

CASE REPORT

Use of microwave ablation in the treatment of patients with multiple primary malignant tumors

Yue Han¹, Na Shao², Xiaoming Xi³ & Xuezhi Hao³

1 Department of Interventional Therapy, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

2 Department of Oncology, Provincial Hospital Affiliated to Shandong University, Jinan, China

3 Department of Medical Oncology, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

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Correspondence

Yue Han, Department of Interventional Therapy, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 17, Panjiayuan Nanli, Chaoyang District, Beijing 100021, China.

Tel: +86 10 8778 7364

Fax: +86 10 8778 7364

Email: doctorhan@163.com

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Abstract

A 56-year-old man was admitted to our hospital in 2007, complaining of an irritating cough. Computed tomography examination demonstrated a mass in the right lung and enlargement of the hilar and mediastinal lymph nodes. Small cell lung cancer was confirmed by pathological examination after fibro-bronchoscope biopsy. The patient was treated with received sequential chemotherapy and radiotherapy. Preventive radiotherapy of the whole brain was performed after complete remission of the lung disease. Seven years after diagnosis, follow-up computed tomography revealed masses in both the liver and kidney. Subsequent percutaneous biopsy confirmed hepatocellular carcinoma in the liver and renal clear cell carcinoma in the kidney. The patient received microwave ablation for the treatment of both liver and renal tumors, and is doing well with no recurrence after two years of follow-up.

Introduction

A multiple primary malignant tumor is defined as the occurrence of two or more primary malignant tumors, where each tumor occurs in a separate site and does not represent extension, recurrence, or metastasis.¹ With the increasing proportion of elderly patients in the general population undergoing regular medical check-ups, the occurrence of multiple primary malignant tumor is becoming more and more frequent.² However, triple primary malignant tumor remains rare and prognosis in these patients is poor. It is important to detect and identify primary tumors or metastases at an early stage. Unlike a metastatic tumor, multiple primary tumors do not represent advanced disease, and each of these tumors should be staged and treated as an independent entity. Management of multiple primary malignant tumors may vary in type,

location, stage, and general patient condition. Percutaneous microwave ablation (MWA), a minimally invasive treatment for cancer, has altered the management of several types of cancer. As an available and improving technology, MWA is emerging as a valuable alternative to radiofrequency ablation (RFA) in the treatment of hepatocellular carcinoma (HCC) and renal clear cell carcinoma (RCC). In this report, we present a case with triple primary cancers occurring in the lung, liver, and kidney, and after chemotherapy, radiotherapy, and MWA the patient achieved long-term survival.

Case Report

A 56-year-old man was admitted to our hospital in March 2007, complaining of an irritating cough. A computed tomography (CT) scan revealed a 4 × 3.6 cm mass in the right superior lung and enlargement of the hilar and

