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# Multipoint Thermal Sensors Associated with Improved Oncologic Outcomes Following Cryoablation

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**Abstract**

***Introduction:*** Cryoablation (CA) is a minimally invasive modality for the management of small renal cortical neoplasms (RCN). Effective ablation is dependent on achieving target temperatures during CA that result in tumor cell death. We investigated long-term oncologic outcomes following CA using multipoint thermal sensors (MTS), which allow precise temperature determination at four points along the needle.

***Methods:*** We performed a retrospective review of 20 patients with <4 cm RCN who underwent *de novo* CA from 2005 to 2009. In 11 procedures, MTS needles were deployed with the goal of obtaining −20°C at the tumor margin, while 9 were done without MTS. Patient demographics, tumor characteristics, and CA procedure data were retrieved and analyzed. Follow-up CT or MRI was used to assess recurrence status.

***Results:*** With a mean follow-up of 45 months, none of the 11 patients experienced a recurrence in the MTS group, compared with 4 of 9 (44.4%) patients in the non-MTS group ($p = 0.026$). Of the biopsy-confirmed renal cancers, none of the 6 in the MTS group, compared with 3 of 6 (50%) in the non-MTS group, recurred ($p = 0.182$). Age, tumor size, surgical approach, tumor histopathology, grade, follow-up time, and skin-to-tumor distance were similar between the MTS and non-MTS groups. The MTS group was also associated with increased total length of freeze ($p = 0.041$), procedure time ($p = 0.020$), cryoprobe utilization ($p = 0.049$), and a greater ratio of cryoprobes used per cm diameter of tumor ($p = 0.003$).

***Conclusions:*** In this small renal mass pilot study, the use of MTS needles to monitor temperature and guide cryoneedle deployment was associated with improved oncologic outcomes.

**Keywords:** cryoablation, multipoint thermal sensor, small renal mass, renal cortical neoplasms, kidney cancer, thermal ablation

## Introduction

Owing, in large part, to advances in cross-sectional abdominal imaging, the incidence of small (<4 cm) renal cortical neoplasms (RCN) has increased significantly in recent years.[1] The natural history of these small renal masses (SRM) has also gradually been elucidated, with 20% of these SRM representing benign lesions and up to 50% to 60% remaining relatively indolent.[2–4] In parallel with the rising incidence of SRM, extirpative surgery has undergone technical advances favoring minimally invasive approaches. Alternative options include active surveillance and thermal ablation, which may provide acceptable long-term oncologic control in addition to improved preservation of renal function.[5,6]

Cryoablation (CA) has recently gained acceptance in the management of SRM.[7,8] The American Urological Association guidelines for stage 1 renal tumors recommend that CA is a viable management option for the <4 cm SRM.[9,10] The recent emergence of intermediate and longer term oncologic follow-up studies demonstrating near equivalent disease-specific survival outcomes of CA compared to extirpation has further cemented the status of ablation in the management of SRM especially among high-risk patients.[11–13]

As CA necessitates the attainment of appropriate freeze temperatures to produce cell injury and cell death, it is thought that inadequate or incomplete freezing may result in tumor persistence and recurrence. In a murine model, Kroeze and colleagues reported that incomplete CA induced hyperproliferation of residual renal tumor cells, highlighting the necessity of complete tumor ablation.[14] Several studies using porcine and canine models have also underscored the value in attaining prolonged, continuous (i.e., 10-minute) target freeze temperatures (generally around −20°C), although the specific temperature nadir remains somewhat controversial.

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Most studies report satisfactory ablation of tumors with temperatures of −16°C to −20°C,[15–18] although some earlier studies recommended −40°C to destroy cancer cells.[19]

While temperature sensors to monitor temperature attainment have been used previously in both urologic and nonurologic cryosurgery, they are not currently standard in CA procedures of the SRM. The current isotherm maps used to guide preoperative planning and cryoprobe placement are developed in nonhuman, nonliving models and, as such, fail to account for individual variations in renal anatomy such as perirenal fat, *in vivo* inflammatory and metabolic factors, and most importantly, intrarenal blood flow. The flow of 37°C blood within or adjacent to the cryoablated region may lead to heat dissipation by the ''heat sink effect'' and complicate attainment of requisite freeze temperatures for the appropriate duration.[20,21]

Multipoint thermal sensor (MTS) needles allow accurate and reproducible temperature determination across multiple points along the needle,[22] providing the surgeon a direct means to ascertain CA temperatures within the area of the RCN. Utilizing MTS needles can help overcome differences in renal tumor microanatomy and vascular distribution, and inform cryoprobe placement and freeze times, hypothetically decreasing the risk of incomplete ablation. In this retrospective report, we evaluate the long-term oncologic outcomes following CA with and without MTS needles.

