Evaluation of Three-Dimensional Printing-Assisted Laparoscopic Cryoablation of Small Renal Tumors: A Preliminary Report

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Purpose: This study aimed to explore the security and feasibility of three-dimensional (3D) printing technology-assisted laparoscopic cryoablation to treat small renal tumors.

Patients and Methods: Four patients recruited from our hospital from April 2016 to August 2017 underwent 3D printing technology-assisted laparoscopic cryoablation. Three-dimensional reconstruction technology was used to mimic cryoablation treatment before operations to determine the number of needles needed for the operation and the depth and angle required for needle insertion into the tumor to preserve nephron integrity. CT scans were used to assess the treatment's efficacy after operation during regular follow-up.

Results: The operation was performed successfully in all cases and all patients recovered without major complications. The operation times ranged from 106 to 118 minutes and blood loss ranged from 50 to 100 mL. The follow-up times were between 8-16 months and the mean time was 13.3 months. Follow-up surveys were conducted regularly based on a standard outpatient protocol. Results showed no abnormal reinforcing signals in cryoablation treated areas.

Conclusion: 3D printing technology-assisted laparoscopic cryoablation is a feasible method for the treatment of renal tumors and may be a way to better preserve nephrons, especially in elderly patients and/or those with comorbidities.

Keywords: laparoscopy; cryoablation; renal cell carcinoma; three-dimentional-printing

INTRODUCTION

Kidney cancer is a globally common malignancy of the genitourinary system. According to cancer statistics from China from 2015, kidney cancer is the third most common malignant tumor of the urinary system in males, and it is the sixth in women.[1] Due to the increase of personal health awareness, regular physical examinations have gradually become routine, therefore the rate of small kidney tumor detection has concurrently increased. However, only about 30% of kidney cancer is diagnosed by the presence of typical symptoms; due to this new methods of treatment for small renal cancer have recently emerged, such as active surveillance, laparoscopic or robot-assisted partial nephrectomy, and high-intensity focused ultrasound radiofrequency ablation and cryoablation, and have been gradually accepted by doctors and patients.[2,3] High-intensity focused ultrasound radiofrequency cryoablation has been used in particular.

Rapidly progressing 3D printing technology is based on computer graphic data and overlays specific materials to make the desired end products, which can vary greatly in size and shape. This technology has been applied in clinical practice for things such as medical model design and the manufacturing of medical equipment. In particular, 3D printing has especially been applied in assisting various surgical operations through the printing of specific auxiliary models for operations, replacements, and surgical instruments.[4,5]

Cryoablation therapy works using the immediate damage seen with cryogenic freezing in conjunction with delayed damage caused by microcirculation disorder, changing the inside and outside environment of tumor cells and inducing cell death or apoptosis. These mechanisms can help to achieve effective tumor treatment. There has been much research conducted to examine the use of this cryoablation technique in the treatment of renal tumors, and findings have confirmed this method's security and approved associated oncologic outcomes.[6-8] Cryoablation is mainly conducted by percutaneous puncture via computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound guidance, or directly under laparoscopy. This procedure heavily relies on doctors' experiences to decide how many needles are needed and the depth and angle required for insertion into the tumor. As a result, it is difficult to precisely freeze the tumor according to the variations in tumor shape. Using too many needles may increase complications and injure healthy tissues; on the other hand too few needles can hinder the effectiveness of cancer therapy. In this study, we explored the use of 3D printing technology to assist preoperative planning and intraoperative cryoablation therapy, achieve precise

