

REVIEW ARTICLE

## Needle tract seeding after percutaneous cryoablation of small renal masses; a case series and literature review

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### ABSTRACT

Neoplastic cell seeding due to needle tumor manipulation during renal mass biopsy (RMB) or thermal ablative treatment is a rare but potentially serious event that can turn an organ-confined and curable tumor in a nonorgan-confined and non-curable disease. Despite the widespread use of percutaneous thermal ablative treatment for small renal masses (SRMs), this complication has been described in few case reports and small case series and has never been reported after ablative treatment alone. We report a series of two patients that underwent cryoablation for SRMs and developed recurrence along the needle tract. Available knowledge on the controversial topic of tumor seeding following needle manipulation are poor. So far, reporting cases of tumor cell seeding due to needle manipulation is useful to permit a better understanding of this complication.

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Seeding; SRMs; cryoablation; renal cell cancer; kidney cancer

## Introduction

Cryoablation represent a therapeutic option for patients with SRMs [1]. Between 2004 and 2015, 1839 patients diagnosed with T1aN0M0 renal cell carcinoma were treated in the United States with thermal ablative techniques, of whom 1381 underwent cryoablation and 457 underwent radiofrequency ablation [2]. Tumor cell seeding is a rare phenomenon that consists of neoplastic cell spillage outside the tumor and implantation in the perinephric tissues. Clinical implication of tumor seeding is not well known. According to available case reports, tumor seeding could manifest as a clinically indolent complication or could significantly change the patient's prognosis [3]. The incidence rate of tumor seeding after RMB for kidney cancer was previously estimated at 0,01% [4], but this value is considered to be an underestimate by many authors [4,5]. We reported here the first case series of two patients treated with percutaneous cryoablation for small renal masses who developed recurrence along the tract of the thermal probes.

## Patients

### Case 1

A 47-year-old male presented initially to our department in 2010 reporting an episode of monosymptomatic hematuria. His medical history, laboratory results and physical examination were unremarkable. Ultrasonography revealed the presence of a 35 mm right complex renal cyst. Cystoscopy and

urine cytological examination were negative for any pathological findings. Computed tomography (CT) showed a cystic lesion with thickened irregular walls and septa characterized by significant contrast enhancement. Three months later, the patient underwent open partial nephrectomy and the cystic lesion was entirely removed without wall breaking. No perioperative complications were reported. Pathological examination demonstrated the presence of a multilocular cystic pT1a RCC with Fuhrman Grade 1. Surgical margins were negative, and no involvement of the collecting system was reported. At 12 months follow-up, abdominal magnetic resonance imaging (MRI) was negative for local and distant recurrences. At two years follow-up, a CT scan showed the presence of an 18 mm cystic renal mass with contrast enhancement at the site of previous surgery. The Institutional multidisciplinary team composed by urologists, medical oncologists and radiologists evaluated the case and proposed a CT-guided percutaneous cryoablative treatment. In order to reduce the risk of cystic rupture connected to the tumor, needle manipulation biopsy was avoided. Two cycles of 10-minute freezing and thawing was performed using two 17-gauge probes. During the procedure, the ice balls entirely covered the cystic mass and a rim of healthy tissue (Figure 1(a)). No intraoperative and perioperative complications occurred. At six months follow-up, no signs of local and distant recurrence were reported. Twelve months after cryoablation, the follow-up MRI revealed an abdominal mass within the posterior flank musculature (Figure 1(b)). Imaging analysis demonstrated that the mass was located along the cryoablation probe tract. Simultaneously, lung nodules