## Methods

### *Patient information and data collection*

This study received institutional review board approval. We retrospectively reviewed and analyzed patients undergoing *de novo* CA for the management of <4 cm RCN from January 2005 to December 2009. Patient information and tumor characteristics were collected from the electronic medical record and analyzed. Data collected included patient age, gender, tumor size, surgery date, creatinine, and follow-up schedule. Data pertaining to the CA procedure, including surgical approach (laparoscopic v. percutaneous), number of cryoprobes used, use of MTS needles, length of freeze, procedure time, and intraoperative/postoperative complications, were determined from operative reports. Tumor histology and Fuhrman grade were determined from pathology reports. Contrast-enhanced CT or MRI was used to evaluate preoperative skin-to-tumor (STT) distance[23] and the presence or absence of recurrence at the most recent follow-up. All complications were graded according to the Clavien–Dindo classification.[24]

### *CA technique*

Our detailed CA technique has previously been described.[25] Briefly, all CA procedures were performed under CT guidance as a collaborative effort between the urologist (R.V.C.) and interventional radiologist (D.V.). For procedures in which MTS needles were used, a 17-gauge IceRod cryoprobe (Galil Medical, St. Paul, MN) was first passed through a 14-gauge angiocatheter for small tumors (≤3 cm). The needle template in all cases was as described in the literature.[26] The MTS (Galil Medical) was then placed through and slightly beyond the tumor, 1 cm away from the cryoprobe or cryoprobe configuration as suggested by the manufacturer, based on their *ex vivo* evaluation. For larger tumors (>3 cm), two MTS needles were placed to encompass the lesion. MTS needle probes are 1.47 mm (17-gauge) in diameter and provide four temperature readings marked at 5, 15, 25, and 35 mm from the tip of the needle with an accuracy of ±5°C. Based on prior literature,[18] the attainment of the adequate freeze temperature was defined as a reading of −20°C on the 5, 15, 25, and/or 35 mm marks on the MTS needle, at the point best representing the tumor margin. After −20°C was attained, a 10-minute freeze was performed followed by a 6-minute thaw. The tumor was then subjected to a second 10-minute freeze following −20°C temperature confirmation with the MTS.

Cryoprobes used in the non-MTS group were 1.7, 2.4, or 3.8 mm Endocare cryoprobes (Endocare, Irvine, CA). Patients underwent two 10-minute freezes separated by a single 6-minute thaw without any temperature sensing modalities. These freeze–thaw cycles were standardized based on evidence from the literature[27,28] and the freeze was terminated only after visualization of the ice-ball extending 1 cm beyond the CT margins of the tumor. In contrast, in the MTS patients, individual freeze and thaw times were subject to change based on the MTS readings.

### *Follow-up and recurrences*

Follow-up CT with contrast was performed immediately following the procedure to assess the technical success and to rule out hematoma and other complications. Subsequent imaging (CT or MRI with contrast) was obtained at 3 to 6 months, and annually thereafter. Given that cryoablated tumors may demonstrate rim enhancement on postprocedural imaging up to 3 months following the procedure, the first set of imaging obtained to evaluate for recurrence was performed after this amount of time had elapsed.[29]

Tumor recurrence was defined by presence of contrast enhancement at the ablation zone on follow-up contrast-enhanced CT or MRI. All recurrences were confirmed by the radiology report and independently by the authors.

### *Statistical analysis*

Categorical data were analyzed by the Fisher's exact test, while continuous data were analyzed by the Wilcoxon rank-sum test or by Student's *t*-test. A $p < 0.05$ was considered statistically significant and all tests were two tailed. Statistical analysis was performed using IBM SPSS Statistics Version 23.0 (IBM Corporation, Armonk, NY).