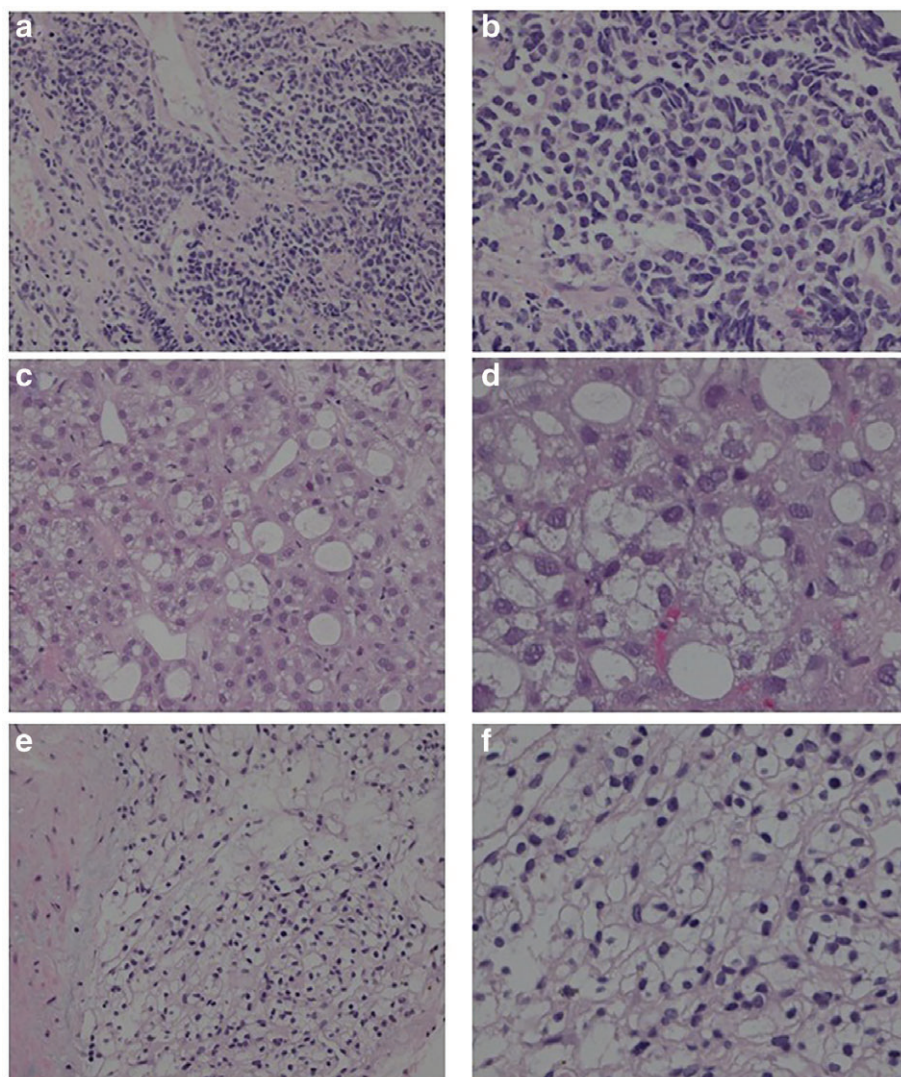
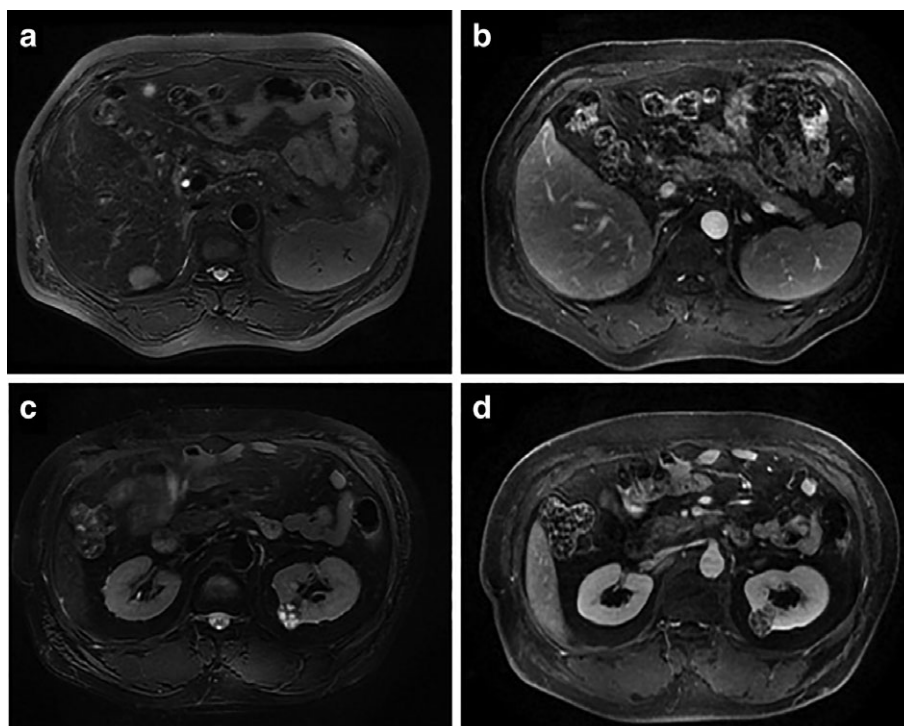


Figure 1 (a,b) Small cell lung cancer was confirmed by pathological examination after fibro-bronchoscope biopsy. (c,d) Hepatocellular carcinoma was determined after percutaneous liver biopsy and (e,f) renal clear cell carcinoma was confirmed after renal biopsy (hematoxylin and eosin staining, original magnification, a,c,e: $\times 200$, b,d,f $\times 400$).

