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Utility of Intra-procedural Contrast Enhanced CT in Ablation of Renal Masses

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Abstract

Purpose—To evaluate the efficacy of radiofrequency ablation (RFA) of renal masses comparing group I without intra-procedural CT and group II with intra-procedural contrast enhanced computed tomography (CT).

Methods and Materials—This is a retrospective review of 45 consecutive patients who underwent RFA of renal masses. If adequate biopsy specimen or follow up were not obtained, they were eliminated from review for calculation of primary technical efficacy. Inclusion criteria were all cases using two "cool tip" electrodes. Baseline demographics (age, body mass index, and gender), renal mass characteristics (diameter, side, location, position, morphology, type of mass, and grade), technical details (repositioning and hydrodissection), and complications were evaluated. Follow-up imaging was evaluated to determine recurrence at the ablation site comparing the two groups.

Results—In the 45 patients with RFA these consisted of 13 in Group I without intra-procedural CTs and group II consisted of 32 intra-procedural CTs. 35 patients met criteria for follow-up and positive biopsy. For calculation of recurrence, 10 were in group I and 25 in group II.

No correlation was found between baseline demographics, renal mass characteristics, and technical results between group I and II. There was a 88.5% overall technical efficacy rate, with a

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96 % primary technical efficacy rate in group II compared with a 70% rate in group I. There was a negative correlation found between these two groups for technical efficacy rate at the $P<0.05$ level.

Conclusion—Intra-procedural CT with contrast provides important information concerning completeness of ablation during the procedure, allowing for probe repositioning and thus attaining a better therapeutic effect.

INTRODUCTION

Percutaneous ablation of hepatic and renal tumors has been used for a number of years. Originally radiofrequency ablation (RFA) was one of the first thermal based methods that found widespread use since first described in 1990 for ex vivo coagulation of liver tissue [1,2]. RFA was originally used most commonly in clinical practice to treat hepatic neoplasms. It was not until 1997 that RFA was reported to provide extensive necrosis of renal tumors both ex vivo and in vivo [3]. Initial case reports of treatment of renal cell carcinoma (RCC) with RFA described the use of sonography for guidance [4,5]. However, more recent publications and larger series describe the almost exclusive use of CT for guidance [6–8]. Still, in most series, the earliest evaluation with CT contrast imaging is not done until 24 hours or later post-procedure. Though prior studies have investigated the use of RFA assisted by intra-procedural CT with contrast in hepatic masses, use of intra-procedural contrast CT for renal masses is less common. The purpose of this study is on the success (outcome) of RFA performed with intra-procedural RFA.

METHODS AND MATERIALS

Patient selection

This retrospective study was approved by our institutional review board (IRB) with the study being Health Insurance Portability and Accountability Act (HIPPA) compliant. After obtaining approval, all patients undergoing renal RFA from December 2010 through March 2018 using two “cool tip” electrodes were included in this study. Other patients using a single electrode or clustered “cool tip” electrode were not included in this series. Renal ablations using other modalities were not considered in this series. All patients had informed consent for their RFA. This study includes 45 consecutive patients who underwent RFA of renal mass and follow-up imaging between December 2010 and March 2018 at a single institution. Originally we performed the initial follow up contrast enhanced CT within 24 hours of the RFA. However, in late 2012 we begin performing a contrast enhanced CT during the procedure, after the initial ablation. All patients were considered candidates for radiofrequency ablation if they had a new solid renal mass with imaging characteristics consistent with RCC. In one patient, two masses were treated for a total of 46 masses. One was not counted, as the smaller of the two masses in our calculations as only one probe was used for treatment, leaving 45 masses in 45 patients. This study divided patients into those that had received no intra-procedural contrast enhanced CT (Group I), and those who had intra-procedural contrast enhanced CT immediately after initial ablation (Group II). Those in group I usually had their initial post ablation CT with 24 hours of their procedure. Patient baseline demographics and renal mass characteristics were obtained for both groups. Biopsy was performed before or at the time of the procedure. If biopsy specimens were inadequate, these patients were not included in calculation of tumor recurrence. Complications of RFA were compared for the two groups. Complications were recorded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events, Version 3 [9].

Complications were classified as major or minor, those requiring no therapy or nominal therapy, and were recorded for those that were major complications, requiring therapy such as transfusion, interventional radiology procedures or operative intervention.

CT-guided biopsy and RFA

All RFAs were performed under general anesthesia using a single radiofrequency generator (Radionics, Covidien) using their "switch box" technology in order to minimize study variables. Electrode applicators were all saline-perfused internally cooled-tip electrodes. This series included only those in which two separate electrodes (Cool-tip RF Ablation Electrodes, Covidien) with 3 centimeter exposed tips were used, to minimize variables. All procedures in this study were limited to one physician with over 20 years of experience in percutaneous ablation, to further limit another variable. Renal mass biopsy was either performed prior to the procedure or immediately prior to the ablation. In both situations biopsies were attempted with 1–3 core samples using 18-gauge automated biopsy device and a 2–4 fine needle biopsies using 22-gauge Chiba type needles. In the cases where biopsy was performed during the procedure, it was followed by ablation performed immediately after the biopsy.