## Results

### *Patient demographics and tumor characteristics*

Twenty patients underwent CA, all by the same surgical team (R.V.C. and D.V.). Eleven patients underwent CA with MTS needles and nine underwent CA without MTS needles. Patient demographics and tumor characteristics are summarized in Table 1.

In the MTS group, 7 of 11 (63.6%) were men, compared with 6 of 9 (66.7%) in the non-MTS group ($p = 0.889$). The median tumor sizes in the MTS and non-MTS groups were 2.1 cm (range 1.4–3.5 cm) and 2.4 cm (range 1.4–3.8 cm), respectively ($p = 0.492$). Of the 11 CA in the MTS group, 1 was performed laparoscopically, while 10 were performed

Table 1. Patient Demographics, Tumor Characteristics, and Procedure Data of All Cryoablations Performed With and Without Multipoint Thermal Sensor Needles

| | *MTS* | *Non-MTS* | p |
|---|---|---|---|
| No. of cryoablated tumors | 11 | 9 | |
| Age, median (range) | 70 (52–77) | 70 (45–86) | 0.568 |
| Male | 7 (63.6%) | 6 (66.7%) | 0.889 |
| Percutaneous/laparoscopic | 10/1 | 9/0 | 0.353 |
| Tumor size, median (range), cm | 2.1 (1.4–3.5) | 2.4 (1.4–3.8) | 0.492 |
| Biopsy-confirmed RCC/oncocytoma/nondiagnostic biopsy | 6/3/2 | 6/2/1 | |
| STT distance, median (range), cm | 9.5 (3.7–14.4) | 8.5 (6.1–10.3) | 0.425 |
| Procedure time, mean (range), minutes | 162.8 (110–225) | 116.2 (60–175) | **0.020** |
| Total length of freeze, mean (range), minutes | 28.9 (19–47) | 21.9 (20–30) | **0.041** |
| Average number of cryoprobes used (range) | 2.7 (1–4) | 1.8 (1–4) | **0.049** |
| Cryoprobes/cm tumor, mean (range) | 1.23 (0.59–1.76) | 0.70 (0.36–1.25) | **0.003** |
| Complications (Clavien–Dindo) | 1 (I) | 2 (II, III) | 0.425 |
| Follow-up, mean (range), months | 48.2 (10.5–79.4) | 40.0 (5.3–126.3) | 0.518 |
| Overall recurrences | 0/11 | 4/9 (44.4%) | **0.026** |
| Recurrences in tumors with STT >10 cm | 0/3 | 1/2 (50%) | 0.400 |

Values that reached statistical significance ($p < 0.05$) are in bold text.
MTS = multipoint thermal sensors; RCC = renal-cell carcinoma; STT = skin-to-tumor.

percutaneously; in the non-MTS group, all 9 of the 9 tumors were performed by the percutaneous approach. Biopsies were performed in all cases either during the CA or in the 4 weeks before the procedure. In the MTS group, biopsies yielded six confirmed renal-cell carcinoma (RCC), three oncocytic neoplasms, and two nondiagnostic findings, whereas in the non-MTS group, there were six RCC, two oncocytomas, and one nondiagnostic result. Of the six biopsy-proven RCC in the MTS group, four had clear cell histology, while two were papillary; of the six biopsy-proven RCC in the non-MTS group, five were clear cell and one was papillary. The Fuhrman grades of the six RCC-confirmed MTS tumors were as follows: II (one tumor), III (three tumors), or unknown (two tumors). The Fuhrman grades in the non-MTS tumors were II (three tumors), III (one tumor), or unknown (two). The median STT distance was 9.53 cm (range: 3.7–14.4 cm) in the MTS group and 8.50 cm (range: 6.1–10.3 cm) in the non-MTS group ($p = 0.425$). There were no major changes in patient creatinine levels following the procedure, with postoperative creatinine values ±0.2 mg/dL of preoperative creatinine levels in all patients.

