhanced imaging, patients received 150 mL of iopamidol solution (Ultravist 370; Schering, Berlin, Germany) by means of intravenous power injection at a rate of 2–3 mL/sec.

MR imaging became available at our hospital during the study period, and five of the eight patients underwent unenhanced and contrast-enhanced MR imaging with a 1.5-T unit (Signa; GE Medical Systems). Follow-up MR images were evaluated and interpreted by means of consensus between three radiologists (J.Z.Z., H.B.S., and K.Q.L., with 10, 7, and 8 years experience with MR imaging, respectively). A consensus interpretation was reached for each patient. Unenhanced MR imaging included T1-weighted spin-echo (366–660/12–20 [repetition time msec/echo time msec], 128–512 × 256–512 matrix, 5–10-mm-thick sections, 1–2-mm intersection gap, two to four signals acquired, and 8–12-minute acquisi-

**TABLE 2**
**Summary of Treatment Data and Follow-Up Results**

| Patient No. | Therapy Time (h) | No. of Therapy Sessions | Changes in Symptoms | Follow-up Time (mo) | Tumor Reduction Rate (%) | Side Effects | Change in Metastasis* | Current Patient Status | Other Details |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 2.0 | 2 | Pain was stopped | 17 | 70 | None | NA | Dead | Patient died of cachexia |
| 2 | 1.0 | 1 | Pain was stopped | 2 | 20 | None | Growth | Dead | Patient died as result of liver metastases |
| 3 | 2.5 | 2 | Pain was stopped | 14 | 50 | None | Growth | Dead | Patient died as result of liver metastases |
| 4 | 1.5 | 1 | Pain was stopped | 11 | 40 | None | NA | Alive | ··· |
| 5 | 1.0 | 1 | Pain was stopped | 10 | 50 | None | Regression | Alive | Multiple liver metastases were ablated with HIFU |
| 6 | 1.0 | 1 | Pain was stopped | 9 | 35 | None | Regression | Alive | Single liver metastasis was ablated with HIFU |
| 7 | 2.0 | 1 | Pain was stopped | 11 | 60 | None | Growth | Dead | Patient died as result of liver metastases |
| 8 | 1.5 | 1 | Pain was stopped | 16 | 70 | None | NA | Alive | ··· |

* NA = not applicable.

tion time), T2-weighted spin-echo (2,000–4,100/70–140, 128–192 × 256 matrix, 5–7-mm-thick sections, 1–3-mm intersection gap, one or two signals acquired, and 4–10-minute acquisition time), and fat-saturated T1-weighted spin-echo (450–733/12–20, 128–192 × 256 matrix, 5–10-mm-thick sections, 1–2-mm intersection gap, one to four signals acquired, and 16-minute 24-second acquisition time) examinations.

After T1- and T2-weighted images were obtained, dynamic contrast-enhanced MR imaging was performed during intravenous injection of 20 mL of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ). Contrast-enhanced MR imaging included multisection dynamic gradient-echo T1-weighted imaging (80–180/1.8–6.0, 60°–90° flip angle, 128 × 256 matrix, 7–10-mm-thick sections, 2–3-mm intersection gap, one signal acquired, and 18–27-second acquisition time) with breath holding and delayed T1-weighted spin-echo imaging (450–733/12–20, 128–192 × 256 matrix, 5–10-mm-thick sections, 1–2-mm intersection gap, one to four signals acquired, and 16-minute 24-second acquisition time) with fat saturation. Areas of low signal intensity or hypoattenuation at MR imaging or CT, respectively, that did not enhance after contrast material administration were considered to represent necrotic tissue. Still-enhancing areas were assumed to reveal residual viable tumor. Follow-up images were obtained every 3–6 months after intervention. Three radiologists (J.Z.Z., H.B.S., K.Q.L.) interpreted these results and reached a consensus for each patient. Changes in tumor size are expressed as a percentage of the initial size of the tumor and were calculated by using the following formula: $\{[(a \times b) - (a' \times b')]/(a \times b)\} \times 100$, where $a$ and $a'$ are the largest tumor diameters before and after high-intensity focused ultrasound ablation, respectively, and $b$ and $b'$ are the perpendicular tumor diameters before and after high-intensity focused ultrasound ablation, respectively.