The two RF electrodes were placed under ultrasound guidance with the patient placed either supine or prone based upon the renal mass location in relationship to surrounding structures as noted on pre-procedure imaging. CT was used to check electrode position and relationship to surrounding structures.. Hydrodissection was performed, when bowel or other structures were in close proximity to the renal mass and the ablation site. Hydrodissection was performed using 100–400 mL of Dextrose (5%) in sterile water. Hydrodissection was used to increase the distance from the renal tumor to adjacent "high-risk" structures (e.g. colon, small bowel, and ureter) to > 4 cm from the RF electrodes. On occasion diluted iodinated contrast material was used for hydrodissection as described by other authors [10]. Contrast enhanced CT was performed either during (Group II) or within 24 hours of the procedure (Group I). These CTs were performed with either a 16-MDCT or 64 MDCT (Light Speed, Light Speed VCT, General Electric, Milwaukee, WI). All CTs included a three-phase renal CT with a base scan, a cortical medullary phase (delay of approximately 40 seconds) and a nephrographic phase (delay of approximately 100 seconds). No excretory phase was routinely performed per our renal mass protocol. Iohexol (Omnipaque 350, GE Healthcare) was injected at a rate of approximately 3 ml/sec for a total of 100ml to 125 ml. In group I, immediately after ablation and before removal of the electrodes, a 3-phase CT scan of the upper abdomen was performed using a renal mass protocol to assess the ablation zone. Additional ablations were performed in either group when it was thought that the ablation zone did not extend beyond the margin of the tumor. Primary technical efficacy is defined as the percentage or target tumors successfully eradicated following the initial procedure as evidenced by imaging follow up as defined by Ahmed et al [11]. All tumors were ablated during a single session.

Follow-up

Patients underwent the institutional standard 3-phase abdominal CT scans using a renal mass protocol at different times after the procedure. Imaging studies were reviewed by a body imaging radiologist and a radiology resident with 35 years and 3 years of experience, respectively, reviewing both the CT reports and images to collect data. Primary treatment effectiveness refers to the lack of residual or recurrent tumor enhancement on follow-up imaging studies [11]. These patients were excluded for calculation of tumor recurrence if a record of contrast-enhanced CT was not available. Follow-up imaging was available for 40 of 45 patients. Glomerular filtration rate (GFR) values before and after ablation were available for all patients as previously discussed. Complications were based upon the Clavien-Dindo grading system [12].

Statistical analysis

Group differences and effects of CT contrast during ablation were estimated and tested using chi square tests for categorical variables and t tests for continuous variables. All statistical analyses were performed using SAS® software version 9.4. The Fisher exact text calculation was used for comparison of tumor recurrence between the two groups. A p-value of less than 0.05 was considered significant.

RESULTS

Of the 45 total patients, 13 had no intra-procedural contrast enhanced CT (group I), and 32 received intra-procedural contrast enhanced CT (group II). Patient baseline demographics and renal mass characteristics are summarized in Tables 1 and 2. Dual probe RFA was used to treat 45 renal tumors, of which 35 (76%) were biopsy-proven RCCs. Technical details are summarized in Table 3. The mean tumor diameter was 2.99 (.65) cm (range, 1.2–5.0 cm). Of the original 45 patients, 35 of the patients (78%) who received follow-up had positive cytology results, no recurrence was observed in 31 (88.5%). There were no major complications in either group I or group II. The following are the demographics for the groups I and II, respectively: 66 y vs. 65 years, BMI 31 vs. 30, females 5 vs. 12, and males 8 vs. 20 (Table 1). None of these variables were found to be statistically significantly different ($p<0.05$) across the two groups.

Renal mass characteristics included mean diameter for Group I versus Group II was as follows 3.25 cm vs. 2.88 cm; side: right 10 vs.14 and left 3 vs. 18; position: anterior 8 vs. 11 and posterior 5 vs. 21; morphology: exophytic 6 vs. 23, endophytic 3 vs. 1, and mixed exophytic-endophytic 4 vs. 8. (Table 2). The following were biopsy results: renal cell carcinoma (RCC) 10 vs. 24, oncocytoma 1 vs. 0, spindle cell carcinoma 0 vs. 1, atypical 0 vs. 2, insufficient specimen 1 vs. 3, and no biopsy due to technical difficulty in performing the biopsy 1 vs. 1. Only the 35 patients with RCC or spindle cell carcinoma were included in the follow up evaluation.

None of the renal mass characteristics were found to be statistically significantly different between the two groups.