### *CA procedure data*

The median number of cryoprobes used intraoperatively was 2.7 (range 1–4) in the MTS group, compared with 1.8 (range 1–4) in the non-MTS group ($p = 0.049$). Additional cryoprobes were added based on initial MTS readings and cryoprobes were repositioned based on MTS data. When the MTS was used, most tumors (9 of 11) underwent freeze times longer than 10 minutes, with 8 of 11 requiring longer than 12 minutes. All tumors in the non-MTS group were frozen for 10 minutes, except for one, which received a 15-minute freeze (due to initial cryoprobe malfunction). The average procedure times as determined by the anesthesia reports were 162.8 minutes (range 110–225) and 116.2 minutes (range 60–175) in the MTS and non-MTS groups, respectively ($p = 0.020$). The average total length of freeze as determined from the operative report was 28.9 minutes (range 19–47) and 21.9 minutes (range 20–30) in the MTS and non-MTS groups, respectively ($p = 0.041$). One postoperative complication (dysuria, nausea, vomiting, Clavien–Dindo I) was observed in the MTS group, while two complications (bleeding requiring 2 U transfusion and small hemothorax, Clavien–Dindo II and III, respectively) were noted in the non-MTS patients.

### *Comparison of biopsy-confirmed RCC*

A comparison of the biopsy-confirmed RCC tumors in the MTS and non-MTS groups is presented in Table 2. When considering only biopsy-confirmed RCC, MTS tumors had a mean tumor size of 1.8 cm compared with 2.3 cm in the non-MTS tumors ($p = 0.017$). MTS tumors were also associated with increased cryoprobe use per cm diameter of tumor (1.38 *vs* 0.69, $p = 0.001$). The biopsy-confirmed RCC MTS group also had increased procedure time (145.3 *vs* 101.5 minutes, $p = 0.085$) and increased numbers of cryoprobes used (2.5 *vs* 1.5, $p = 0.065$).

### *Recurrences*

The mean follow-up time for the entire cohort was 44.5 months (range 5.3–126.3). Mean follow-up times for the MTS and non-MTS groups were 48.2 months (range 10.5–79.4) and 40.0 months (range 5.3–126.3) ($p = 0.518$), respectively. At the most recent follow-up, none of the 11 patients in the MTS group experienced a recurrence, while 4 of 9 patients had recurrent tumors in the non-MTS group ($p = 0.026$). Of the biopsy-proven RCC, none of the 6 recurred in the MTS group compared with 3 of the 6 in the non-MTS group ($p = 0.182$). The three RCC tumors that recurred had clear cell (2) and papillary (1) histology. The sizes of recurrent RCC tumors were 2.0, 2.2, and 2.4 cm.

The mean time to recurrence was 42.8 months, with the individual recurrences occurring at 5.3, 8.2, 31.6, and 126.3 postoperative months. There were no biopsies recorded for any of the recurrent tumors. One patient developed multiple metastases to the rib cage and lung despite a negative metastatic work-up before CA, and died shortly thereafter. The

Table 2. Comparison of Multipoint Thermal Sensor and Non-Multipoint Thermal Sensor Cryoablation in Biopsy-Confirmed Renal-Cell Carcinoma Tumors

| | *MTS* | *Non-MTS* | p |
|---|---|---|---|
| No. of biopsy-confirmed tumors | 6 | 6 | |
| Age, median (range) | 59 (52–77) | 68 (45–86) | 0.402 |
| Male | 3 (50%) | 5 (83.3%) | 0.545 |
| Tumor size, median (range), cm | 1.8 (1.4–2.2) | 2.3 (2–3) | **0.017** |
| Percutaneous/laparoscopic | 5/1 | 6/0 | 1.000 |
| RCC histology: clear cell/papillary | 4/2 | 5/1 | 1.000 |
| Fuhrman grade: II/III/not specified | 1/3/2 | 3/1/2 | |
| STT distance, median (range), cm | 10.9 (8.0–14.4) | 9.1 (6.1–10.3) | 0.173 |
| Procedure time, mean (range), minutes | 145.3 (110–217) | 101.5 (60–152) | 0.085 |
| Follow-up, mean (range), months | 69.1 (61.8–79.3) | 51.8 (5.3–126.3) | 0.411 |
| Complications (Clavien–Dindo) | 1 (I) | 1 (II) | 1.000 |
| Average number of cryprobes used (range) | 2.5 (2–3) | 1.5 (1–3) | 0.065 |
| Cryoprobes/cm tumor, mean (range) | 1.38 (1.11–1.76) | 0.69 (0.45–0.83) | **0.001** |
| RCC recurrences | 0/6 | 3/6 (50%) | 0.182 |
| Median STT distance in recurrences, median (range), cm | — | 9.7 (8.5–10.1) | |

other three recurrences were managed by active surveillance due to patient's choice (1) or were lost to follow-up (2).