mediastinal lymph nodes. Small cell lung cancer was confirmed by pathological examination after fibro-bronchoscope biopsy (Fig 1a,b). A comprehensive CT scan ruled out distant metastatic disease, thus the clinical stage was classified as limited. Between April and November 2007, the patient received three courses of standard chemotherapy composed of etoposide and cisplatin (EP), and then received sequential intensity modulated radiation therapy (IMRT; total dose: 60Gy/30f), which involved the primary lesion in the right lung and the hilar and mediastinal lymph node areas. The patient then received another three courses of EP chemotherapy. A CT scan in December 2007 demonstrated that the primary lesion in the right lung and the metastatic lymph nodes had disappeared, signaling a complete response according to World Health Organization standard criteria. Three months later, the patient received preventive radiotherapy of the whole brain.

Follow-up CT scans showed no evidence of recurrence until September 2014 when new tumors were found in the right posterior segment of the liver and in the upper pole left kidney. We performed enhanced magnetic resonance imaging (MRI) of the abdomen, which suggest the presence of malignant neoplasms (Fig 2). The patient had a history of chronic viral hepatitis B, and his alpha-fetoprotein level had elevated to 385 ng/mL, which supported a diagnosis of primary liver cancer. As is well known, enhanced CT and MRI cannot provide sufficient information to distinguish metastatic and primary tumors. Hence, our team performed image-guided percutaneous liver and renal biopsies to make a pathological diagnosis. Pathology determined the liver tumor as HCC (Fig 1c,d) with immunohistochemistry (IHC): hepatocyte (3+), carcinoembryonic antigen (–), caudal type homeobox 2 (–), cluster of differentiation 31 (CD31) (1+), AE1/AE3 (3+),

Figure 2 Magnetic resonance imaging of the abdomen. Abnormal signals were detected in (a,b) the right posterior segment of the liver and (c,d) in the upper pole of the kidney, with slight contrast enhancement.



Ki-67 (5%), and the kidney tumor RCC (Fig 1e,f) with Fuhrman grade 2, with IHC: AE1/AE3 (3+), CD10 (1+), cytokeratin (CK)18 (3+), CK7 (+), paired box 2 (PAX2) (2+), PAX8 (1+), P504 (+), S100 (–), Vim (3+). After further comprehensive radiologic examination, neither regional lymph node metastasis nor distant metastasis was found. Thus, the clinical tumor node metastasis stage was classified as T1N0M0 for both the HCC and RCC. According to the Barcelona Clinic liver cancer staging classification, the patient was at stage A.

Our team then performed curative image-guided percutaneous ablation for the treatment of both HCC (Fig 3) and RCC (Fig 4). We used the microwave system at 2450 MHz with water circulative-cooling. Ultrasound was performed to act as a guide for the HCC treatment and showed a liver mass of about 2.8×2.0 cm, located in the hepatic dome (liver segment VI). When the patient inhaled, the mass was invisible on ultrasound because of the aerated alveoli. To solve this problem, our team applied artificially induced right hydrothorax to allow the ultrasound image to be clearly visible and to protect the lung from active heating. With the patient in the supine position, an MWA needle was used to puncture the lower side of the lesion at an output power of 55 w for 3.5 minutes. Another needle was injected into the upper side of the lesion at an output power of 55 w for 5.5 minutes. We then performed contrast-enhanced ultrasound examination, which showed that the lesion was fully ablated. The

patient complained of pain after ablation, which was relieved by symptomatic treatment. There were no other complications, such as bleeding, pneumothorax, infection or hemoglobinuria. The patient was hospitalized for five days for HCC treatment, and the follow up CT scan revealed no disease recurrence or metastasis (Fig 5a,b).

One month later, we applied CT-guided MWA for management of the RCC. A preoperative CT scan showed that the lesion was 3.0×2.5 cm in size, located in the upper pole of the left kidney. With the patient placed in a half right supine position, two guided 22G needles were inserted into the tumor at pre-determined angles and depths. After a CT scan confirmed the accuracy of the puncture route, one MWA needle punctured the middle of the lesion at an output power at 55–60 w for seven minutes. The second needle was inserted into the upper side of the lesion, at an output power of 55–60 w for four minutes. The follow-up CT scan showed that the RCC was completely ablated, and the patient was in good health without any postoperative complications. He was hospitalized for five days for the treatment of RCC, and the follow up CT scan found no disease recurrence or metastasis (Fig 5c,d).