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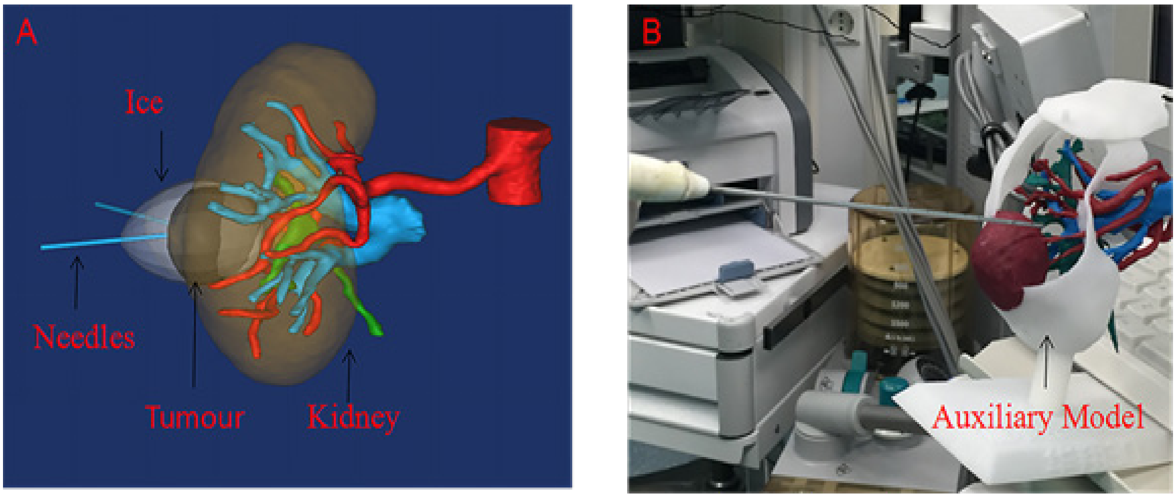

Figure 1: 3D printing assisted cryoablation therapy: A: Renal CT scan data was extracted to develop 3D reconstruction of the kidney, and then a cryoablation procedure was simulated to figure out the number of needles needed and the angle and depth required for insertion into the tumor to find the optimal plan. B: The kidney model was created through 3D printing technology to guide intraoperative manipulation.

freezing of tumors, and preserve the maximum number of normal renal units, so as to benefit the patients.

PATIENTS AND METHODS

Study Population

This study included four cases, including two male and two female patients, aged 50 to 75 years old. One patient had only one kidney due to the resection of renal cancer on the other kidney. In the four patients, one tumor was located in the upper lobe, one tumor was located in the renal hilum, and the remaining two were located in the lower lobes. Tumor diameters ranged from 3.8 to 2.4 cm. One patient had a history of five cycles of chemotherapy for pelvic mucinous adenocarcinoma. In another patient, severe hydronephrosis was detected in the other kidney due to kidney stones. One patient suffered from high blood pressure and a contralateral renal cyst. Urinary system CT scans with additional enhancement and 3D reconstruction were conducted on all patients before operations, in order to assess the malignancy of the renal tumor. Renal biopsy and pathological diagnosis confirmed all tumors were renal clear cell carcinoma. Pathological diagnoses for two cases were confirmed by pre-operative biopsy and the remaining two by biopsy during laparoscopy before cryoablation.

Instruments and Equipment

The 3D printing technology adopts the medical image control system (Materialise Mimics 18.0) software and uses a hs402p 3D printer with FS3200PA Nylon Powder printing material. The American hydrogen helix