There were no significant differences in tumor characteristics of the recurrent and nonrecurrent groups within the non-MTS group. In particular, there were no differences in tumor size, number of cryoprobes used, and STT distance; these results are displayed in Table 3.

## Discussion

In the current study, we were able to demonstrate significantly improved long-term oncologic outcomes following CA with MTS needles, which allow precise determination of ice-ball temperature. Strikingly, our analysis revealed that none of the 11 patients undergoing CA with MTS needles experienced recurrence, compared with 4 of the 9 patients in the non-MTS group. There were no significant differences in patient and tumor characteristics between the MTS and the non-MTS groups, including patient age, gender, tumor size, surgical approach, STT distance, biopsy results, and complications, although the MTS group was associated with increased cryoprobe utilization and increased procedure time. Of note, none of the 6 MTS patients with biopsy-proven RCC had a recurrence compared with 3 of the 6 non-MTS patients with biopsy-proven RCC.

The vascular differences within renal tumors and in the surrounding milieu are believed to impact the treatment success of CA.[30] These differences may manifest in variable heat dissipation by the heat sink effect, due to warm blood flow impeding adequate CA freeze temperatures in the more vascular areas of the tumor. The thermal sinks created by continued circulation may in turn be cryoprotective and result in incomplete ablation, particularly in the absence of *in vivo* temperature monitoring.[20,21] The use of the MTS provides a standardized mechanism to account for the vagaries in tumor blood flow, ensure target temperature attainment throughout the tumor, and minimize the risk of incomplete ablation.

In our study, we noted recurrence in 4 of 20 tumors, a relatively high recurrence rate compared with similar studies from other institutions.[8,11] While multiple reports have reported effective long-term outcomes post-CA of greater than 90%, it is possible our findings may be related to the flux of a small sample size, the alteration in the type of cryoprobe used in the two groups, or the possible higher success rate in those series in which renal mass biopsy was not performed, and hence, upward of 20% of the lesions treated were benign and incapable of recurrence. The original pathologies of the four recurrences in this study were three biopsy-confirmed RCC and one oncocytoma. Three of the four recurrences in the non-MTS group also failed within 3 years, indicating that these were likely true recurrences relating to the CA and not *de novo* tumors arising in the same region.

Our finding that additional cryoprobes were utilized in the MTS group suggests that the MTS data helped improve and optimize cryoprobe placement during the CA procedure. Breda and colleagues determined that the use of a single 1.47 mm cryoneedle was inadequate for complete ablation of most SRM. Instead, an elliptical ice-ball with a triangular template of three cryoprobes resulted in the most consistent tissue destruction.[31] As the use of multiple cryoprobes appears to allow synergistic expansion of ice-ball diameter inducing

Table 3. Comparison of Recurrences *Vs* Nonrecurrences in the Biopsy-Confirmed Tumors Within the Non-Multipoint Thermal Sensor Group

| | *Recurrences* | *Nonrecurrences* | p |
|---|---|---|---|
| No. of biopsy-confirmed tumors | 3 | 3 | |
| Tumor size, median (range), cm | 2.2 (2.0–2.4) | 2.4 (2.2–3.0) | 0.279 |
| Average number of cryprobes used (range) | 1.67 (1–3) | 1.67 (1–2) | 1.000 |
| Median STT distance in recurrences, median (range), cm | 9.7 (8.5–10.1) | 6.4 (6.1–10.3) | 0.271 |
| Cryoprobes/cm tumor, median (range) | 0.50 (0.45–1.25) | 0.67 (0.45–0.83) | 0.781 |

greater areas of tissue necrosis, the increased cryoprobe utilization with the MTS likely contributed to more complete ablation and improved outcomes; however, this increased area of CA resulted in clinically insignificant injury to surrounding normal renal parenchyma based on postoperative creatinine levels. Thus, we surmise that the use of fewer cryoprobes in the absence of the MTS may result in inadequate probe distribution and hence poorer outcomes.