## Results

### Treatment Data

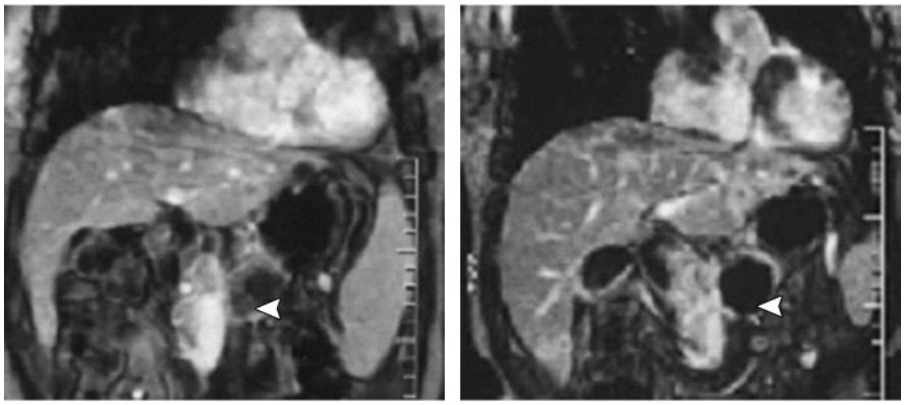
High-intensity focused ultrasound treatment was successfully performed in all patients. Two patients underwent two high-intensity focused ultrasound sessions, and six patients underwent one high-intensity focused ultrasound session (mean, 1.25 sessions). Among five patients with liver metastasis, two underwent high-intensity focused ultrasound ablation of the hepatic neoplasm immediately after treatment of the pancreas was finished. The remaining three patients underwent no intervention for their hepatic disease. Acoustic focal peak intensities ranged from 10 000 to 15 000 W per square centimeter. The scanning speed was 1–3 mm per second, and the track length was 10–15 mm. High-intensity focused ultrasound treatment time ranged from 1.0 to 2.5 hours (mean, 1.56 hours). The treatment data are summarized in Table 2.

### Laboratory Evaluation

In all patients, blood samples were obtained daily for 7 days after high-intensity focused ultrasound. Neither the amylase level nor the bilirubin level showed a statistically significant increase over baseline values during this period. There were no differences between the pre- and postinterventional values of serum aspartate transaminase and alanine aminotransferase levels, even in the two patients who underwent ablation of liver metastasis immediately after high-intensity focused ultrasound ablation of the pancreatic tumor, while still anesthetized.

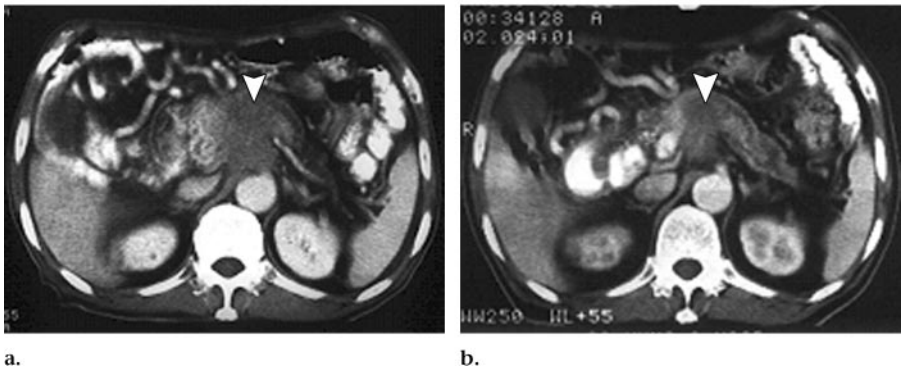
### Postinterventional Imaging

Follow-up color Doppler US was performed in all patients. When we compared the Doppler US images obtained before with those obtained after high-intensity focused ultrasound, no change in gray scale was seen. The target lesion was hypovascular in six patients; thus, Doppler US was not sufficiently sensitive for evaluating any changes in the tumor blood vessels. Obvious regression of the treated lesions, however, was observed during the follow-up period. Contrast-enhanced follow-up CT was performed in three patients, and a hypoattenuating region without contrast enhancement was seen in only one patient after high-intensity focused ultrasound ablation. Five patients underwent contrast-enhanced MR imaging before and after high-intensity focused ultrasound. In three of these five patients, postprocedural MR imaging re-



a. b.