Hydrodissection was required in 12/45 (27%) (std= 7%) of tumors. More cases in group II (9) were hydrodissected compared to group I (3) (Table 3) (Figures 1 and 2). Twelve cases in group II were repositioned compared to only 2 in group I. However, repositioning and hydrodissection showed no statistical difference between the two groups.

There were no grade II or higher complications in either group [12]. All complications were minor, such as minor hemorrhage requiring no more than analgesia and no other therapeutic intervention.

Group 1 consisted of 10/13 patients with follow-up imaging and positive biopsy for RCC and Group 2 consisted of 25/32 patients who had follow-up imaging with renal or spindle cell carcinoma. All patients without follow up imaging had no other tumor recurrence in review of their electronic medical records. However, these patients are not counted in our statistical analysis. It was found that 1/25 with intra-procedural CT had tumor recurrence (4%) at a follow up CT. This patient is still undergoing watchful waiting of the tumor recurrence. Of the 10 patients who did not receive intra-procedural CT, 3/10 (30%) has incomplete ablation on the contrast CT performed within 24 hours of the procedures. These were residual untreated disease. One of these patients was successfully re-ablated (Figure 3), one had a nephrectomy, and one had continued watchful waiting. There was correlation was found between intra-procedural CT and primary technical efficacy rate ($P = 0.061$) when using $P<0.05$. There was a 96% technical efficacy rate when using intra-procedural CT compared to a 70% technical success when using post procedural CT. Those patients in group I with post-procedural CT had a mean follow-up of 2 years and 5 months, and those with intra-procedural CT had a mean follow-up of 1 year and 4 months.

DISCUSSION

RCC is the most common malignant cancer of the kidney and it accounts for 3% of all cancers in adults [13]. Currently, surgery is the method of choice for treatment of localized RCC. However, a significant number of patients are not suitable for surgery because of comorbid illnesses. Given the surgical constraints, image-guided ablative treatment of small renal tumors with RFA, cryotherapy, and microwave has developed at a rapid pace over the last decade [14]. In fact, RFA is the most commonly used percutaneous ablation technique used in inoperable patients with RCC [15]. It preserves more normal organ tissue and is less expensive than surgery [16–18]. However, RFA still has some limitations regarding ablation size, procedure time, and heat sink effect from adjacent vessels [15]. Though it is a safe procedure with a serious complication rate of <1% [19] and like most other procedures, major complications include hemorrhage, infection, and injury to adjacent organs [19,20]. Patient positioning and hydrodissection may help to displace the adjacent bowel to prevent injury [15] and were found to not be utilized differently in the two groups.

Imaging technique is paramount in all steps of tumor ablation [21]. Baseline MR or CT scans are typically performed 1–2 weeks prior to ablation to permit accurate comparison with post-ablation images. Contrast enhanced ultrasound (CEUS) is often used as the primary pretreatment imaging modality to localize the tumor and for correct placement of the electrodes. On the other hand, post-ablation images with contrast enhanced CT or MRI are typically performed within 1 week after the RFA to detect potential residual viable tumor tissue that requires immediate retreatment. Close follow-up imaging is usually performed every 3 months for 1 year after ablation [15] and then every 4–6 months in the following years [22]. However, there has been no consensus on when to obtain follow-up imaging whether at the time of the procedure, the next day, or in three weeks.

A number of studies have studied the clinical impact of using intra-procedural imaging when performing RFA of solid tumors. As an example, Mauri et. al. [23] treated 148 hepatocellular carcinomas (HCC) in 93 patients by RFA and performed immediate assessment by intra-procedural CEUS 5–10 min following the ablation. Intra-procedural CEUS detected incomplete ablation in 34 of 93 (36.5 %) patients, who underwent additional treatment during the same session. At 24 hours, complete ablation was found in 88 of 93 (94.6 %) patients [23]. Cost-effectiveness analysis revealed an advantage for the use of intra-procedural CEUS in comparison (4,639 euros) with standard treatment (6,592 euros) with a 21.9 % reduction of the costs to treat the whole sample. A second session of treatment was spared in 29 of 93 (31.1 %) patients. Mauri et al. concluded intra-procedural use of CEUS has a relevant clinical impact, reducing the number of re-treatments and the related costs per patient [23].

Likewise, Shyn et. al. [25] investigated whether nitrogen 13 (^{13}N) ammonia perfusion positron emission tomography (PET) performed during liver tumor ablation can be used to intra-procedurally to assess ablation margins. They reported 11 of 11 (100%) ablation margins were fully assessable by using intra-procedural perfusion PET.

Intra-procedural CT with contrast when performing RFA of liver has been shown to provide early assessment of the ablation zone [26,27]. There have been differences in the timing of performance of contrast CT after thermal ablation including microwave ablation. For instance, Chan P el al. performed contrast enhanced CT immediately after ablation. They then “organized” a second session immediately if there was residual mass [28].