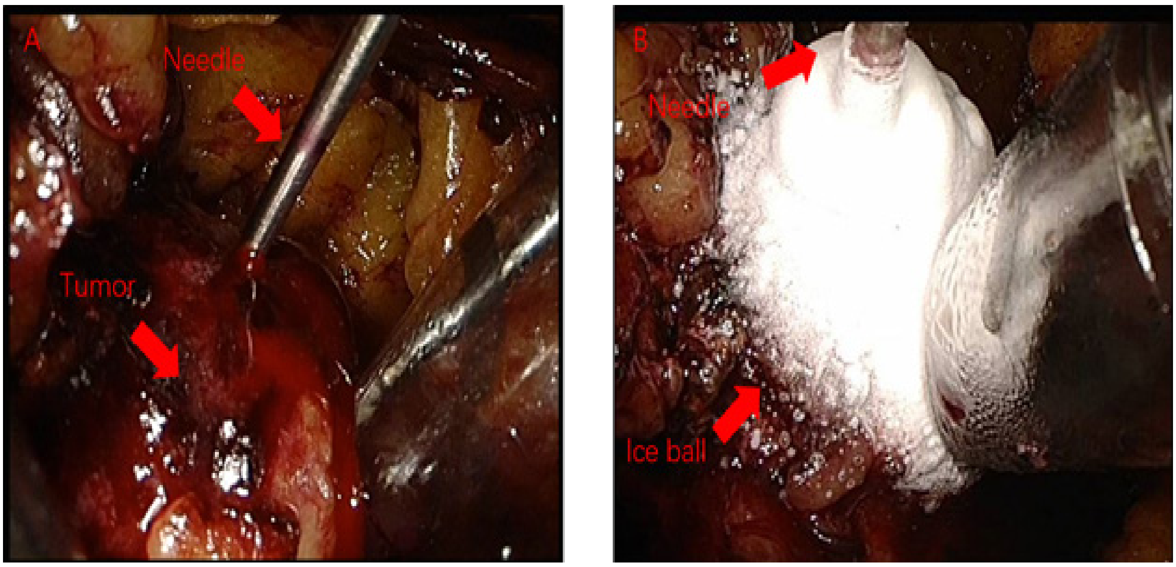

Figure 2: Laparoscopic renal tumor cryoablation: A: Needles were inserted into the tumor under laparoscopy according to the scheme predetermined with the help of 3D printing technology before surgery. B. An ice ball was formed that reached more than one centimeter beyond the tumor's edge during cryoablation therapy.

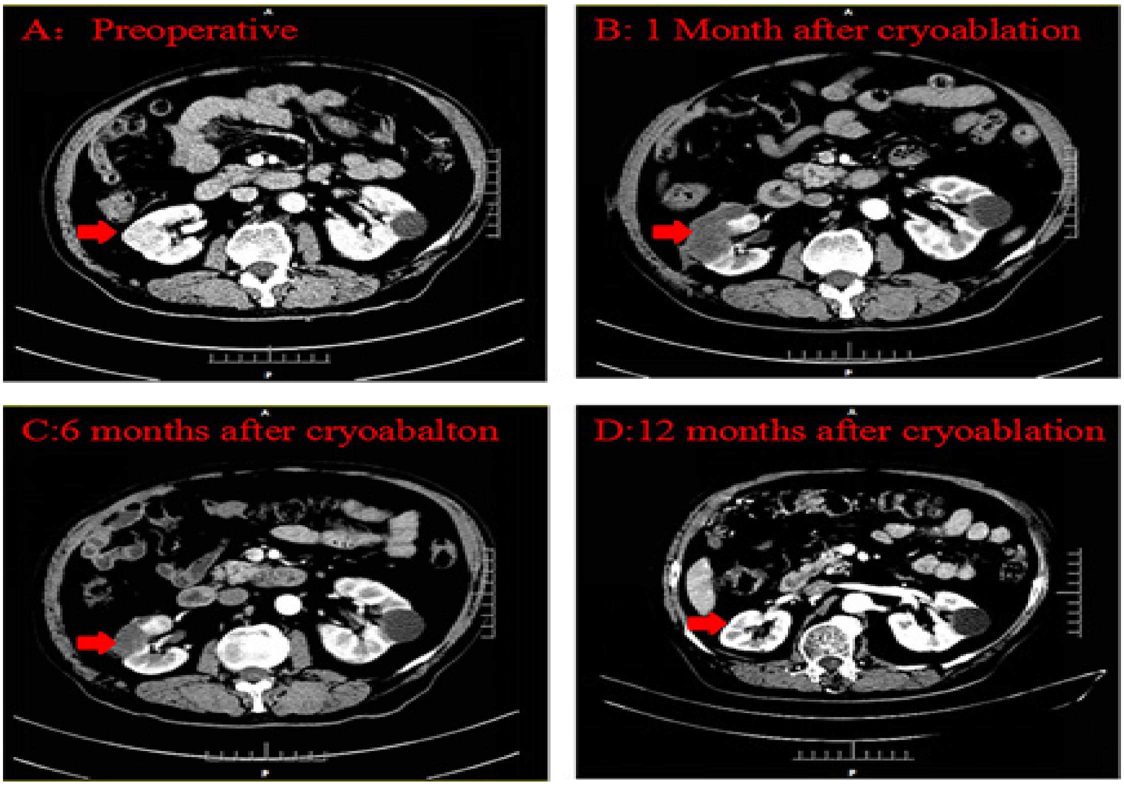

Figure 3: Typical images of the effect of cryoablation therapy in the same patient: **A:** Significant uneven enhancement was seen in the center of the right renal before surgery. **B:** Postoperative renal CT examination showed no obvious enhancement in the frozen region after one month, and large necrotic tumor tissue was seen. **C:** There was no obvious enhancement in the operational area after six months, but necrotic tumor tissue decreased. **D:** 12 months after surgery, there was almost no necrotic tissue in the treated area, and no obvious abnormal enhancement was observed, indicating the efficacy of tumor therapy. Tumor area and frozen area were marked with red arrow.

knife system (Cryocare Surgical System) was used for cryoablation treatment.