Discussion

Multiple primary malignant tumors are defined as tumors that are clearly malignant, topographically separate and

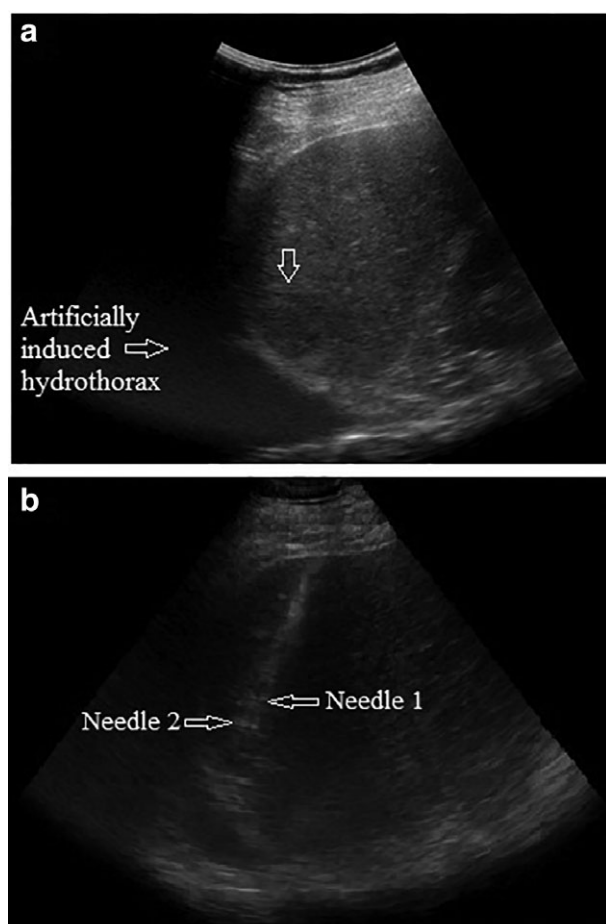


Figure 3 A hypoechoic lesion in the right posterior segment of the liver was detected by ultrasonic examination. (a) Artificially induced right hydrothorax to make the ultra sound-image clear and protect the lung from active heating. (b) Ablative needles were advanced into the upper and lower sides of the lesion.

distinct, and the probability that one is a metastatic lesion from the other has been ruled out.^{1,2} According to these criteria, this case was determined as a triple primary malignant tumor. To our knowledge, no similar cases of triple primary cancer (small cell lung cancer, HCC, and RCC) in which the patient achieved long-term survival have been reported. It has been proven that individuals who develop a malignancy might be at a greater risk of developing a second. On the one hand, the agents or factors that caused the first malignancy may still be at work, while on the other, chemotherapy and radiotherapy used in cancer treatment are known carcinogens.^{3–6} The mechanisms require further exploration.