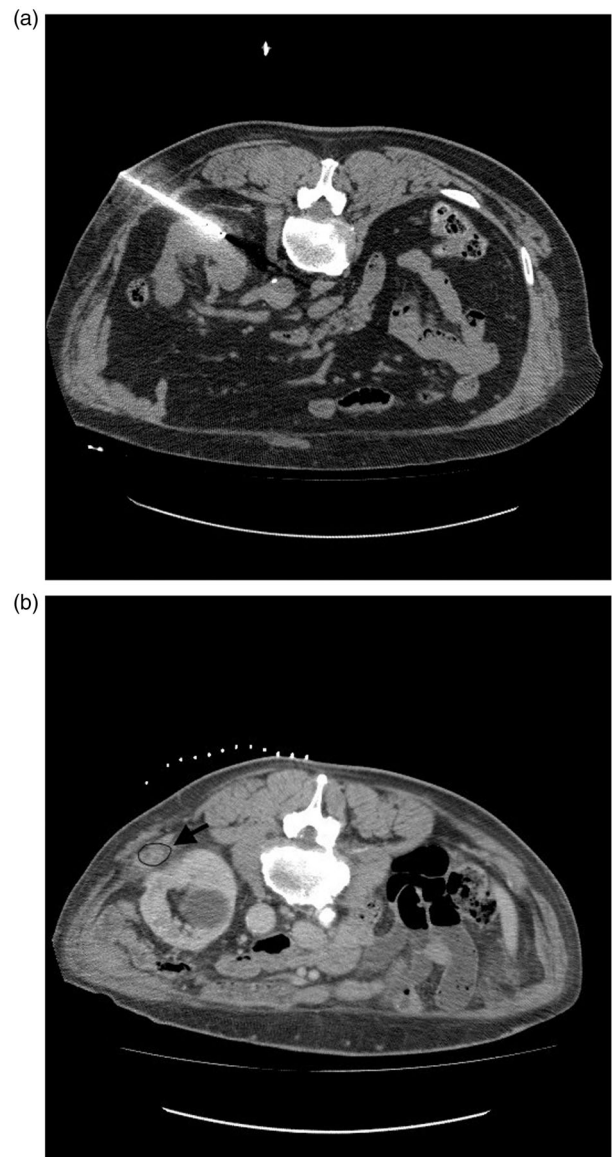


**Figure 1.** (a) Case 1. CT scan during renal cryoablation showing the probe passed through the right flank. Patient was placed in prone position during the procedure. (b) Case 1. RMN at 12 months after percutaneous cryoablation demonstrating a recurrent tumour mass in the right flank musculature along the the cryoprobe tracts. The mass was biopsied with evidence of undifferentiated renal cell carcinoma.

compatible with metastasis were also present. The lumbar lesion was surgically biopsied, and pathological examination was consistent with undifferentiated renal cell carcinoma. Three months later, chest and abdominal CT scans demonstrated the rapid progression of the disease. The patient underwent chemotherapy with limited response. Cancer induced death six months later.

### Case 2

A 66-year-old male with a history of right nephrectomy in 2002 and left partial nephrectomy in 2007, both for papillary RCC (pRCC), presented for a scheduled follow-up visit in 2010. At this visit, the surveillance abdominal CT-scan reported the presence of two masses smaller than 1 cm in the middle third of the left kidney with the features of the papillary tumor at MRI. Within 8 weeks, the patient underwent cryoablation of both masses. Two cycles of 10-minute freezing and thawing were performed using two 17-gauge



**Figure 2.** (a) Case 2. CT scan during renal cryoablation showing the probe passed through the right flank. Patient was placed in prone position during the procedure. (b) Case 2. CT scan at 14 months after percutaneous cryoablation demonstrating 2 nodules of tumor seeding in the right flank musculature along the cryoprobe tracts. The mass was biopsied with evidence of papillary renal cell carcinoma.

