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Inflammatory Nodules Mimic Applicator Track Seeding After Percutaneous Ablation of Renal Tumors

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OBJECTIVE. The objective of our study was to report the occurrence of benign inflammatory nodules that develop in or near applicator tracks after percutaneous radiofrequency ablation and cryoablation of renal tumors.

CONCLUSION. Benign inflammatory nodules occur rarely after percutaneous ablation of renal tumors and may mimic tumor seeding of the applicator track.

Renal cell carcinoma constitutes approximately 3% of adult malignancies and is the sixth leading cause of cancer deaths in the United States [1]. Detection has increased with advances in abdominal imaging, and many renal cancers are small and amenable to minimally invasive therapies [2]. Partial nephrectomy is now being used to treat small (< 4 cm) renal tumors, with 5-year survival rates similar to radical nephrectomy [3].

Percutaneous ablation of renal tumors using either radiofrequency ablation or cryoablation involves nephron-sparing techniques that aim to further decrease procedure-related morbidity relative to partial nephrectomy and allow patients who are not surgical candidates to be treated. Although longer follow-up data will be required before percutaneous ablation becomes the standard of care, initial results have been promising [4–6].

Implantation ("seeding") of tumor cells within the applicator track is a potential complication of percutaneous ablation that has been reported in one patient after radiofrequency ablation of a renal cell carcinoma [7]. We report six patients who had benign imaging findings that initially suggested applicator track seeding.

Materials and Methods

In a retrospective study of 253 patients, we reviewed CT and MR images after 310 percutaneous renal tumor ablation procedures performed over 7 years at two partnering institutions. This study was approv4ed by our single institutional internal review board; informed consent was waived. Ablations were performed on 287 tumors (mean, 3.0 cm; range, 1.0–8.9 cm) in 173 men and 80 women with an average age of 69 years (age range, 22–89 years). Renal tumors included renal cell carcinoma ($n = 276$), angiomyolipoma ($n = 1$), leiomyosarcoma ($n = 1$), oncocytoma ($n = 7$), and transitional cell carcinoma ($n = 2$). All tumors were biopsy-proven except for 31 tumors that were diagnosed as renal cell carcinoma by imaging criteria alone. Images were reviewed to identify patients with findings within or adjacent to the applicator track that were suggestive of applicator track seeding. Positive findings (i.e., nodular enhancement occurring more than 24 hours after the ablation) were tabulated. Enhancement was determined by measuring attenuation before and after administration of IV contrast material. Enhancement with MRI was defined as an increase in signal intensity by more than 20% [8]; when available, subtraction MRI was used also. Enhancement with CT was defined as an increase in attenuation of more than 10 H [9]. Imaging findings, pathology, and clinical follow-up of patients with positive findings were reviewed.

Radiofrequency Ablation Procedures

Of 310 procedures, 235 were performed using radiofrequency ablation guided by CT (LightSpeed, GE Healthcare; $n = 224$) or sonography (Logic 700, GE Healthcare; $n = 11$) on 205 renal tumors (mean, 3.2 cm; range, 1.0–8.9 cm) [4]. Prophylactic antibiotics were not administered before the procedure. The skin was prepared and draped using sterile technique. For most cases ($n = 205$), a 200-W generator with impedance-controlled pulsed current was used with internally cooled straight single or cluster electrodes ($n = 190$) or with a switching controller allowing three straight single electrodes ($n = 15$) (Cool-tip, Valleylab) with multiple overlapping 12-minute ablations to treat the entire tumor. The remaining cases were performed using a 150- to 200-W generator and multitined expandable electrodes with ($n = 4$) or

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without ($n = 26$) saline instillation (3–5 cm) (StarBurst XLi or StarBurst XL, RITA Medical Systems) and a target temperature of 105°C, also with multiple overlapping ablations. In a minority of cases, dextrose 5% in water (D5W) was injected with fine (20-gauge) needles to prevent burning adjacent structures. The electrode track was ablated to reduce the risk of hemorrhage in patients with central tumors, coagulopathy, or evidence of bleeding during the procedure. Track ablation was performed at operator discretion in a minority of cases with 200–300 mA of current, allowing the temperature to reach over 50°C as the electrode was slowly and incrementally withdrawn. To avoid skin pain or burns, track ablation was discontinued when the active tip of the electrode was within 1–2 cm of the skin. Thirty tumors required a second radiofrequency ablation session because CT scans at 1 month showed residual tumor.