**Figure 1.** Dynamic contrast-enhanced gradient-echo T1-weighted MR images (180/6.0, 90° flip angle, 128 × 256 matrix, 10-mm-thick sections, 2-mm intersection gap, one signal acquired, and 18-second acquisition time) obtained with breath holding in 48-year-old man who underwent high-intensity focused ultrasound ablation for advanced pancreatic cancer. The tumor was 4.5 × 4.5 cm in diameter and located in the body of the pancreas. **(a)** Image obtained before high-intensity focused ultrasound shows the blood supply in the pancreatic lesion (arrowhead). **(b)** Image obtained 2 weeks after high-intensity focused ultrasound shows no evidence of contrast enhancement in the treated lesion (arrowhead), which is indicative of complete coagulation necrosis in the pancreatic cancer.



a. b.

**Figure 2.** **(a, b)** Transverse contrast-enhanced conventional CT scans obtained **(a)** 1 month before and **(b)** 9 months after high-intensity focused ultrasound ablation for advanced, unresectable pancreatic cancer (arrowhead) in 78-year-old man. The lesion was 7.5 × 6.5 × 6.0 cm in diameter and located in the head and the body of the pancreas. There was an obvious regression in lesion size after high-intensity focused ultrasound.

vealed an obvious absence of contrast enhancement in the lesion, which is indicative of the coagulation necrosis induced by high-intensity focused ultrasound in the treated region (Fig 1).

Either CT or MR imaging was performed after intervention to assess tumor size from both the maximum transverse and the longitudinal dimensions of the lesion in each patient. It was noted that high-intensity focused ultrasound had obvious effectiveness in the control of tumor growth. During the follow-up period, tumor regression was detected in all patients, and the reduction rate ranged from 20% to 70% (mean, 49.4%) compared with the initial size of the tumor before high-intensity focused ultrasound (Table 2, Fig 2). Among the five patients with liver metastases, two of them underwent simultaneous high-intensity focused ultrasound to ablate hepatic lesions with diameters of 2–4 cm. Follow-up contrast-enhanced MR imaging demonstrated a positive therapeutic response, and no tumor blood supply was observed in the treated liver lesions 2 weeks after high-intensity focused ultrasound.

### Pain Relief

Before high-intensity focused ultrasound, all patients had obvious visceral pain that necessitated management with oral analgesic drugs. The pain associated with unresectable pancreatic cancer, however, had resolved within 24–48 hours after a single session of high-intensity focused ultrasound, and the pain relief persisted during the follow-up period. Two patients who were still experiencing some pain from their original liver metastasis required less medication to control the pain compared with the initial pretreatment dose.

### Survival

At the time of this writing, four patients had died (median survival time, 11 months; range, 2–17 months) and four were alive (mean follow-up time, 11.5 months; range, 9–16 months). The overall median survival time was 11.25 months (range, 2–17 months). One patient died as a result of cachexia, and three patients died of hepatic dysfunction caused by liver metastases untreated with high-intensity focused ultrasound. Control of the growth of liver metastases was observed in the two patients who underwent high-intensity focused ultrasound treatment for metastatic liver disease.

### Complications

No skin burns caused directly by high-intensity focused ultrasound were observed in this group, and no deaths had occurred 1 month after high-intensity focused ultrasound. During the hospital stay, no signs of tumor hemorrhage, large blood vessel rupture, or gastrointestinal perforation were detected in any patient. No dilatation of the common bile duct or pancreatic duct was visible at follow-up imaging. There was no evidence of postinterventional pancreatitis, peritonitis, or jaundice in any patient during the follow-up period.

## Discussion

Several energy sources, such as radiofrequency, microwave, cryotherapy, and laser, have been used to induce coagulation necrosis of a target tumor in clinical practice. With most of these techniques, the energy is applied percutaneously with needle applicators. The energy is, therefore, concentrated around the applicator, and there is heterogeneous distribution of heat through a target lesion. The result is that a maximum tumor diameter of 5 cm can be generally treated. As a noninvasive treatment, high-intensity focused ultrasound is not restricted by these lim-

itations. It does not require the insertion of an applicator into a target tissue, and an extracorporeal source can be used to treat large-volume tumors with real-time imaging guidance. Ultrasound energy deposited in the target tumor induces coagulation necrosis. Both the thermal and the cavitation effects caused by ultrasound energy are responsible for tissue damage (23).

In our study, eight patients with advanced and unresectable disease were treated with high-intensity focused ultrasound. After high-intensity focused ultrasound, the serum amylase level was measured as a surrogate marker for traumatic pancreatitis. The amylase level showed no statistically significant elevation over that at baseline in the 7 days after high-intensity focused ultrasound. No severe side effects (eg, tumor hemorrhage, large blood vessel rupture, peritonitis, obstructive jaundice, and gastrointestinal perforation) were observed in any patients during the follow-up period.

