Renal mass biopsy and thermal ablation: should biopsy be performed before or during the ablation procedure?

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Abstract

Purpose: To determine if renal mass biopsy should be performed before or during the ablation procedure with emphasis on complications and rate of ablation for renal cell carcinomas (RCC), benign tumors, and small renal masses without a histologic diagnosis.
Methods: This HIPAA-compliant, single-center retrospective study was performed under a waiver of informed consent from the institutional review board. Two hundred eighty-four consecutive patients with a small renal mass (≤4.0 cm) treated with percutaneous thermal ablation between January 2001 and January 2015 were included. Two cohorts were identified based upon the timing of renal mass biopsy: separate session two weeks prior to ablation and same session obtained immediately preceding ablation. Clinical and pathologic data were collected including risk factors for non-diagnostic biopsy. Two-sided t test, χ^2 test or Fischer's exact tests were used to evaluate differences between cohorts. Univariate and multivariate logistic regression models were constructed.
Results: A histologic diagnostic was achieved more frequently in the separate session cohort [210/213 (98.6%) vs. 60/71 (84.3%), $p < 0.0001$]. The rate of ablation of RCC was higher in the separate session group [201/213 (94.4%) vs. 46/61 (64.7%), $p = 0.001$]. The rate of ablation for benign tumors [14/71 (19.7%) vs. 6/213 (2.8%), $p < 0.0001$] and small renal masses without a histologic diagnosis [3/213 (1.4%) vs. 11/71 (15.5%), $p < 0.0001$] was higher in the same session cohort. There were no high-grade complications in either cohort.
Conclusion: Performing renal mass biopsy prior to the day of ablation is safe, increases the rate of histologic diagnosis, and reduces the rate of ablation for benign tumors and small renal masses without a histologic diagnosis.

Key words: Renal mass biopsy—Renal cell carcinoma—RCC—Tumor ablation—Oncocytoma

The detection of small renal masses (≤4.0 cm) has increased dramatically over the last 50 years, largely due to increased utilization of cross-sectional imaging [1]. Large surgical and renal mass biopsy series have shown that 10–33% of small renal masses are benign, predominantly oncocytomas and fat poor angiomyolipomas [2]. Percutaneous renal mass biopsy is now widely considered to be safe with biopsy and surgical specimen histologic concordance rates approaching 100%, when coupled with immunohistochemistry [3]. However, the consistent limitation of renal mass biopsy is the 15–22% non-diagnostic rate [4–6].

Thermal ablation is an alternative treatment to surgery for many patients with clinical T1a renal cell carcinoma (RCC), especially elderly, medically comorbid,

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and patients with syndromes causing recurrent multifo-cal RCC [7–9]. For patients considering ablation, renal mass biopsy is recommended [7–10]. Biopsy may be performed in a separate session prior to the ablation procedure or during the same session as ablation. However, the optimal time to perform biopsy is currently unknown. Biopsy performed at the time of ablation may be viewed as more efficient or potentially less risky be-cause biopsy and ablation are accomplished during a single procedure. Unfortunately, this combined ap-proach may result in a higher rate of ablation for benign or indeterminate pathology. Further, this approach may not allow appropriate risk stratification. For example, patients with favorable RCC histology could be triaged to ablation while patients with unfavorable histology to surgery. Therefore, the purpose of this study is to determine if renal mass biopsy should be performed be-fore or during the ablation procedure with emphasis on complications and rate of ablation for renal cell carci-nomas (RCC), benign tumors, and small renal masses without a histologic diagnosis.

Methods

This HIPAA-compliant, single-center retrospective study was performed under a waiver of informed consent from the institutional review board.

The medical records of 341 consecutive patients who underwent thermal ablation for a previously untreated small renal mass (≤4.0 cm) between 1/2001 and 1/2015 were reviewed. Fifty-seven patients were excluded from the study. Percutaneous thermal ablation was performed for 37 patients without a renal mass biopsy and 20 pa-tients had renal mass biopsy performed during a laparoscopic ablation procedure. Therefore, 284 patients were included in our study.

The study design was overlapping with renal mass biopsy performed either in a separate session approxi-mately 2 weeks prior to ablation, or in the same session, immediately preceding the ablation. Tissue specimens were placed in a 10% formalin solution and processed according to the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guideli-nes [11]. Genitourinary pathologists reviewed pathology specimens and immunohistochemistry was performed to facilitate diagnosis when appropriate. Tissue samples were considered non-diagnostic when fibrosis/sclerosis, necrosis, or only benign renal parenchyma was found at histology. The ablation procedure proceeded without the knowledge of the tissue diagnosis when biopsy was per-formed in the same session.