Cryoablation Procedures

Of 310 procedures, 75 were percutaneous cryoablations of 82 renal tumors (mean, 2.6 cm; range, 1.0–6.6 cm) guided by a 0.5-T open-configuration MRI system (Signa SP, GE Healthcare) [5]. During seven procedures, two tumors were targeted. Before the cryoablation procedure, the skin was prepared and draped using sterile technique. Prophylaxis for infection was provided with 1 g IV cefazolin sodium (Ancef, SmithKline Beecham Pharmaceuticals) administered every 8 hours for 24 hours. A cryoablation delivery system (CryoHit, Galil Medical) was used with 13- or 17-gauge cryoprobes. Depending on the size of the lesion, one to seven (mean, three) cryoprobes were placed in tandem alongside an MRI-compatible 22- to 20-gauge biopsy needle (MRI-compatible biopsy needle, E-Z-EM). A freeze-thaw-freeze cycle (15-minute freeze, 10-minute passive thaw, 15-minute freeze) was used. During freezing, probe-tip temperatures reached a nadir of approximately −130°C. If the ice ball did not encompass the tumor entirely and include a 5-mm margin of tissue beyond the tumor, additional cryoprobes were placed. To prevent freezing adjacent structures, normal saline was injected using fine (20- to 22-gauge) needles before five of 75 cryoablation procedures. During 18 of 75 procedures, external manual compression was used to displace bowel loops [10].

Follow-Up Imaging

All patients underwent CT or MRI before ablation, with and without IV contrast material; these results formed a baseline comparison for subsequent imaging. CT (LightSpeed [GE Healthcare] or Somatom Volume Zoom, Somatom Sensation 16, or Somatom Sensation 64 [Siemens Medical Solutions]) was performed with 2.5- to 5-mm collimation at 220–240 mA and 140 kVp. MRI (Signa, GE Healthcare) included the following sequences: transverse T2-weighted imaging with fast spin-echo (TR_{range}/TE, 3,267–7,000/100; echo-train length, 12; section thickness, 4 mm; gap, 1 mm; field of view, 30–36 cm), breath-hold fast-recovery fast spin-echo (1,200–2,996/91–94; echo-train length, 17–22; section thickness, 5 mm; gap, 1 mm; field of view, 32–40 cm), and/or single-shot fast spin-echo (17,240–53,380/184–190; section thickness, 5 mm; gap, 1 mm; field of view, 32–40). We also used transverse T1-weighted imaging with a spin-echo sequence (500–800/14; section thickness 4–5 mm; gap, 1 mm; field of view, 30–36 cm) or a spoiled gradient-recalled echo (GRE) sequence (300–400/2.2, 4.7; dual echo; flip angle, 90°; section thickness, 5 mm; gap, 1 mm; field of view, 32–40 cm) and transverse fat-suppressed T1-weighted dynamic imaging with a spoiled GRE sequence (260–435/4.2; flip angle, 75°; section thickness, 4–6 mm; gap, 1 mm; field of view, 34–40 cm) or a 3D fast-acquisition multiple-excitation spoiled GRE sequence (5.2–7.3/1.5–2.2; flip angle, 10°; section thickness, 2.5 mm [effective]; gap, 0 mm; field of view, 32–40 cm) before and after IV gadolinium administration (gadopentetate dimeglumine; Magnevist, Berlex).