Abboud et. al [29] compared microwave and radiofrequency ablation of renal cell carcinoma and did not perform immediate post procedure contrast CT until 1 month following ablation. They defined primary treatment success at the initial 1 month CT. They defined primary effectiveness as treatment success without reoccurrence. They had treatment success of 88% for microwave and 80% for RFA groups (P= 0.29). Technical success simply addresses whether the tumor was treated according to protocol and covered completely the ablation zone. Technical efficacy addresses complete macroscopic ablation of the tumor by imaging follow up [11]. There was a 70% technique efficacy with one treatment in 70% for those patients in which CT was performed at the 24 hour mark and 96% technique efficacy if intra-procedural CT was performed. This difference demonstrates the value of intra-procedural CT in ensuring more complete ablation when using thermal ablation techniques, when compared to other series.

The current study is unique in that we investigated the clinical impact of two groups of patients. In the early portion of the study, the first contrast enhanced CT of the kidneys within 24 hours of the procedure and not contemporaneously with the ablation. In the latter portion of the study, contrast enhanced CT was performed at the time of the procedure. In comparing the two groups, 30% of the patients in group I, experienced recurrence. All of these were noted on the CT performed within 24 hours of the procedure. One patient had successful repeat RFA, one had a nephrectomy, and one underwent watchful waiting. This rate of incomplete ablation is not much different than the rate found when using intra-procedural CEUS (22). However, only 4% of group II experienced recurrence. The intra-procedural CT was used to access complete tumor ablation and in 38% of the patients the RF electrode was repositioned in group II. Thus, in these patients a repeat ablation at another setting (anesthesia) was avoided. Therefore, preliminary data suggests RFA of RCC with intra-procedural CT allowed immediate assessment of ablation and is associated with a high initial success rate and a low tumor recurrence rate. The 96% technical success rate in this series compares well with other success rates recorded in the literature [28].

There were several limitations of this study. There were a small number of subjects included in this series. There was only a single operator included in this study. Having only one operator did eliminate any variables in comparing operator experience. The patients were not randomized in any order, which could have been a co-variable as a learning curve for the single operator. However, this operator has had over 20 experience of experience in performing renal ablation. This is a single institution study with a relatively short median follow-up period. Different biological characteristics of renal tumors may influence survival. However, there was no significant difference in demographics and tumor characteristics between two groups, and the results of the two groups could be comparative. These results should be applicable to patients undergoing renal microwave ablation, which has a widely utilized ablation technique[28].

In conclusion, intra-procedural CT with contrast of the RFA of RCC shows clinical promise. In this limited study, use of intra-procedural contrast CT lead to a higher success rate of complete tumor ablation, no increased complications, and limited incomplete ablation, compared to the group in which contrast CT was performed after the procedure. Multi-institutional studies with a larger sample size are needed to validate this proposed clinical benefit and to determine exactly how much intra-procedural contrast enhanced CT reduces the number of re-treatments.