The decision for each patient to undergo thermal ablation was made in consensus by a team of subspe-cialty radiologists and urologists experienced in tumor ablation and kidney surgery, respectively. Decision to perform thermal ablation was based upon age, comor-bidities, proximity of tumor to non-target anatomy, and tumor histology, if available. Thermal ablation was performed by one of six radiologists (1–19 years of experience).

Separate session renal mass biopsy procedure

Renal mass biopsy procedures were performed with US by 1 of 12 abdominal radiologists (1–19 years of expe-rience) or CT by 1 of 7 abdominal radiologists (1–19 years of experience). Procedures were performed under conscious sedation with fentanyl and/or midazo-lam and local anesthesia (sodium bicarbonate buffered 1% lidocaine) as prescribed and supervised by the attending radiologist. An 18-gauge core needle device with adjustable throw (BioPince, Argon Medical De-vices, Plano, TX) without (US-guidance) or with a 17-gauge introducer (CT-guidance) was used for all biopsies. Core length, generally 2.3 cm, and number of passes were determined by the performing radiologist based upon renal mass size, proximity of non-target anatomy, and gross evaluation of the specimen. Routine post procedure care included two hours of bed rest with vital sign monitoring. The procedure was repeated in the event of a non-diagnostic biopsy.

Same session renal mass biopsy procedure

Renal mass biopsy, immediately followed by ablation, was performed with US or CT-guidance by 1 of 6 abdominal radiologists (1–19 years of experience) who performs both renal mass biopsy and thermal ablation. The biopsy technique and devices used were the same as the separate session biopsy cohort. Because ablation was performed during the same session as biopsy, there were several intraprocedural differences between the cohorts including: the use of general anesthesia, placement of a urinary bladder catheter and administration of pre-pro-cedure antibiotics (routine clinical care at our institu-tion), hydrodisplacement when non-target anatomy was in proximity to the index tumor or expected zone of ablation, and overnight observation (also routine clinical care at our institution). Because biopsy was generally performed prior to hydrodisplacement, the use of GA was the primary procedural difference between the co-horts.

Thermal ablation procedure

The thermal ablation procedure was performed in a CT suite (GE Optima 580W, Waukesha, WI) under general anesthesia. Immediately prior to the procedure, an in-dwelling bladder catheter was placed and a single dose of intravenous prophylactic antibiotics to cover skin organisms (first generation cephalosporin or clin-damycin, weight-based dosing) was administered.

Ultrasound (US) (GE LOGIQ E9, Waukesha, WI) or computed tomography fluoroscopy (CTF) (GE Lightspeed 580, Waukesha, WI) or a combination of US and CTF were used for applicator placement. Hydrodisplacement was used in cases when non-target anatomy was within 1 cm of the tumor or within the expected zone of ablation. For hydrodisplacement, faintly radiopaque (2% iohexol solution) normal saline was manually infused through an 18- or 20-gauge introducer placed between the tumor and non-target anatomy until an adequate margin of safety was achieved. Ultrasound or CT was used for real-time monitoring of the ablation zone and proximity to non-target anatomy during the procedure. Contrast-enhanced CT (CECT) was obtained immediately after the ablation procedure to evaluate technical success and to assess for complications. There were no staged treatments and treatment intent was curative for all cases.

Data collection and analysis

Clinical and pathologic data for each patient was collected from an institutional database by two authors (SAW, EJA). Clinical data collected included patient age, gender, and Charlson comorbidity index. The Charlson comorbidity index predicts one-year mortality based upon a tiered scoring system of 22 health disorders [12]. Potential factors associated with non-diagnostic biopsy were recorded for each patient: tumor diameter, cystic vs. solid ($\leq$10 HU vs. $\geq$10 HU), renal mass enhancement ($\leq$20 HU vs. $\geq$20 HU), tumor polarity (superior vs. mid vs. lower pole), anterior vs. posterior location, endophytic vs. exophytic (tumor extending beyond renal capsule), image guidance (US vs. CT), skin-to-tumor distance, number of core biopsies obtained, and patient body mass index (BMI) [13]. Pathologic data collected included tumor histology. Complications were classified according to the Clavien–Dindo system [14]. Clinical and imaging follow-up with contrast-enhanced CT or MRI was obtained at target intervals of 3–6, 12, and 18 months after ablation, with annual imaging thereafter. Two fellowship trained abdominal radiologists experienced (1–5 years) in tumor ablation (SAW, VKW) reviewed imaging in consensus for complications, including tumor seeding.