After ablation, CT or MRI using the same protocol as the preprocedural examination was performed at 24 hours and/or 1 month and then every 3 months for the first year and every 6–12 months thereafter. Most patients who underwent radiofrequency ablation were followed up with CT, and most patients who underwent cryoablation were followed up with MRI. There were some patients treated with radiofrequency ablation who were followed up with MRI instead of CT because of renal insufficiency. Some patients treated with cryoablation were followed up with CT if CT was requested for another indication; one patient had a cardiac pacemaker implanted in the interval, and therefore, could no longer be followed up with MRI. The mean length of follow-up was 2.6 years for radiofrequency ablation procedures and 1.8 years for cryoablation procedures.

Results

A new, enhancing nodule (mean, 2.5 cm; range, 1.3–4.9 cm) was visible within or adjacent to the applicator track after six (1.9%) of 310 procedures. Nodules were first visible 2–52 months after the ablation procedure (mean, 13 months; median, 6.5 months) and appeared as ring-enhancing lesions ($n = 4$; mean diameter, 1.6 cm) or ill-defined enhancing soft-tissue masses ($n = 2$; mean diameter, 4.1 cm).

Applicator track nodules occurred after four (1.7%) of 235 radiofrequency ablation procedures and two (2.7%) of 75 cryoablation procedures. Nodules occurring after radiofrequency ablation were ring-enhancing ($n = 2$; mean size, 1.4 cm) or ill-defined enhancing regions of soft tissue ($n = 2$; mean size, 4.1 cm) (Fig. 1). These findings were first visible at 3, 6, 7, and 52 months and were adjacent to the ablated renal tumor within the perinephric space alone ($n = 3$) or within the perinephric space and abdominal wall ($n = 1$, Fig. 1).

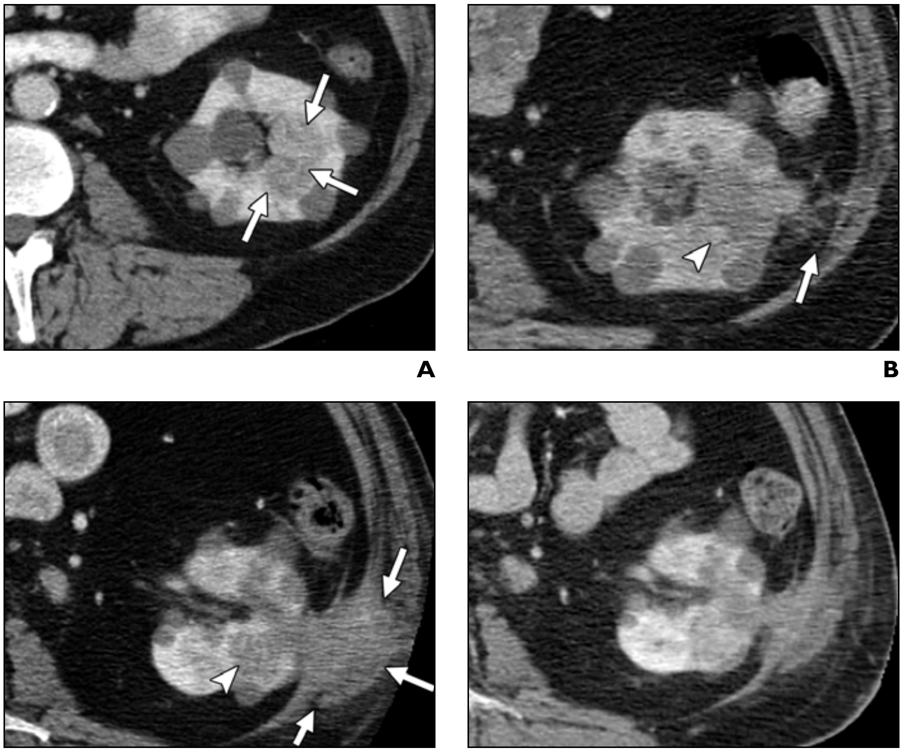
The nodules occurring after cryoablation ($n = 2$) were ring-enhancing (mean size, 1.8 cm) and first visible at 2 and 9 months, respectively (Fig. 2). The nodules were located within the subcutaneous fat and associated with a tram-tracking pattern of enhancement along the cryoprobe track on subsequent imaging examinations (Fig. 2) or on both previous and subsequent examinations. Nodules after radiofrequency ablation were not associated with tram-tracking along the electrode track.