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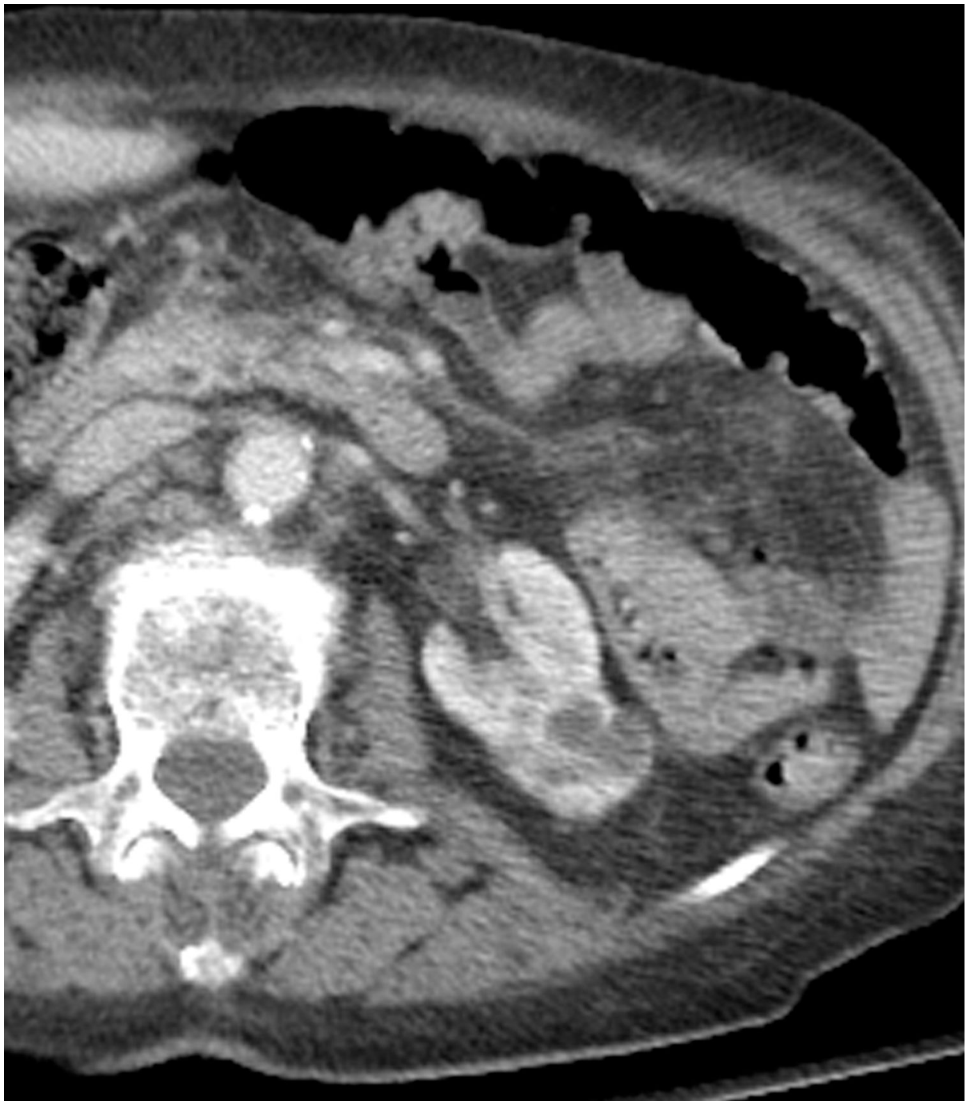
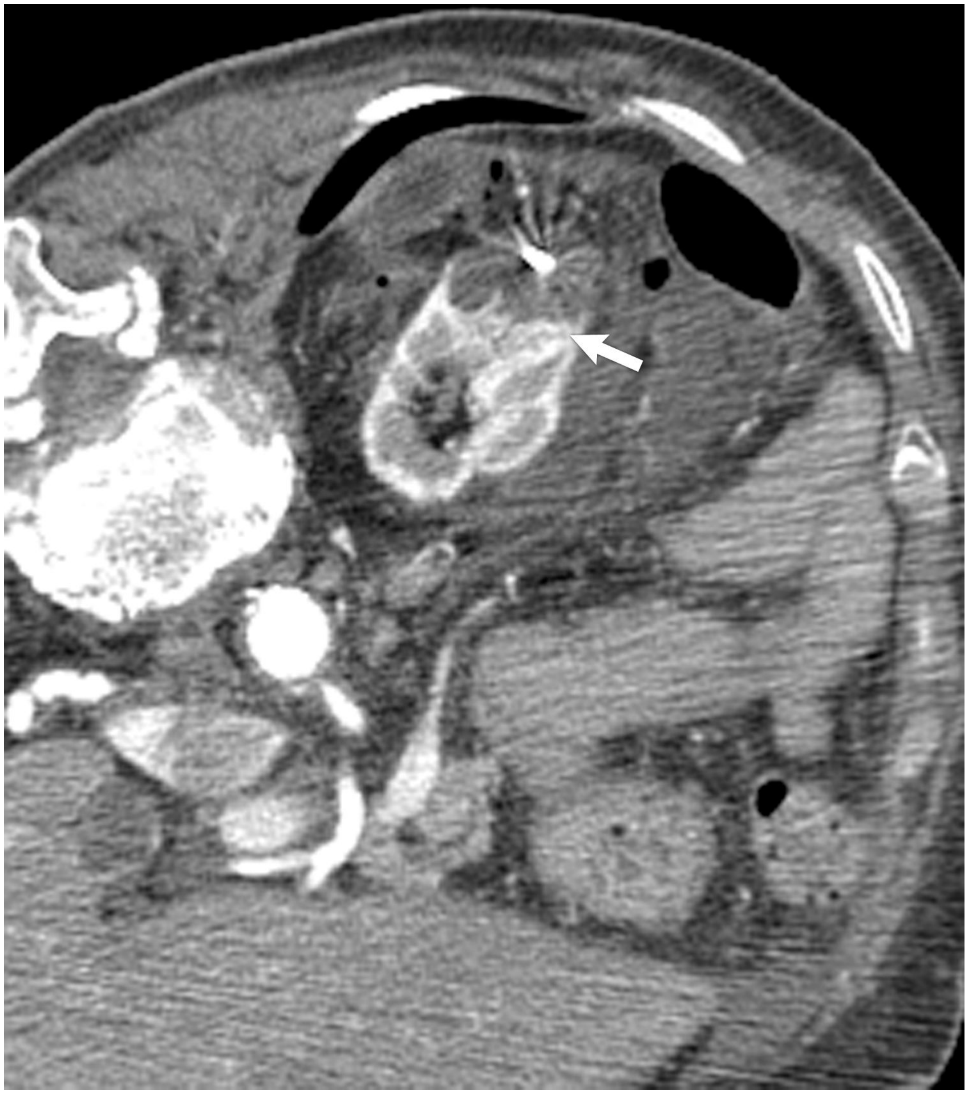