3D Printing Technology

Medical imaging control system software used data of renal CT scans to reconstruct the kidney, including the tumor, in 3D, then mimicked the punctures of the cryoablation therapy according to the size and location of the tumor. In the simulation, we aimed to calculate the number of needles needed and the best angle and depth for insertion into the tumor in order to find the best scheme. The best scheme is defined as the technique that uses the least amount of needles to completely freeze the tumor, as shown in **Figure 1A. A 3D** model of a kidney was utilized to guide intraoperative surgical operations, as shown in **Figure 1B**.

Laparoscopic Renal Tumor Cryoablation

The four cases underwent laparoscopic surgery via a retroperitoneal approach with the guidance of a preoperative auxiliary model recreated by 3D printing technology. We chose laparoscopic guidance over percutaneous access via ultrasound guidance during cryoablation because we had direct vision, and this technique could improve the accuracy of positioning and reduce side pain. Furthermore, some studies had shown that percutaneous renal cryoablation had higher rates of surgical failure and higher recurrence rates than laparoscopic cryoablation.[9-11] The renal tumor cryoablation procedure was conducted according to the preoperative simulation optimization scheme with the guidance of the preoperative auxiliary model recreated using 3D printing technology (**Figure 2A**).

A hydrogen helium knife system (Cryocare Surgical System) was used in cryoablation therapy. Needles were inserted into the tumor under laparoscopy according to the scheme determined using 3D printing technology before the operation, and the tumor was subjected to a quick freeze for 10 minutes, making an ice ball that reached more than one centimeter beyond the tumor's edge. The tumor was thawed after 10 minutes; after a total of two cycles of freezing and thawing, the needles were slowly removed (**Figure 2B**). Great attention was paid to respiratory movements during the whole operation process to avoid probe offset and intraoperative bleeding.

Evaluation of Oncologic Outcomes

Follow-up was conducted routinely during outpatient. Patients had to do renal enhancing CT scans, chest radiographs, abdominal ultrasonography, and routine laboratory tests; if any problem was found, further investigation was done. Treatment effectiveness was assessed through renal enhancing CT scans to check for abnormal enhancing signals in the frozen areas of the kidney. Postoperative serum creatinine levels were also monitored.

The present study was approved by the ethics committee of Hunan Cancer Hospital and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients.

RESULTS

Clinical Outcomes

Operation times ranged from 106 to 118 minutes. Intraoperative blood loss ranged from 50 to 100 mL. Preoperative serum creatinine ranged from 70.7 to 80.1 umol/L. The serum creatinine one week after surgery was between 68.5 and 84.4 umol/L. Patient characteristics and surgical indicators were shown in **Table 1**.

Follow-up

Follow-up time was between 8 to 16 months, with an average time of 13.3 months. Renal enhancing CT scans were conducted routinely after surgery, and no obvious tumor signals were found in the frozen areas of all patient cases; the typical images of one of the patients are shown in **Figure 3**. Postoperative serum creatinine levels were stable (**Table 2**) and no obvious distant metastases were detected.

DISCUSSION

The main use of 3D printing technology in the clinical field is printing out specific anatomical models to assist surgical operations.[5] In clinical applications to urology, 3D printing technology is applied to assist partial nephrectomies,[12] adrenal partial resections,[13] percutaneous nephrolithotomies,[14] prostate needle biopsies,[15] and more. In partial nephrectomies, the auxiliary kidney model printed out via a 3D printer could accurately display the size and location of the tumor, the infiltrating depth of the tumor, and the anatomic relationship between renal artery, renal vein, and collecting system. This information gained from the kidney model can facilitate preoperative surgical planning and intraoperative guidance, which could reduce intraoperative complications and improve success rate and precision of surgery.[12,16]