Continuous variables were summarized as medians and interquartile ranges (IQR). Categorical data were summarized with frequency counts and percentages. Patient and tumor characteristics for diagnostic and non-diagnostic biopsies were assessed using a two-sided t test, χ^2 test, or Fischer's exact test as appropriate. Univariate and multivariate logistic regression models were constructed to evaluate association between biopsy outcomes and imaging features. A p value of <0.05 was considered to be significant for all statistical tests.

Results

Procedure/patient data

Renal mass biopsy was performed in a separate session than ablation for 213/284 (75.0%) patients and in the same session as ablation for 71/284 (25.0%) patients. There was no significant difference in gender, age, or Charlson comorbidity index between patient cohorts. Among the seven radiologists who performed at least ten biopsies, there was no association between experience and rate of non-diagnostic biopsy ($p = 0.82$) (Appendix)

Of the potential factors associated with a non-diagnostic biopsy, there was no significant difference between cohorts in median tumor diameter ($p = 0.11$), solid or cystic tumors ($p = 0.44$), radiographic enhancement ($p = 0.53$), exophytic or endophytic tumors ($p = 0.99$), US or CT image guidance ($p = 0.22$), or patient BMI ($p = 0.71$). Patients in the same session cohort were more likely to have superior pole and anterior tumors ($p = 0.02$ and $p = 0.01$, respectively). Skin-to-tumor distance was longer in the separate session cohort (9 vs. 8 cm, $p = 0.004$). Lastly, the median number of biopsy passes was higher in the separate session cohort (2 vs. 1, $p < 0.0001$). Patient and procedural characteristics are summarized in Table 1.

Tumor histology

The rate of histologic diagnosis was significantly higher in the separate session biopsy cohort [210/213 (98.6%) vs. 60/71 (84.3%), $p < 0.0001$]. Of the patients receiving biopsy in a separate session than ablation, a histologic diagnosis was confirmed on the initial biopsy in 195/213 (91.5%). Biopsy was repeated in a separate session for all 18 patients who received a non-diagnostic biopsy. A histologic diagnosis was confirmed on repeat biopsy in 15/18 (83.3%). Figure 1 The three patients (1.4%) who experienced a second non-diagnostic biopsy proceeded to thermal ablation without a histologic diagnosis. Repeat biopsy was not possible for patients in the same session cohort who received a non-diagnostic biopsy 11/71 (15.5%) because of interval thermal ablation (Figure 2).

Clear cell was the predominant RCC subtype in both separate session and same session cohorts followed by papillary and chromophobe ($p = 0.27$). Ablation of histologically confirmed RCC was higher in the separate session cohort [201/213 (94.4%) vs. 46/61 (64.7%), $p = 0.001$]. The rate of ablation for benign tumors was higher in the same session cohort [14/71 (19.7%) vs. 6/213 (2.8%), $p < 0.0001$]. Ablation was performed for 13 oncocytomas and 1 fat poor angiomyolipoma in the same session cohort and 6 oncocytomas and 0 fat poor angiomyolipomas in the separate session group. Further, the rate of small renal masses without a histologic diagnosis was higher in the same session group [3/213