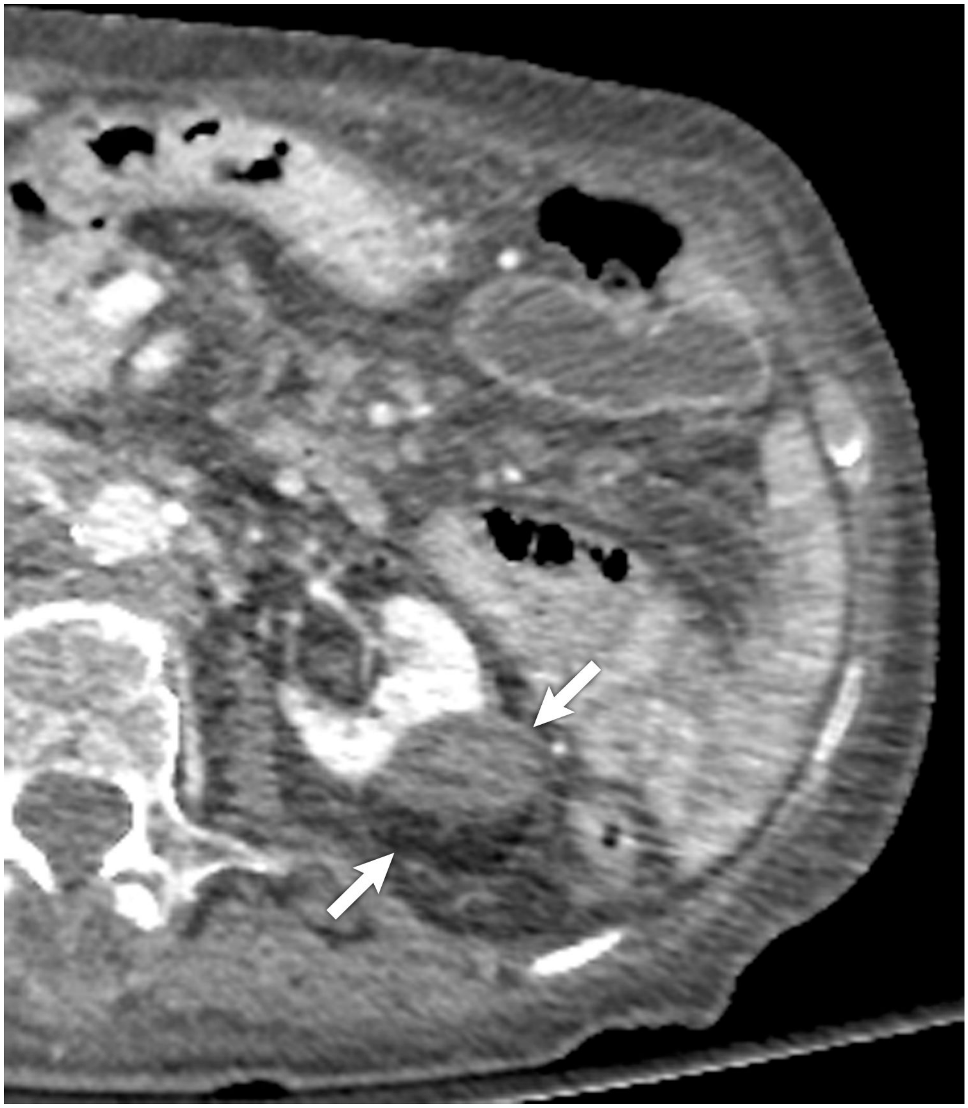


Figure 1.