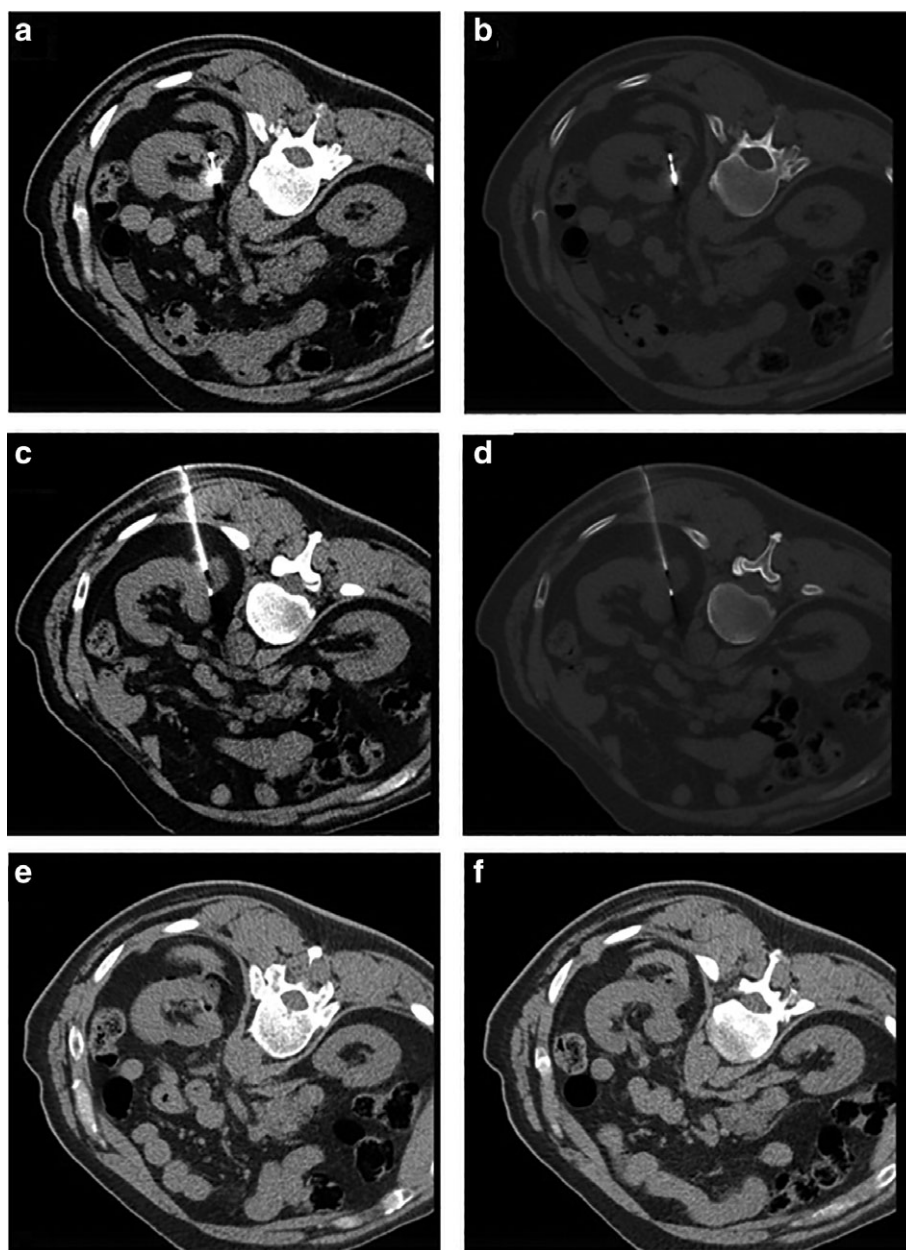
The patient received sequential chemotherapy and radiotherapy for the treatment of SCLC. In Sharouni *et al.*'s study, a patient with SCLC who had received sequential chemotherapy and radiotherapy achieved median survival

of 14.0 months and a five-year overall survival rate (OS) of 10.5%.⁷ It has been 10 years since our patient was diagnosed with SCLC, which is rare long-term survival of SCLC. He had been in a stable condition after achieving complete remission (CR) for more than six years before a follow up CT examination revealed the liver and renal masses. A history of hepatitis B and an elevated alpha-fetoprotein level supported a diagnosis of primary liver cancer. We performed percutaneous biopsy, and pathologic analysis confirmed the synchronous double primary tumors. Fortunately, both the liver and kidney tumors were at very early stages. As a result, the importance of regular examination and accurate diagnoses should be emphasized.

Microwave ablation, an extremely promising and improving heat-based thermal ablation modality, is emerging as an alternative to RFA in the treatment of hepatic and renal malignancies.^{8,9} Microwaves can generate very high temperatures in short time periods, potentially leading to improved treatment efficiency and larger ablation zones.¹⁰ According to a recent study, no significant difference between RFA and MWA therapy for the treatment of early stage HCC was found in terms of CR, rates of residual foci of untreated disease, and recurrence rate.¹¹ In tumors ≥ 3.5 cm, the five-year OS and disease-free survival rates of patients treated with MWA are better than those treated with RFA.¹² Facciorusso *et al.* reported similar efficacy between MWA and RFA techniques, and indicated the apparent superiority of MWA in larger liver tumors.¹³ Although the efficiency of MWA for the treatment of HCC and RCC has been proven by clinical research, there is less cumulative data on MWA compared to RFA.^{14,15}