probes (Figure 2(a)). Ice balls entirely covered the cystic masses and a rim of healthy tissue. No intraoperative and perioperative complications occurred. In the following years, the patient underwent three ulterior cryoablative treatments for local recurrence. In November 2017, the follow-up ultrasonography showed a  $2.7 \times 1.6$  cm suspicious hypoechoic solid lesion in the posterior perinephric fat. Chest and abdominal CT scan revealed another smaller lesion in the perinephric fat (Figure 2(b)). Percutaneous biopsy of both nodules was performed, and histological examination was consistent with pRCC. The multidisciplinary team composed of urologists, medical oncologists and radiologists proposed a CT-guided percutaneous cryoablative treatment. Two cycles of 4.5-minute freezing and thawing were performed on the known lumbar mass using two 10-gauge probes, and two cycles of 3-min freezing and thawing were performed on the

Table 1. Previous reported cases of renal cancer seeding after needle manipulation (RCC: Renal Cell Carcinoma).

Authors and sources	Number of cases	Age (Years)	Procedure that comported the tumor needle manipulation	Histology	Diagnosis of the recurrences	Recurrence site and time to recurrence (when disposable)	Treatment	Disposable data about follow-Up
Macklin et al.; Eur Urol. 2018 [4]	7	66	Percutaneous biopsy	Clear renal cell carcinoma Fuhrman GGrade IV	Pathological examination after open partial nephrectomy	Perinephric fat	-	Died from metastatic disease.
		73	Percutaneous biopsy	Papillary RCC Fuhrman grade III	Pathological examination after open partial nephrectomy	Perinephric fat	-	Free from recurrence at 12 months follow-up
		44	Percutaneous biopsy	Papillary RCC type 2 Fuhrman grade III	Pathological examination after open partial nephrectomy	Perinephric fat	-	Free from recurrence at 36 months follow-up
		71	Percutaneous biopsy	Papillary RCC Fuhrman grade III	Pathological examination after robotic partial nephrectomy	Perinephric fat	-	Free from recurrence at 18 months Follow-up
		49	Percutaneous biopsy	Papillary RCC Fuhrman grade III	Pathological examination after robotic partial nephrectomy	Perinephric fat	-	Free from recurrence at 9 months Follow-up
		60	Percutaneous biopsy	Papillary RCC Fuhrman grade III	Pathological examination after robotic partial nephrectomy	Perinephric fat	-	Free from recurrence at 11 months follow-up
		74	Percutaneous biopsy	Papillary RCC Fuhrman grade II	Pathological examination after open partial nephrectomy	Perinephric fat	-	Free from recurrence at 6 months follow-up
Andersen et al.; Urol Case Rep. 2016 [14]	2	40	Percutaneous biopsy	RCC	Imaging pathological examination after surgical excision	4 years after in the cicatrix, 7 years after in the Psoas muscle	Surgical excision	Free from recurrence at time of the article
		60	Percutaneous biopsy	RCC	Imaging pathological examination after surgical excision	2 years after and 3 years after in the abdominal wall, 3.5 years after in the 12th rib and in the Psoas muscle	Surgical excision	New recurrence at 4.5 years
Iguchi et al.; Diag and Int Im. 2016 [15]	1	NA	Percutaneous biopsy	RCC	NA	8 months	-	NA
Chang et al.; Korean J Urol. 2015 [16]	1	66	Percutaneous biopsy	Clear cell RCC. Fuhrman grade II	Pathological examination after partial nephrectomy	Perinephric fat	-	3 months after patient was free from recurrences
Soares et al.; Case Rep Urol. 2015 [17]	1	50	Percutaneous biopsy	Low-grade renal cancer	Pathological examination after partial nephrectomy	Perinephric fat	-	1 month after patient was free from recurrences
Viswanathn et al.; J Can Urol Assoc. 2015 [3]	2	63	Percutaneous biopsy and percutaneous cryoablation	Clear cell RCC. Fuhrman grade II	Follow-up imaging	Flank musculature 10 months after cryoablative treatment	Medical treatments	Metastatic spread tumor induced death 2 years after recurrence diagnosis
		53	Percutaneous biopsy	Papillary RCC	Pathological examination after partial nephrectomy	Perinephric fat	-	5 years after surgery patient was free from recurrence
Van De Kamp et al.; J Can Urol Assoc. 2015 [11]	1	65	Laparoscopic guided biopsy and cryoablation	Clear Cell RCC, Fuhrman grade I	Follow-up imaging	Multiple recurrences In retroperitoneal fat 5 years after cryoablative treatment	Radical nephrectomy	5 years after surgery patient was free from recurrence

(continued)

Table 1. Continued.