Table 1. Patient and procedural characteristics

Characteristics	Separate session ($n = 213$)	Same session ($n = 71$)	P value
Median age (IQR)	66 (59–72)	66 (59–72)	0.88
Gender n (%)			0.38
Male	147 (69.1)	45 (63.4)	
Female	66 (30.9)	26 (36.6)	
Median BMI (IQR)	30.8 (27.0–37.3)	31.4 (27.1–34.4)	0.71
Median CCI (IQR)	4 (3–5)	3.5 (2–5)	0.77
Median tumor diameter cm (IQR)	2.5 (2.0–3.4)	2.5 (1.9–2.8)	0.11
Guidance modality n (%)			0.22
US	168 (78.9)	61 (85.9)	
CT	45 (21.1)	10 (14.1)	
Median # of biopsy passes (IQR)	2 (2–3)	1 (1–2)	<0.0001
Median skin-to-tumor distance cm	9 (7.3–11)	8 (6.5–9.5)	0.004
Tumor characteristics n (%)			
Endophytic	57 (26.8)	19 (26.8)	0.99
Exophytic	156 (73.2)	52 (73.2)	
Solid	184 (86.4)	64 (90.1)	0.44
Cystic	29 (13.6)	7 (9.9)	
Radiologic enhancement n (%)			0.53
≤20 HU	11 (5.2)	2 (2.8)	
≥20 HU	190 (89.2)	63 (88.7)	
Uncharacterized	12 (5.6)	6 (8.5)	
Location n (%)			
Anterior	97 (45.5)	45 (63.4)	0.01
Posterior	116 (54.5)	26 (36.6)	
Superior pole	66 (31.0)	35 (49.3)	0.02
Mid pole	88 (41.3)	21 (29.6)	
Inferior pole	59 (27.7)	15 (21.1)	

(1.4%) vs. 11/71 (15.5%), $p < 0.0001$]. Tumor histology results are summarized in Table 2.

Complications

Asymptomatic perinephric hematomas were not considered adverse events. There were no Clavien-Dindo Grade II or greater complications in either cohort. One patient in the separate session cohort was monitored overnight after experiencing an episode of hypotension associated with conscious sedation that resolved spontaneously after intravenous fluid administration. No patients required a blood transfusion, developed a pneumothorax or required an additional procedure due to the biopsy or ablation procedure. Further, there was no biopsy tract tumor seeding identified in either cohort.

Discussion

Percutaneous biopsy is safe and establishes a pathologic diagnosis for patients with small renal masses treated with thermal ablation. Our study identifies several tangible benefits to performing renal mass biopsy separate from the ablation procedure. First, confirmation of renal mass histology is improved. Prince et al. showed that the non-diagnostic rate of repeat biopsy is similar to the non-diagnostic rate of the initial biopsy, meaning that in most cases, a diagnosis can be obtained by repeating the biopsy [13]. In our study, repeating the biopsy procedure was the primary source of our improved diagnostic rate in the separate session group. Unfortunately, when

biopsy and ablation are performed in the same session, repeat biopsy cannot be performed. Hence, the non-diagnostic rate was more than tenfold higher when biopsy and ablation were performed in the same session.

The optimal number of core biopsy samples has not been defined [15]. In our study, the median number of passes was lower in the same session cohort. The attenuation of acute blood and soft tissue is similar on unenhanced CT. As a result, exophytic or partially exophytic tumors can become obscured when biopsy is performed in the same session as ablation. Similarly, the presence of a perinephric hematoma, intratumoral bleeding, and retroperitoneal gas following US-guided biopsy can distort tissue planes and obscure renal tumors. Precise and accurate placement of ablation applicators is the most important predictor for treatment success and complications. Therefore, preserving tumor conspicuity is critically important when performing thermal ablation. Hence, we likely attempted to preserve tumor conspicuity by limiting biopsy passes. Regardless, the diagnostic rate of 84.3% in our same session group is similar to large renal mass biopsy series where 2–5 passes were used [16–20].