Tumors in the MTS group were first evaluated for −20°C attainment throughout the tumor before each 10-minute freeze. The target temperature in this study was chosen to be −20°C based on previous reports.[15–17] Consistent with the literature, no failures occurred once the target temperature was recorded by the MTS. However, the MTS group underwent significantly longer freeze times and overall procedure times, requiring on average 47 minutes longer to perform than without the MTS. The MTS also increases the cost of the procedure, as the MTS is $500 and either one or two MTS needles are used per CA. Nevertheless, our findings suggest that a freeze protocol failing to incorporate *in vivo* temperature confirmation within the tumor by the MTS may result in undertreatment during CA and the more expensive option of needing to repeat the treatment or proceed to more invasive therapy.

There are several limitations to this study. First, this was a retrospective analysis with a limited sample size. In addition, there was temporal separation of the MTS and non-MTS groups, with the non-MTS group occurring earlier. While this may appear to represent a ''learning curve'' for CA, it was likely not a significant concern as our surgical team had more than 5 years of CA experience before the study start date. Different cryoprobes (Endocare for non-MTS and IceRod Galil for MTS) were used in the MTS *vs* non-MTS groups due to hospital supply decisions. Finally, the MTS needles introduce the potential for technical error, with manufacturer-stated temperature accuracy of ±5°C. Despite these limitations, we believe our findings support the routine use of MTS in the setting of CA and may thereby render a situation in which patient outcomes are equivalent to partial nephrectomy. However, given our small sample size and the aforementioned confounding factors, a prospective randomized study comparing MTS and non-MTS CA treatments is much needed.

## Conclusions

The use of MTS needles during CA to guide CA therapy was associated with improved long-term oncologic outcomes. Increased cryoprobe utilization was also observed when MTS needles were deployed. Further prospective studies with a larger patient cohort are needed to test this observation.

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## Author Disclosure Statement

Dr. Clayman has previously served as a consultant for Endocare and received support for laboratory studies; he has also participated in a meeting with Galil, Inc.

## References

1. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: A need to reassess treatment effect. J Nat Cancer Inst 2006;98:1331–1334.
2. Chawla SN, Crispen PL, Hanlon AL, Greenberg RE, Chen DY, Uzzo RG. The natural history of observed enhancing renal masses: Meta-analysis and review of the world literature. J Urol 2006;175:425–431.
3. Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MA. The natural history of incidentally detected small renal masses. Cancer 2004;100:738–745.
4. Ramanathan R, Leveillee RJ. Ablative therapies for renal tumors. Ther Adv Urol 2010;2:51–68.
5. Haber GP, Lee MC, Crouzet S, Kamoi K, Gill IS. Tumour in solitary kidney: Laparoscopic partial nephrectomy vs laparoscopic cryoablation. BJU Int 2012;109:118–124.
6. Pierorazio PM, Johnson MH, Patel HD, Sozio SM, Sharma R, Iyoha E, et al. Management of renal masses and localized renal cancer: Systematic review and meta-analysis. J Urol 2016;196:989–999.
7. Castro A, Jr., Jenkins LC, Salas N, Lorber G, Leveillee RJ. Ablative therapies for small renal tumours. Nat Rev Urol 2013;10:284–291.
8. Dominguez-Escrig JL, Sahadevan K, Johnson P. Cryoablation for small renal masses. Adv Urol 2008;2008:479495.
9. Mues AC, Landman J. Small renal masses: Current concepts regarding the natural history and reflections on the American Urological Association guidelines. Curr Opin Urol 2010;20:105–110.
10. Campbell SC, Novick AC, Belldegrun A, Blute ML, Chow GK, Derweesh IH, et al. Guideline for management of the clinical T1 renal mass. J Urol 2009;182:1271–1279.
11. Zargar H, Atwell TD, Cadeddu JA, de la Rosette JJ, Janetschek G, Kaouk JH, et al. Cryoablation for small renal masses: Selection criteria, complications, and functional and oncologic results. Eur Urol 2016;69:116–128.
12. Klatte T, Shariat SF, Remzi M. Systematic review and meta-analysis of perioperative and oncologic outcomes of laparoscopic cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal tumors. J Urol 2014;191:1209–1217.
13. Thompson RH, Atwell T, Schmit G, Lohse CM, Kurup AN, Weisbrod A, et al. Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses. Eur Urol 2015;67:252–259.
14. Kroeze SG, van Melick HH, Nijkamp MW, Kruse FK, Kruijssen LW, van Diest PJ, et al. Incomplete thermal ablation stimulates proliferation of residual renal carcinoma cells in a translational murine model. BJU Int 2012;110(6 Pt B):E281–E286.
15. Chosy SG, Nakada SY, Lee FT, Jr., Warner TF. Monitoring renal cryosurgery: Predictors of tissue necrosis in swine. J Urol 1998;159:1370–1374.
16. Campbell SC, Krishnamurthi V, Chow G, Hale J, Myles J, Novick AC. Renal cryosurgery: Experimental evaluation of treatment parameters. Urology 1998;52:29–33; discussion 33–34.
17. Schmidlin FR, Rupp CC, Hoffmann NE, Coad JE, Swanlund DJ, Hulbert JC, et al. Measurement and prediction of thermal behavior and acute assessment of injury in a pig model of renal cryosurgery. J Endourol 2001;15:193–197.