Compared to RCC, HCC has a high malignancy level, high mortality, and rapid progression, thus we treated the HCC in our patient first. According to literature, patients with early stage HCC (i.e. Barcelona Clinic liver cancer stage 0–A) should be considered for any available curative treatments, including liver transplantation, hepatic resection, and ablation.¹⁶ Hepatic resection is the mainstay of curative treatment for early stage HCC and has achieved the best outcomes.¹⁶ With advances in image guided ablation techniques, the long-term outcomes reported for patients treated with thermal ablation shown that five-year OS rates were comparable with those achieved using surgery in patients with potentially respectable tumors.¹⁷ Although partial nephrectomy is still considered the gold standard treatment for stage T1a (< 4 cm) RCC, surgical complications should also be considered when a surgical course is decided. In recent years, ablation has shown significant promise and increasing clinical utility as more studies have demonstrated its safety and efficacy for the treatment of RCC. For stage T1a RCC in poor surgical

Figure 4 Figure 4 Two ablative needles were inserted into the upper (**a**, abdomen; **b**, bone) and lower sides (**c**, abdomen; **d**, bone) of the lesion in the right kidney. (**e,f**) A computed tomography scan revealed that the neoplasm of the right kidney had been sufficiently ablated.



candidates (including patients with significant surgical risk or in patients where preservation of nephrons is critical), ablation is the preferred treatment. For stage T1a RCC in otherwise healthy patients, ablation could also be considered. Recent literature has demonstrated that renal mass ablation is safe with a similar in efficacy to surgical resection in carefully selected patients.^{18,19} For early stage RCC, according to a recent study, ablation resulted in equal clinical outcomes compared to surgical resection.^{20,21} Percutaneous ablation is a less invasive treatment, and is associated with lower complication rates and shorter hospitalization compared to surgery. However, until now, no

data has unequivocally supported percutaneous ablation as a replacement for resection for the first-line treatment of early stage HCC. Although MWA is acknowledged as a viable option for RCC ablation, it still lacks supporting clinical data.

In conclusion, we report a rare case of multiple primary malignant tumors. Over 10 years, this patient developed primary malignant tumors in his lung, liver, and kidney. The patient has survived without recurrence because of diligent surveillance; accurate diagnosis; and positive, correct, individualized therapy. Further study is warranted to improve our understanding of why such patients are

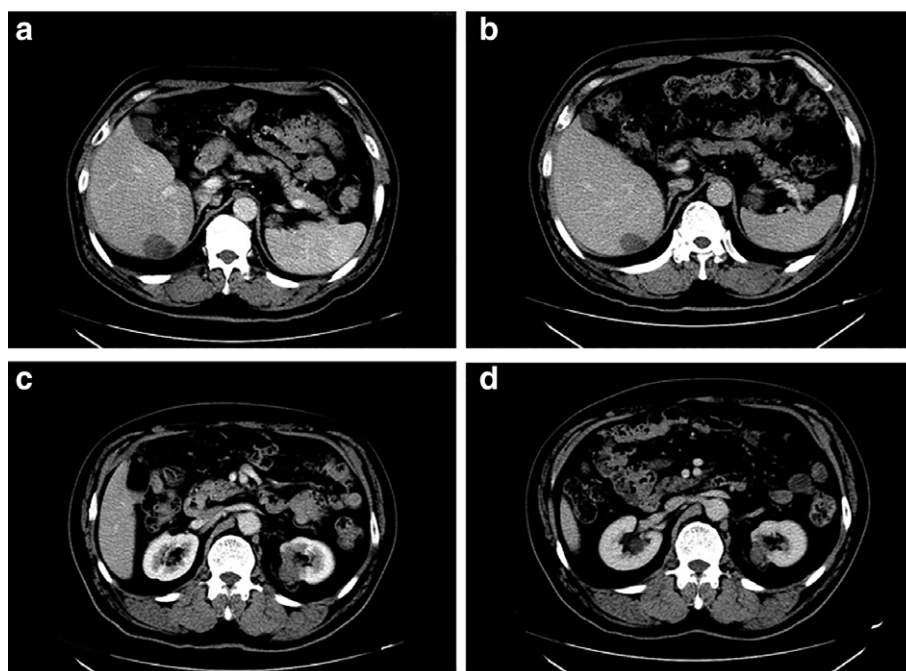


Figure 5 One month after ablation, contrast enhanced computed tomography showed no recurrence in either the (a) liver or (b) kidney. At the two year follow-up, computed tomography showed no recurrence in either the (c) liver or (d) kidney.

susceptible to multiple primary tumors. The advantages of MWA for the treatment of patients with multiple primary malignant tumors require further supportive evidence.

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Disclosure

No authors report any conflict of interest.

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