External manual compression of the bowel was performed during one of the cryoablation procedures associated with an applicator track nodule. No cases were associated with the injection of D5W or saline.

Among patients who developed an applicator track nodule, self-limited hematuria was observed after one radiofrequency ablation, and a small perinephric hematoma developed after another radiofrequency ablation that persisted 3 months after the procedure. The hematoma was in the same area as the applicator track nodule that appeared 3 months later. A small perinephric hematoma was visible at 24 hours after one cryoablation procedure and resolved by 1 month. This hematoma was not in the same area as the applicator track nodule. No major complications as defined by Goldberg et al. [11] occurred after procedures associated with an applicator track nodule.

Four nodules (three after radiofrequency ablation, one after cryoablation) were biopsied percutaneously under CT guidance. Of these, one was also surgically resected. At pathology, three nodules showed signs of a chronic, reactive inflammatory process, such as perivascular lymphoplasmacytic infiltrate, histiocytes, granulation tissue, and fibrosis. A nodule after radiofrequency ablation that occurred after a persistent hematoma consisted of marked acute inflammation and granulation tissue consistent with an organizing abscess. None of the nodules showed evidence of malignancy.

Of the six nodules, two were no longer visible 4 months after detection. Three either substantially decreased in size or no longer enhanced within 3 to 6 months. The remaining nodule, which was found on biopsy to be consistent with an organizing abscess, decreased in size at 3 months and therefore was not treated with antibiotics; it has remained stable at 12 months.



A B C D

Fig. 1—42-year-old man with von Hippel-Lindau disease referred for CT-guided percutaneous radiofrequency ablation of 3.4-cm renal cell carcinoma.
A, Axial CT scan before ablation shows enhancing tumor (*arrows*) in left mid to lower pole.
B, CT scan 1 month after ablation shows soft-tissue stranding (*arrow*) adjacent to applicator track. Dense arterial enhancement (*arrowhead*) is seen within treated tumor, consistent with residual disease.
C, CT scan 7 months after ablation procedure. A new, enhancing 4.9 × 4.1 cm nodule (*arrows*) is located in perinephric space and abdominal wall along applicator track. Percutaneous biopsy of nodule showed chronic inflammation with histiocytes, granulation tissue, and fibrosis, with no evidence of malignancy. Arrowhead indicates residual disease within treated tumor.
D, CT scan 2 months later shows applicator track nodule decreased in size to 4.0 × 3.2 cm.

Discussion

To our knowledge, this is the first series of clinical observations that describes the development of tumorlike nodules in the applicator track after renal ablation. Tumor seeding of the applicator track after renal tumor ablation has occurred in only one case [7]. Indeed, tumor seeding also is rare after percutaneous biopsy of renal tumors [12]. Nevertheless, seeding is an important complication and should be looked for on patient follow-up. Although we encountered no cases of tumor seeding, benign inflammatory findings suggestive of tumor seeding occurred after 1.9% of percutaneous renal tumor ablation procedures, prompting biopsy after 1.3% of procedures.

The appearance of the inflammatory nodules provides some insight into their origin. Nodules after cryoablation were located in the subcutaneous tissues peripheral to the abdominal wall and were associated with a tram-tracking pattern of enhancement along the path of the cryoprobe. Although the distal 4 cm of each cryoprobe reaches temperatures as low as −130°C, the rest of the probe's shaft reaches temperatures as low as −35°C. It is likely that the tissues adjacent to the shaft were affected to some degree. A tubular pattern of tissue injury may have occurred along the probes leading to the nodules observed in this study. This pattern led to a tram-tracking appearance of enhancement when the imaging plane was in the same plane as the probe track. In other cases, tissue injury appeared as ring-enhancing nodules when the imaging plane was perpendicular to the probe track.