Authors and sources	Number of cases	Age (Years)	Procedure that completed the tumor needle manipulation	Histology	Diagnosis of the recurrences	Recurrence site and time to recurrence (when disposable)	Treatment	Disposable data about follow-up
Giorgadze et al.; Diagn Cytopathol. 2013 [18]	1	NA	Core biopsy and fine needle aspiration	Papillary RCC	NA	Retropertoneal recurrence four years after Biopsy	NA	NA
Sainani et al.; J Vasc Interv Radiol. 2013 [9]	1	61	Percutaneous biopsy and percutaneous cryoablation	Papillary RCC	Follow-Up Imaging	Perinephric fat 4 years after cryoablative treatment	Percutaneous Tc guided cryoablation of the recurrences	38 months after the recurrences treatment, patient was free from recurrence.
Mullins et al.; J Can Urol Assoc. 2013 [19]	1	68	Percutaneous biopsy	Papillary RCC Fuhrman Grade I	Pathological examination after partial nephrectomy	Perinephric fat	-	3 months after patient was free from recurrence.
Akhavain et al.; BMJ Case Rep. 2012 [12]	1	84	Percutaneous biopsy and percutaneous cryoablation	Clear cell RCC, Fuhrman not reported	Follow-up imaging	Perinephric and subcutaneous fat 3 months after cryoablation	Observation	1 years patient was alive with multiple chest and abdominal metastasis
Shenoy et al.; Acta Radiol. 1991 [20]	1	40	Percutaneous needle aspiration	Cytologic examination negative for malignant cells	Hematuria	Subcutaneous fat 1 year after needle aspiration	Radical nephrectomy and surgical excision of the subcutaneous nodule	NA
Kiser et al.; J Urol. 1986 [10]	1	48	Percutaneous CT-guided needle aspiration	Papillary RCC	Intraoperative during partial nephrectomy	Nodule of 5 mm at the psoas muscle 24 days after needle aspiration	Local excision	18 months after patient was free from recurrence
Wehle et al.; J Urol. 1986 [21]	1	37	Percutaneous biopsy	Papillary RCC	Follow-up	Flank mass 4 Years	Local radiotherapy	Metastatic spread tumor induced death 10 months after recurrence diagnosis
Auvert et al.; Prog Clin Biol Res. 1982 [22]	1	59	Percutaneous biopsy	Oncocytoma	Follow-up	Lumbar subcutaneous 7 years	Local excision	No data reported about follow-up
Gibbons et al.; J Urol. 1977 [23]	1	56	Percutaneous needle aspiration	RCC	Follow-up	Muscular nodule 20 months after Needle Aspiration	Local excision	No data reported about follow-up

smaller adjacent mass. No intraoperative and perioperative complications occurred. At last check-up, 12 months after the treatment of the extrarenal recurrences, follow-up was negative for relapses.