18. Young JL, Khanifar E, Narula N, Ortiz-Vanderdys CG, Kolla SB, Pick DL, et al. Optimal freeze cycle length for renal cryotherapy. J Urol 2011;186:283–288.
19. Tatsutani K, Rubinsky B, Onik G, Dahiya R. Effect of thermal variables on frozen human primary prostatic adenocarcinoma cells. Urology 1996;48:441–447.
20. Young JL, Clayman RV. Cryoprobe isotherms: A caveat and review. J Endourol 2010;24:673–676.
21. Ladd AP, Rescorla FJ, Baust JG, Callahan M, Davis M, Grosfeld JL. Cryosurgical effects on growing vessels. Am Surg 1999;65:677–682.
22. Beemster PW, Lagerveld BW, Witte LP, de la Rosette JJ, Pes MP, Wijkstra H. The performance of 17-gauge cryoprobes in vitro. Technol Cancer Res Treat 2008;7:321–327.
23. Vernez SL, Okhunov Z, Dutta R, Kaler K, George A, Moreira D, et al. PD46-03 evaluation of skin-to-tumor distance as a predictor of tumor recurrence following percutaneous cryoablation of renal cortical neoplasms. J Urol 2016;195:e1124.
24. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surgery 2004;240:205–213.
25. Abraham JB, Gamboa AJ, Finley DS, Beck SM, Lee HJ, Santos RJ, et al. The UCI seldinger technique for percutaneous renal cryoablation: Protecting the tract and achieving hemostasis. J Endourol 2009;23:43–49.
26. Tay KJ, Kim C, Polascik TJ. Chapter 29: Renal cryosurgery. In: Smith JA Howards SS, Preminger GM, Dmochowski RR, eds. Hinman's Atlas of Urologic Surgery, 4th ed. Philadelphia, PA: Elsevier Health Sciences, 2016, pp. 241–247.
27. Auge BK, Santa-Cruz RW, Polascik TJ. Effect of freeze time during renal cryoablation: A swine model. J Endourol 2006;20:1101–1105.
28. Woolley ML, Schulsinger DA, Durand DB, Zeltser IS, Waltzer WC. Effect of freezing parameters (freeze cycle and thaw process) on tissue destruction following renal cryoablation. J Endourol 2002;16:519–522.
29. Kawamoto S, Solomon SB, Bluemke DA, Fishman EK. CT and MR imaging appearance of renal neoplasms after radiofrequency ablation and cryoablation. Semin Ultrasound CT MR 2009;30:67–77.
30. Lagerveld BW, van Horssen P, Pes MP, van den Wijngaard JP, Streekstra GJ, de la Rosette JJ, et al. Immediate effect of kidney cryoablation on renal arterial structure in a porcine model studied by imaging cryomicrotome. J Urol 2010; 183:1221–1226.
31. Breda A, Lam JS, Riggs S, Leppert JT, Gui D, Said JW, et al. In vivo efficacy of laparoscopic assisted percutaneous renal cryotherapy: Evidence based guidelines for the practicing urologist. J Urol 2008;179:333–337.

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**Abbreviations Used**

CA = cryoablation
CT = computed tomography
MRI = magnetic resonance imaging
MTS = multipoint thermal sensors
RCC = renal-cell carcinoma
RCN = renal cortical neoplasms
SRM = small renal mass
STT = skin-to-tumor