Inflammatory nodules after percutaneous radiofrequency ablation were less defined, not associated with a tram-tracking appearance, and located adjacent to the ablated tumor in the perinephric region or abdominal wall musculature along the electrode track. One nodule may have been due to ablation of the electrode track, which was occasionally performed at the operator's discretion on electrode removal to prevent track seeding and bleeding at the end of the procedure. Another nodule was ultimately diagnosed as an organizing abscess that developed from a postprocedure hematoma. Although the finding persisted for several months, no infectious organism was isolated. Infections after radiofrequency ablation of renal tumors are rare, prompting many to perform radiofrequency ablation without antibiotics [4, 7, 13]. Indeed, prophylactic antibiotics were used only before cryoablation procedures in our series. Nevertheless, subclinical infection is one possible cause of applicator track nodules. Therefore, antibiotics may help prevent the appearance of application track nodules, although antibiotics before cryoablation did not prevent occurrence entirely.

Because needle track seeding cases are so rare after renal tumor ablation, it is difficult to suggest how to discriminate them from the benign inflammatory nodules we encountered. Benign inflammatory nodules may become visible from several months to years after the ablation. Three of the six applicator track nodules appeared more than 6 months after the ablation. In fact, one was first detected on MRI 52 months after radiofrequency ablation. Therefore, one cannot rely solely on delayed onset to diagnose cases of tumor track seeding.

The frequency of nodules after cryoablation (2.7%) was greater than the frequency after radiofrequency ablation (1.7%). However, the finding is rare; determination of the true incidence of this finding would require more cases. Also, most patients were followed up with MRI after cryoablation and CT after radiofrequency ablation. MRI may be more sensitive in detecting changes in soft tissue because of its greater soft-tissue contrast. A study using the same postprocedure imaging technique would be needed to determine if there is a true difference in the incidence of inflammatory nodules after the two ablation methods. Other confounding variables such as size and number of applicators preclude drawing any definitive conclusion regarding differences in the incidence of this finding between radiofrequency ablation and cryoablation.

Among patients who developed applicator track nodules, percutaneous biopsy was performed before tumor ablation and along similar tracks as the applicators. Therefore, the possibility that the inflammatory nodules were caused by the biopsy procedure cannot be excluded. However, percutaneous tumor ablation is more likely to lead to tissue injury and inflammation than percutaneous biopsy.

Limitations of this study include its retrospective design and observer subjectivity. Dur-