Second, ablation of benign tumors can be minimized when biopsy is performed in a separate session. In our study, approximately 1 in 5 patients in the same session cohort underwent ablation for a benign tumor compared to less than 3% in the separate session cohort. These results are similar to other contemporary ablation series where biopsy and ablation were performed in the same
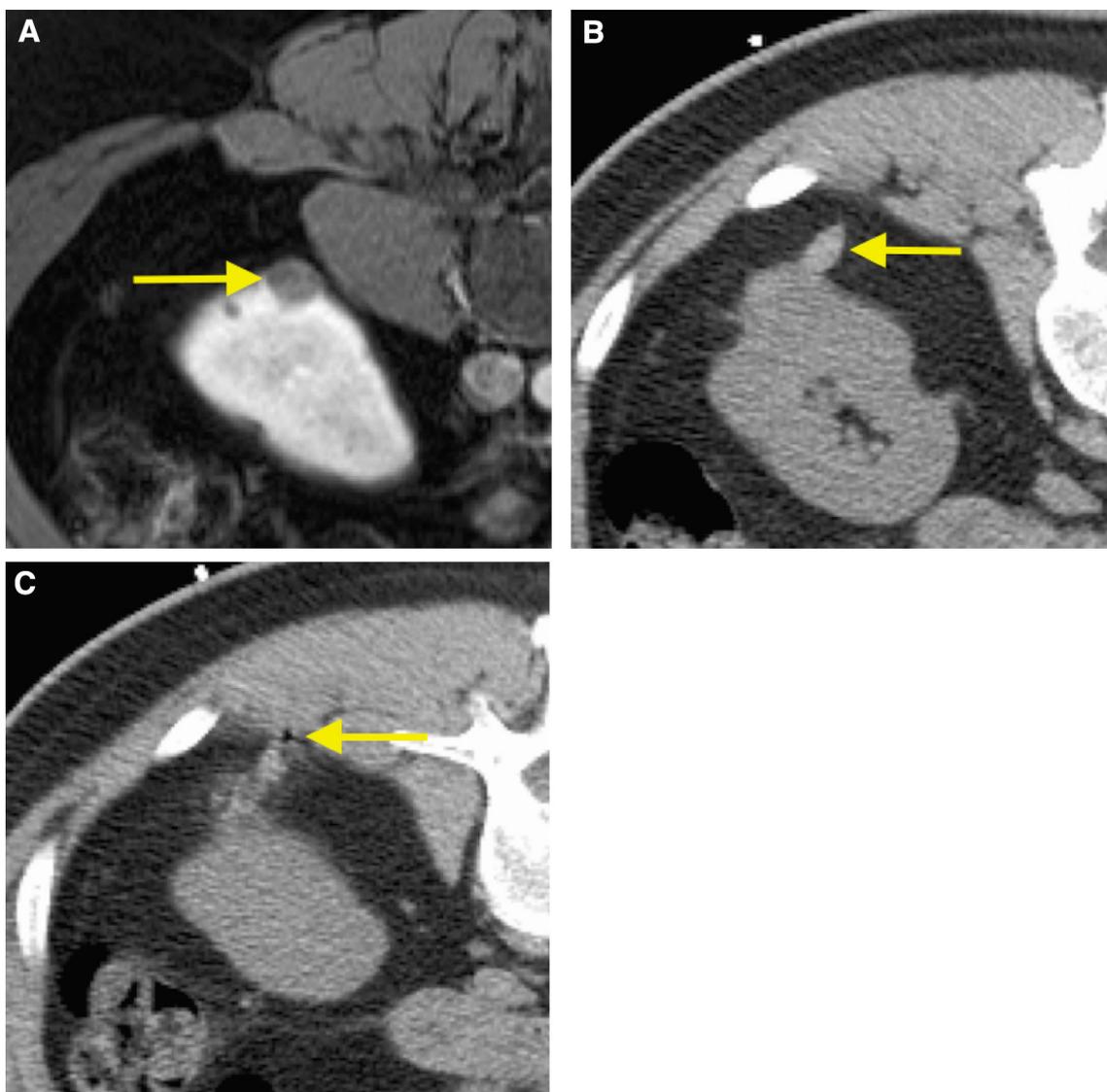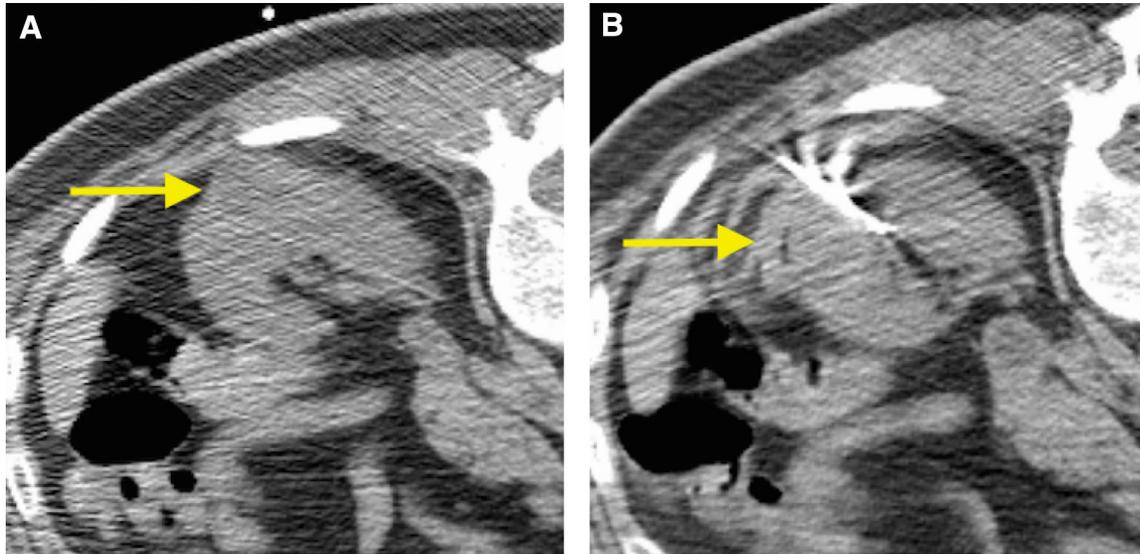
Fig. 1. Separate session renal mass biopsy for a 64-year-old man with a small renal mass. Axial enhanced T1-weighted, fat-saturation MRI of the abdomen (**A**) with the patient prone demonstrates a partially exophytic small renal mass (≤4.0 cm) arising from the lower pole of the right kidney (*arrow*). At US-guided biopsy, the mass became obscured after the first pass, due to intratumoral bleeding, a perinephric hematoma (*arrow*) and retroperitoneal gas (*arrow*) as see on axial unenhanced CT (**B**, **C**). Because the first renal mass biopsy was non-diagnostic, the patient returned for repeat, separate session renal mass biopsy where tumor histology was confirmed as a papillary renal cell carcinoma. The patient proceeded to percutaneous thermal ablation approximately 2 weeks later.