## Discussion

Cryoablation represents an attractive, minimally invasive therapeutic option for the management of SRMs [1]. Available evidence does not allow definitive conclusions regarding oncological outcomes because of that The European Association of Urology guidelines prudently states that should be considered only for old and/or comorbid patients [6]. In both cases of this article, cryoablation was used to treat the local recurrence of RCCs. Treatment protocols for RCC local relapse after nephron-sparing surgery are lacking. According to available evidence, it seems that resection may lead to good disease control and improve survival if no sarcomatoid features are present [7]. In both cases, the decision to opt for the cryoablation was supported by both the multidisciplinary team and the patient's will. In the first case, considering the reduced diagnostic accuracy of the biopsy in cystic lesions and the additional risk of tumor rupture, biopsy was avoided [8]. One could argue that puncture of the cyst with a cryoprobe could lead to a considerable risk of tumor seeding. Felker et al. reported a series of 16 patients treated with radiofrequency ablation for histologically proven malignant cystic mass without any case of tumor seeding at a mean follow-up of 24 months [9]. At the time of tumor seeding diagnosis, lung nodules suggestive of metastatic disease were also present; however, no other abdominal metastases were detectable. The presence of a single abdominal metastatic mass in the lumbar muscular wall along the cryoprobe tract is an extremely rare event, and so we considered the mass as tumor seeding. In the second case, the neoplastic nodules were localized in the perinephric fat and the muscular wall along the needle tract. Chest and abdomen CT did not report any other suspicious nodules. Sainani reported a similar case of tumor seeding due to percutaneous biopsy of a pRCC, in this case, the nodules of tumor seeding were successfully treated with percutaneous cryoablation [10]. Tumor seeding after RTB or thermal ablative treatments are anecdotally reported with varying oncological outcomes (Table 1). In some cases, the spread cells have an indolent behavior and are incidentally discovered within the perirenal fat at the pathological examination after nephrectomy [8,11]. In other cases, the disseminated tumor cells presented an aggressive behavior and evolved to metastatic disease [4,12,13]. Different behaviors are likely due to the different biological features. Many strategies to reduce the risk of seeding have been suggested, such as the utilization of coaxial needle technique or the 'hot withdrawal' of the needle tract after RTB or radiofrequency ablation. However, efficacy of these strategies has never been definitively proven [5,8]. Recently, Macklin et al. reported seven cases of histologically proven tumor seeding after RMB despite the use of the coaxial needle technique [5]. The presence of nodules along the cryoprobe tract after

tumor ablation should not be directly interpreted as tumor seeding. In a series of 253 patients who underwent percutaneous cryoablation or radiofrequency ablation for renal tumors, Lokken et al. reported six patients with benign inflammatory nodules that mimicked seeding [14]. Suspicious nodules should be biopsied to distinguish between inflammatory masses and tumor seeding. Studies on cryoablation of SRM are continuously increasing in number but only a few cases of seeding have been reported. This study represents the largest reported series of histologically confirmed tumor seeding after cryoablation without previous RTB. In our institutions, between June 2011 and February 2018, 110 percutaneous cryoablations for SRMs were performed. Fifty-six masses were histologically proven malign RCC, 36 were benign lesions, in eight cases biopsies were nondiagnostic, and in 10 cases, biopsy was avoided. Incidence of seeding after cryoablation of SRMs in our institutions, excluding benign tumor, is 2.7%. All the cryoablation treatments as the oncological surveillance were performed by the same team of urologists and radiologists. Follow-ups were scheduled according to internal protocol based on the European Association of Urology guidelines [6]. The analysis of this case series does not permit us to reach any general conclusion about tumor seeding, however, as observed by other authors, the previously proposed value of 0,01% is probably underestimated [4].

## Conclusions

Over the recent years, the use of cryoablation for the treatment of small renal tumor is increasing and it is likely that this will rise further. This article's objective is absolutely not to deter clinicians from using cryoablation to treat SRMs. Cryoablation, as with RTB and other procedures that could comport tumor needle manipulation, is helping patients and surgeons to avoid the concrete risks produced by surgery and anesthesia for unnecessary intervention. Advantages produced by these procedures exceed morbidity due to the risk of tumor seeding. Nevertheless, unfortunately, tumor seeding seem not anecdotal as previously stated. We believe that reporting cases of tumor seeding could help to better understand and manage this challenging complication. Finally, we emphasize the importance of careful inspection of the perinephric fat, the posterior abdominal wall, the subcutaneous fat and other tissues along the ablation probe tract during oncological surveillance in order to identify and treat the possible case of tumor seeding as early as possible.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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