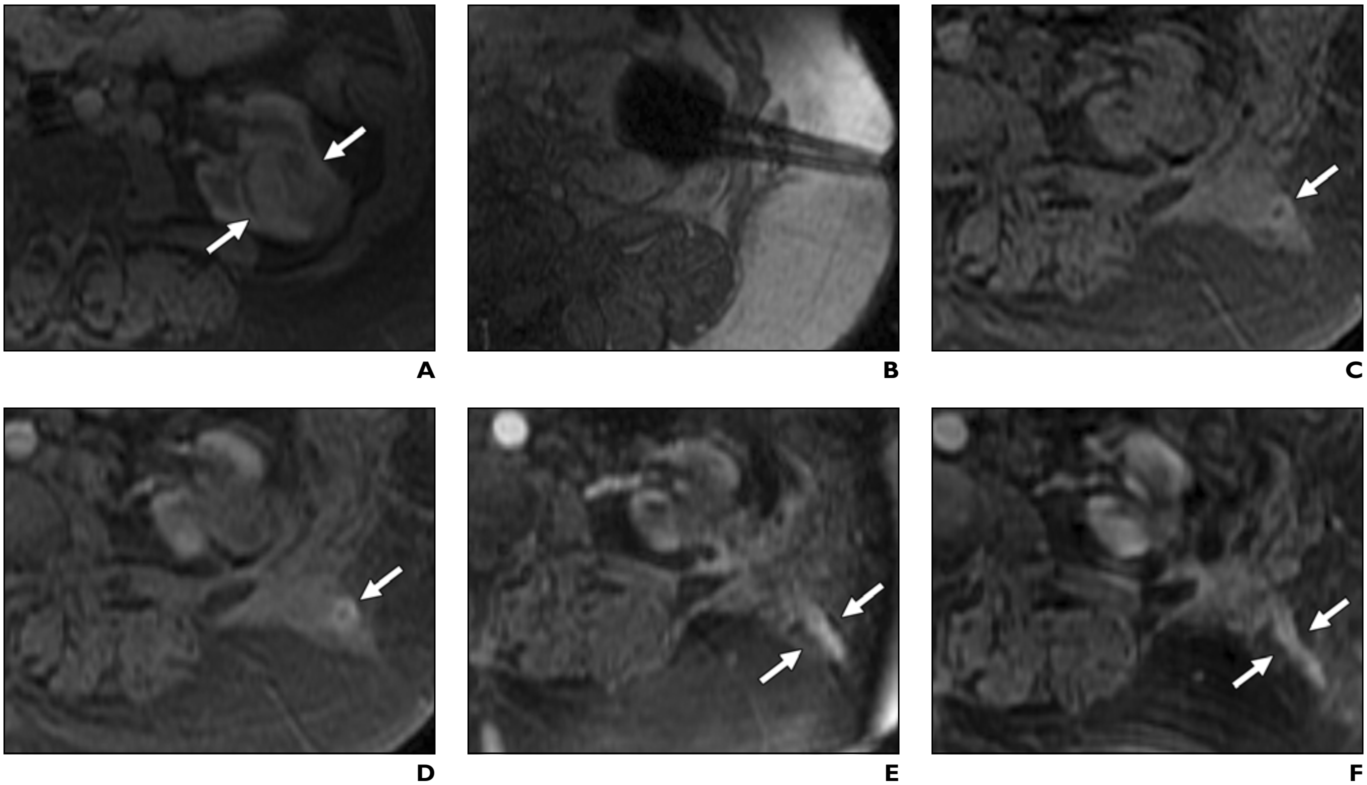


Fig. 2—71-year-old woman referred for percutaneous cryoablation of 5.0-cm renal cell carcinoma.
A, Axial T1-weighted, fat-suppressed, dynamic sequence image (TR/TE, 310/4.2) shows heterogeneously enhancing tumor (*arrows*) before cryoablation.
B, Axial gradient-recalled echo image (51/10) shows cryoprobes and ice ball formation during cryoablation.
C, Axial unenhanced T1-weighted, fat-suppressed image (260/4.2) acquired 9 months after cryoablation procedure shows new 1.3-cm nodule (*arrow*) within applicator track.
D, Axial gadolinium-enhanced T1-weighted, fat-suppressed image (260/4.2) shows enhancement (34.8%) of nodule (*arrow*). Percutaneous biopsy revealed fibroadipose tissue with mild perivascular lymphoplasmacytic infiltrate and no evidence of malignancy.
E, On axial fast-acquisition multiple-excitation image (4.4/1.9) acquired 13 months after tumor cryoablation, discrete applicator track nodule detected 4 months earlier is not visible. Enhancing tram-tracking pattern of soft-tissue stranding (*arrows*) now follows ablation track.
F, Axial fast-acquisition multiple-excitation image (4.4/1.9) acquired 17 months after tumor cryoablation shows tram-tracking enhancement (*arrows*) is stable along applicator track. It has remained stable at 34 months.

ing review of the images, we included only cases with findings that were suggestive of tumor. Indeed, four of the six applicator track nodules detected in the study had been biopsied, suggesting that nodules were likely to arouse suspicion among other practicing radiologists.

In conclusion, patients may develop new benign enhancing nodules in or around the applicator track that mimic tumor seeding. These nodules should be biopsied and not diagnosed presumptively as tumor seeding.

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