session [21–24]. Table 3 Importantly, benign tumors are not all equal. Angiomyolipomas (AML), fat containing renal tumors have no malignant potential. Therefore, ablation can be avoided for AMLs less than 4 cm because there is minimal risk for spontaneous hemorrhage [25, 26]. Oncocytomas are benign tumors that represent 3–7% of solid renal masses [27]. When renal mass size is stratified to ≤4 cm, the incidence of oncocytoma increases to 18% which corresponds to the rate of oncocytoma in our same session cohort [28]. Hybrid tumors composed of oncocytoma and malignant RCC are uncommon, accounting for <3% of all oncocytomas [27–29]. These hybrid tumors are composed of low-grade RCC generally considered to have minimal metastatic potential [30–32]. Therefore, an active surveillance strategy is prudent in the elderly and comorbid populations [32, 33]. With this management strategy, misdiagnosed oncocytic/eosinophilic neoplasms and hybrid tumors with accelerated growth kinetics can be subsequently ablated. During active surveillance, six patients (2.8%) with oncocytomas, in our separate session cohort, demonstrated accelerated growth suggesting discordant histology. Therefore, these patients were treated with thermal ablation.

Fig. 2. Same session renal mass biopsy and percutaneous thermal ablation for a 65-year-old man with a small renal mass. Axial unenhanced CT of the abdomen (**A**) with the patient prone demonstrates a partially exophytic small renal mass (≤4.0 cm) arising from the posterior, interpolar right kidney (*arrow*). **B** After the first biopsy pass, the renal mass became obscured by a perinephric hematoma (*arrow*) as seen on CT. The ablation applicator was placed in the expected location of the tumor with CT-guidance (**C**) and the assistance of anatomic landmarks. The renal mass biopsy was non-diagnostic; therefore, clinical and imaging follow-up were based upon the presumptive diagnosis of renal cell carcinoma.

Third, ablation of small renal masses without a histologic diagnosis can be avoided when biopsy is performed separate from the ablation procedure. In our study, 99% of patients in the separate session cohort had a histologic diagnosis compared to 84% in the same session group. Without a histologic diagnosis, the default diagnosis must be RCC, even though 10–33% of small renal masses are benign [2, 5]. Because most small renal masses including RCC grow at a rate of 0.2–0.4 cm/year, this presumptive diagnosis requires both long-term clinical and imaging follow-up to evaluate for local recurrence and metastases [34]. Hence, a subset of patients are unnecessarily exposed to medical radiation and iodinated contrast, incur insurance and out-of-pocket expenses associated with physician and radiology appointments, in addition to the anxiety of a cancer diagnosis. Furthermore, benign tumors do not require ablation. Therefore, procedural risks associated with ablation, including anesthesia and decline in renal function, could have been avoided.

Lastly, knowledge of tumor histology improves informed consent [35]. Patients with a definitive cancer diagnosis are better able to weigh the risks and benefits of all treatment options without the confusion of hypothetical scenarios. Expectant management or active surveillance could be recommended for benign tumors including oncocytomas, while ablation or partial nephrectomy could be recommended for low- and high-grade RCC, respectively.