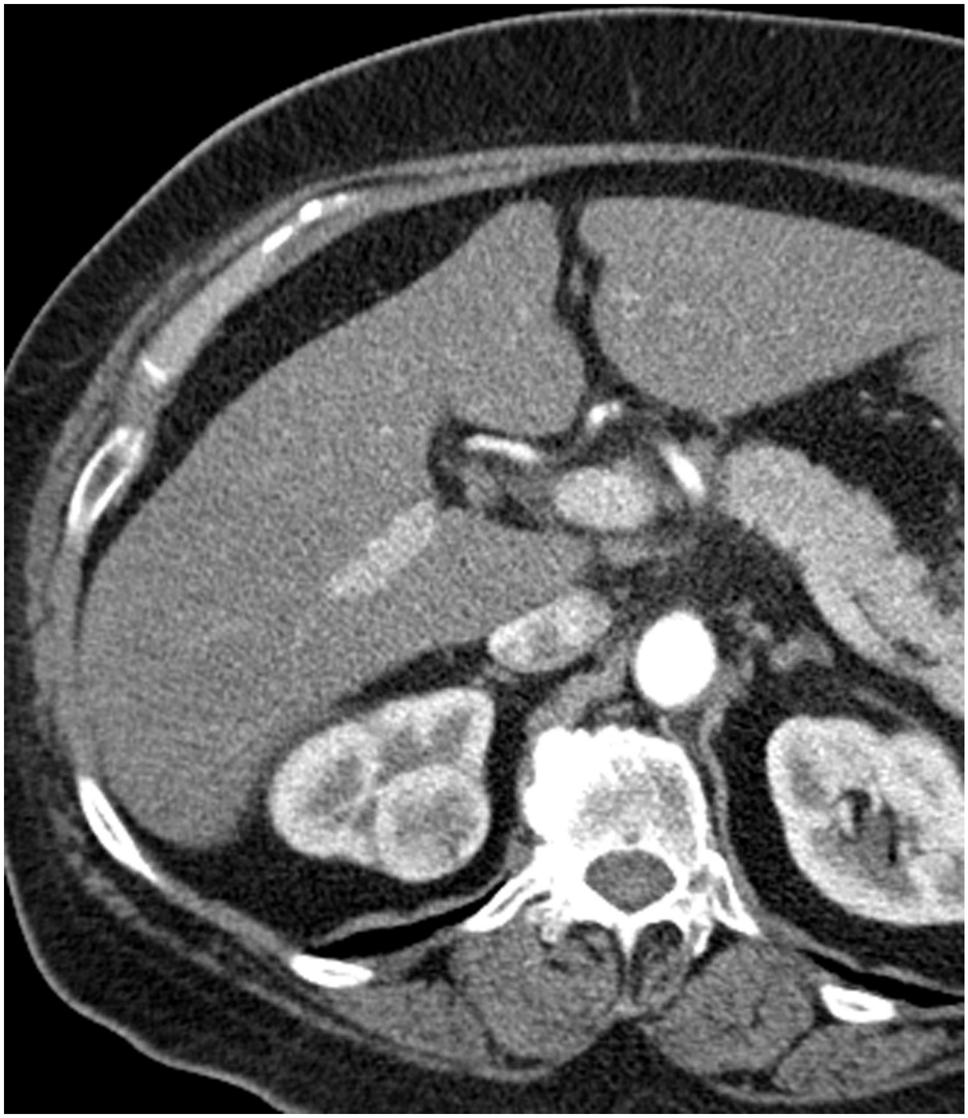
61-year-old female with left Fuhrman grade 1 clear cell RCC showing value of intra-procedural contrast enhanced CT

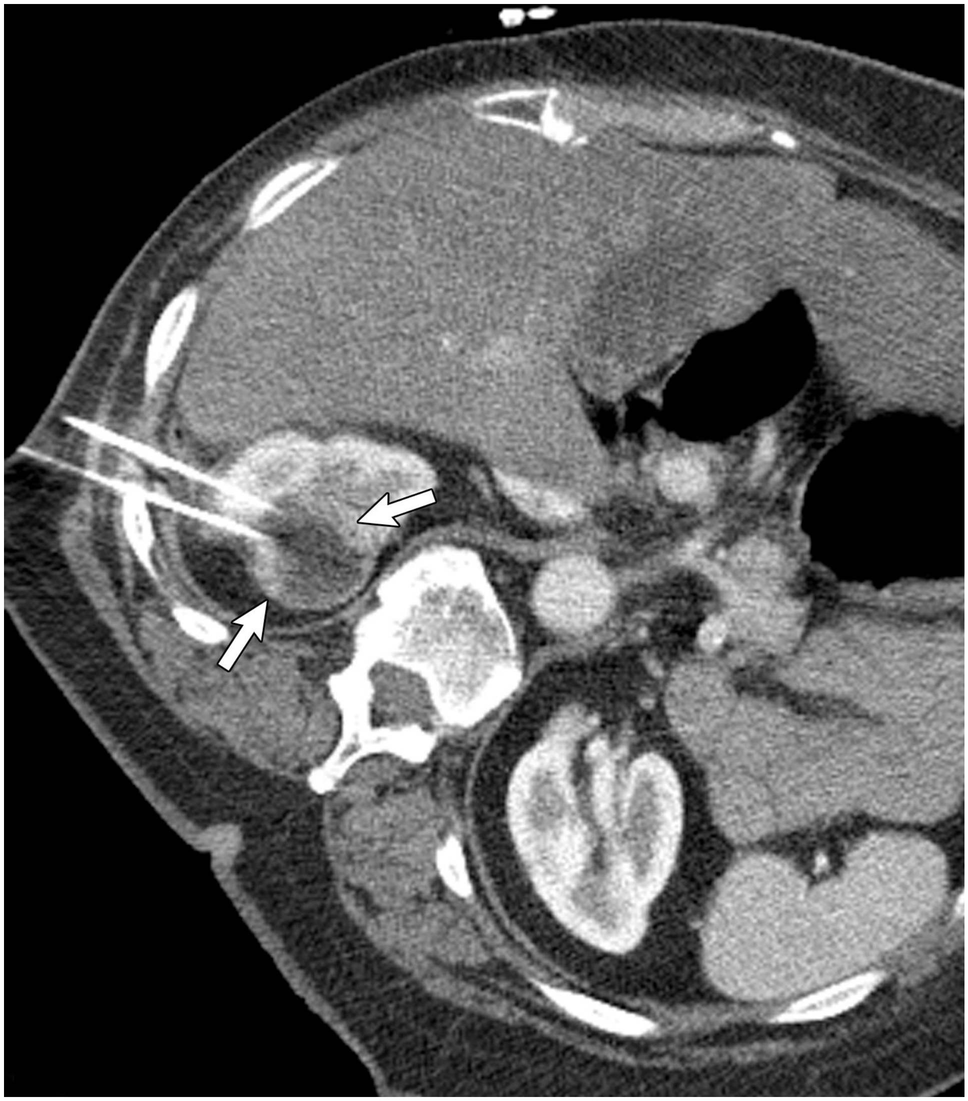
Figure 1A: Pre-procedural contrast-enhanced CT demonstrates necrotic appearing tumor in the left kidney (arrow).