The application of laparoscopic cryoablation in the treatment of renal tumors is well established, can achieve great efficacy in cancer treatment, and also has an advantage in protecting renal function. In 2010, Guazzoni et al. performed a study that included 44 cases of renal cell carcinoma patients who underwent laparoscopic cryoablation and found that the tumor specific survival rate was 100% and overall survival rate was 93.2% through the average follow-up of 5 years.[17] Tsivian and Tanagho et al. monitored the renal function of patients who underwent laparoscopic cryoablation therapy and found no significant change in patients' renal function.[18,19] Cryoablation has its own advantages, like easy implementation, no intraoperative thermal ischemia damage, and no need for incision and suture of renal parenchyma, which can better preserve renal function. This method is significant to patients with kidney deficiency and poor general conditions who need to retain maximum renal function.

Laparoscopic partial nephrectomies are the most widely used operation in nephron sparing surgery with a highly satisfactory efficacy. This technique requires high proficiency on the surgeons part to block the renal blood supply, resect the tumor, and suture the rest of renal parenchyma during the operation. Laparoscopic cryoablation, on the other hand, is simpler than a laparoscopic partial nephrectomy and causes less damage to the kidney. European urology guidelines recommend cryoablation for elderly and/or comorbid patients with small renal masses. A number of studies have compared oncological outcomes and operational parameters between these two methods, but there are no consistent conclusions. A systematic review and meta-analysis showed that, compared to a laparoscopic partial nephrectomy, laparoscopic cryoablation could better protect renal function and reduce complications, but the local recurrence rate (OR = 13.03) and distant metastasis rate (OR = 9.05) was significantly higher than that of a laparoscopic partial nephrectomy.[20] On the other hand, the author also pointed out that patients selected for laparoscopic cryoablation had poorer general conditions and were older than those receiving a laparoscopic partial nephrectomy, and the isolated kidney rate was higher in the laparoscopic cryoablation group as well. Therefore, surgeons have to be very careful and choose the most beneficial method for the patient based on the individual conditions of each patient. For elderly patients and those with serious complications, cryoablation is the preferred choice. Here we integrated 3D printing technology with laparoscopic cryoablation, which can further promote the advantages of cryoablation and provide better protection of renal function.

This study aimed to explore the feasibility of using 3D printing technology-assisted laparoscopic cryoablation to precisely preserve normal renal tissue. Although these two technologies are applied in treatment separately, this is the first time that we combined these two techniques to treat renal tumors. The combination of these two technologies integrated their individual advantages, making nephron sparing more accurate. The following is a summarization of the advantages of 3D printing-assisted laparoscopic cryoablation. First, before operations, cryoablation therapy can be mimicked on the computer through 3D reconstruction to figure out the point of insertion and the depth and angle of needles needed to design the optimal cryoablation scheme. Next, 3D printing technology can provide a kidney model that can be used to communicate with patients, which could increase the patients' understanding of renal anatomy and the surgical operation, thus increasing the patients' trust in their surgeons. The model can also provide intraoperative guidance, improving the success rate of the operation, shortening operation time, and reducing intraoperative haemorrhage and other complications. Under laparoscopic guidance, the tumor was fully exposed, side damage was reduced, and there was sufficient vision to do an accurate renal tumor puncture. During the operation, surgeons could refer to the 3D printing model of patients' kidneys and easily confirm puncture point and depth. The most important advantage is that the optimal cryoablation therapy scheme can effectively preserve renal units and reduce injury to normal renal tissue. Therefore, we think that the combination of 3D printing technology and laparoscopic cryoablation, which are already widely applied in renal tumor treatment separately, could better preserve patients' renal function and is worth further application in clinical. However, this study, which only included four cases, is a preliminary exploration of this method. Additional studies using larger sample sizes and prospective randomized trials are needed to prove the feasibility and effectiveness of this method.

CONCLUSIONS

Our study suggested that it is feasible and safe to use 3D printing technology-assisted laparoscopic cryoablation to treat small renal tumors, which is a new technique for nephron sparing surgery, especially for elderly and/ or comorbid patients. Further prospective studies with larger sample sizes should be conducted to confirm this technique.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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