Retrospective studies are subject to bias, which is a limitation of this study. Patients selected for same session biopsy and ablation may have had tumors that were more suspicious at imaging or in technically challenging locations due to proximity of non-target anatomy. This may partially explain why there were more superior pole and anterior tumors in the same session cohort. However, biopsy was generally performed prior to hydrodisplacement maneuvers. Radiologists who perform biopsy and ablation may have greater technical expertise that could lead to a higher rate of histologic diagnosis. However, the diagnostic rate between radiologists who do and do not perform ablation was similar in our study. There are subsets of patients where the same session biopsy and ablation is almost certainly preferable. Patients at increased risk for bleeding and/or recipients of anticoagulation medications may have been triaged to same session biopsy and ablation in order to mitigate the risk of bleeding or an embolic episode, respectively. Since this was not a randomized study, the choice of biopsy technique and timing relative to ablation was at the discretion of the radiologist performing the procedures. Therefore, direct comparison of results and complications based on technique is not possible.

In conclusion, our study suggests that renal mass biopsy should be performed in a separate session before the ablation procedure. Patients should be counseled that performing biopsy for a small renal mass prior to the day of ablation is safe, increases the rate of histologic diag-

Table 2. Tumor histology results

Characteristics	Separate session ($n = 213$)	Same session ($n = 71$)	P value
Histologic diagnosis n (%)			
Yes	210 (98.6)	60 (84.3)	<0.0001
No	3 (1.4)	11 (15.5)	
Initial biopsy	195 (91.5)	60 (84.3)	
Repeat biopsy	15/18 (83.3)	N/A	
RCC subtype (confirmed) n (%)			0.27
Clear cell	155 (76.0)	36 (80.0)	
Papillary	38 (18.6)	6 (13.3)	
Chromophobe	6 (2.9)	1 (2.2)	
Other	5 (2.5)	3 (6.6)	
Benign histology n (%)			<0.0001
Oncocytoma	6 (2.8)	13 (18.3)	
Fat poor angiomyolipoma	0 (0)	1 (2.2)	
Other	0 (0)	0 (0)	
Ablation of RCC (confirmed) n (%)	201 (94.4)	46 (64.7)	<0.0001

Table 3. Contemporary ablation series with same session biopsy and ablation

Characteristics	Tracy et al. [24]	Best et al. [22]	Atwell et al. [21]	Breen et al. [23]
Patients n	243	159	445	171
Median tumor diameter cm	2.4	2.4	2.1	3.3
Non-diagnostic biopsy n (%)	16 (6.5)	9 (5.7)	153 (34.4)	36 (21.1)
Thermal ablation of: n (%)				
Oncocytoma	21 (8.6)	18 (11.3)	48 (10.8)	23 (13.5)
Unconfirmed RCC	37 (15.2)	27 (17.0)	201 (45.2)	59 (34.5)

nosis, and reduces the rate of ablation for benign tumors and small renal masses without a histologic diagnosis.

Appendix

Renal mass biopsy is performed with ultrasound (US) and computed tomography (CT) guidance. At our institution, all abdominal radiologists perform US-guided renal mass biopsy ($n = 12$), a subset of these radiologists perform CT-guided renal mass biopsy ($n = 7$) and a subset of these radiologists perform thermal ablation ($n = 5$). Radiologists who perform CT-guided biopsies and thermal ablations perform more procedures, a variable than may impact the rate of positive histologic diagnosis. This table explores the variable of expertise. Of the seven radiologists who performed more than ten renal mass biopsies, there was no significant difference in the rate of positive histologic diagnosis among radiologists with expertise in US, US and CT, or US, CT and thermal ablation.

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Radiologist	Histologic diagnosis, n (%)		Biopsy modality (CT or US)	Performs ablation (Yes or No)	P value
	Yes	No			
1	30 (88.2)	4 (11.8)	US and CT	Yes	0.82
2	14 (93.3)	1 (6.7)	US	No	
3	12 (100)	0	US and CT	No	
4	65 (90.3)	7 (9.7)	US and CT	Yes	
5	14 (100)	0	US and CT	Yes	
6	11 (100)	0	US	No	
7	25 (89.3)	3 (10.7)	US and CT	Yes	

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