Although the ultimate goal of high-intensity focused ultrasound in patients with cancer is cure, all of our patients had advanced pancreatic cancer. Five patients had liver metastases, and three had unresectable pancreatic cancer; thus, a curative approach with high-intensity focused ultrasound ablation was not realistic. Therefore, high-intensity focused ultrasound was performed as a palliative treatment in all cases. Postinterventional imaging showed that there was obvious regression of the treated tumors, with an average reduction rate of 49.4%. The median survival time was 11.25 months (range, 2–17 months). After high-intensity focused ultrasound treatment, one patient died of cachexia caused directly by cancer and three patients died as a result of hepatic metastases; however, the survival times of 17 and 14 months for two of these patients were relatively long. Four patients were still alive as of the time of this writing. Two of these patients underwent high-intensity focused ultrasound ablation of both primary pancreatic cancer and liver metastases concurrently. Follow-up imaging showed that both the primary and the metastatic tumors were treated successfully, and a survival benefit was achieved in these patients. These results suggest that high-intensity focused ultrasound could substantially improve the quality of life and increase the survival time in patients with advanced-stage pancreatic cancer.

Pain management for patients with locally advanced pancreatic cancer is an ongoing challenge. This pain can be both neuropathic and inflammatory, resulting from both tumor expansion and tumor invasion of the celiac and mesenteric plexus (24–26). Nonsteroidal anti-inflammatory drugs and narcotic analgesics are principally used for pain control in clinical practice. At disease progression, however, they may not be sufficient. Therefore, anesthetic block of the celiac plexus by means of injection of a chemical solution (27,28), external radiation therapy (29,30), and chemotherapy (31,32) are used to palliate pain in patients with advanced pancreatic cancer. These modalities can achieve pain control, but the duration of pain relief is limited.

Because almost 70% of patients with pancreatic cancer are at least 65 years old at diagnosis, side effects related to external radiation and antitumor drugs may be very severe. In our study, the most striking change in the patients was that the preoperative pain disappeared immediately after high-intensity focused ultrasound treatment. Severe pancreatic pain was stopped in all patients. Because ionizing radiation is not used with high-intensity focused ultrasound, this treatment is not restricted by the limitation of radiation dose and may be used repeatedly. Although the mechanism is still unclear, high-intensity focused ultrasound might be an effective treatment option for pain control, particularly in patients with tumors infiltrating the celiac plexus and in whom conventional pain treatments are not considered an effective option.

In our study, results of follow-up showed that there were no signs of obstruction from bile and pancreatic ducts in the patients treated with high-intensity focused ultrasound because most cancers were located in the body or the tail of the pancreas. However, there remained a substantial possibility of biliary obstruction or biliary duct damage caused by the thermal ablation, especially in those patients with tumors in the pancreatic head. Therefore, to reduce the risk of complications, an endobiliary stent should be routinely placed before high-intensity focused ultrasound in patients with cancers in the pancreatic head.

Anesthesia might be considered one disadvantage of high-intensity focused ultrasound treatment in clinical applications. Anesthesia is used for two predominant reasons: to prevent the patient from experiencing pain and to ensure immobilization of the treated pancreas. Anesthesia, however, can raise the potential risks to patients, particularly those in a weakened state with advanced-stage carcinoma. However, all patients in our study—even an 86-year-old patient—tolerated anesthesia, and no related complications were detected after high-intensity focused ultrasound ablation.

Our study had several weaknesses. The small population of patients who underwent high-intensity focused ultrasound treatment may have limited our clinical experience and statistical analysis of the follow-up results, particularly those related to the high-intensity focused ultrasound therapeutic parameters used for the treatment. Another limitation is that the imaging equipment that we used to assess the follow-up results, compared with current state-of-the-art equipment, was not good enough to enable us to determine treatment effectiveness. This work would be improved in our future study. Finally, because some pancreatic cancers—particularly early-stage or small tumors—cannot be detected with US, it is impossible to perform US-guided high-intensity focused ultrasound in patients with these malignancies.

Because most patients with pancreatic cancer have unresectable disease and no effective modality offers survival benefits for them, the results from our study are very encouraging. In summary, our preliminary experience suggests that high-intensity focused ultrasound is safe and feasible for the treatment of patients with unresectable cancer in the body and the tail of the pancreas. A randomized clinical trial, however, is essential to determine the future role of this treatment in patients with pancreatic malignancy.

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