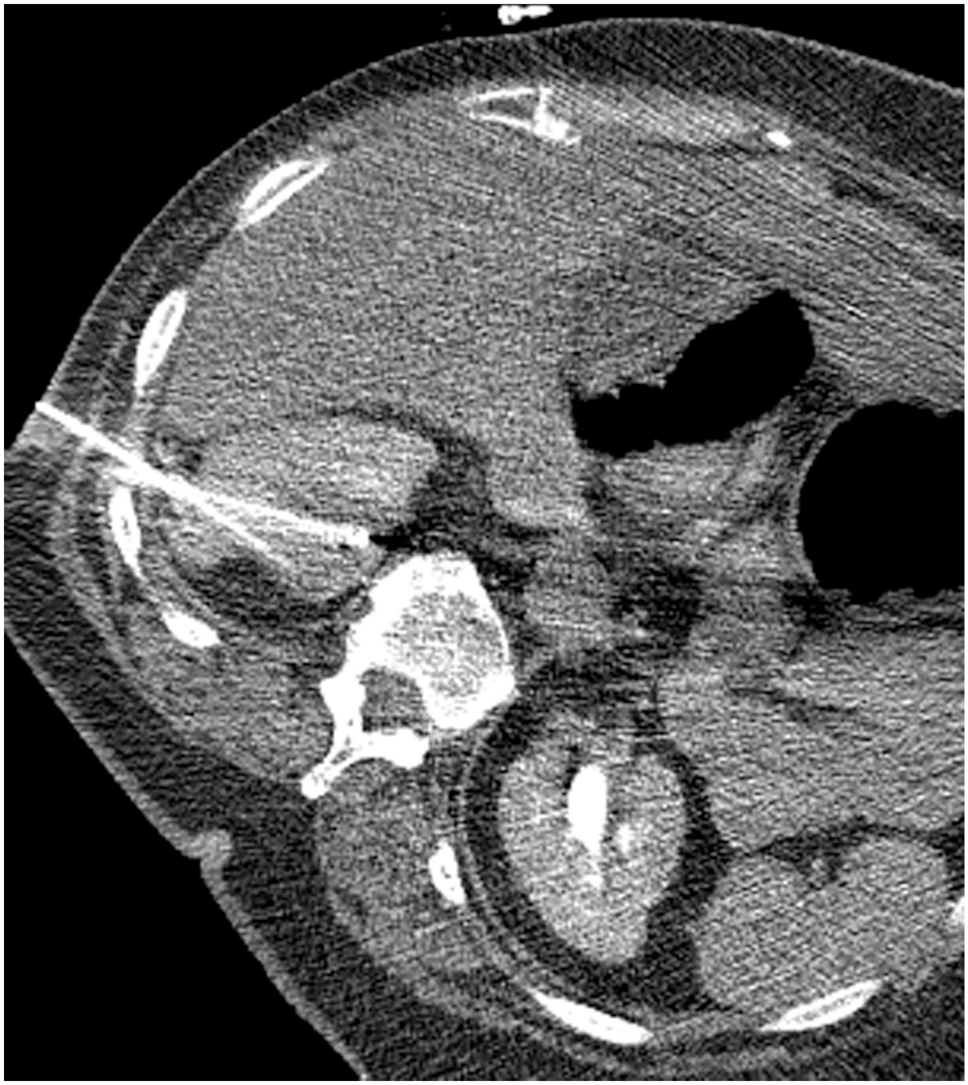
Figure 1B: Arterial phase contrast enhanced CT after hydrodissection and ablation demonstrates one of the 2 RF electrodes in place. There appears to be residual tumor (arrow).

Figure 1C: Because of this finding the 2 RF electrode were repositioned for further RF ablation (arrow).

Figure 1D: One-year follow-up CT demonstrates no enhancement of the prior renal mass with residual changes noted within the perineal fat (arrows).







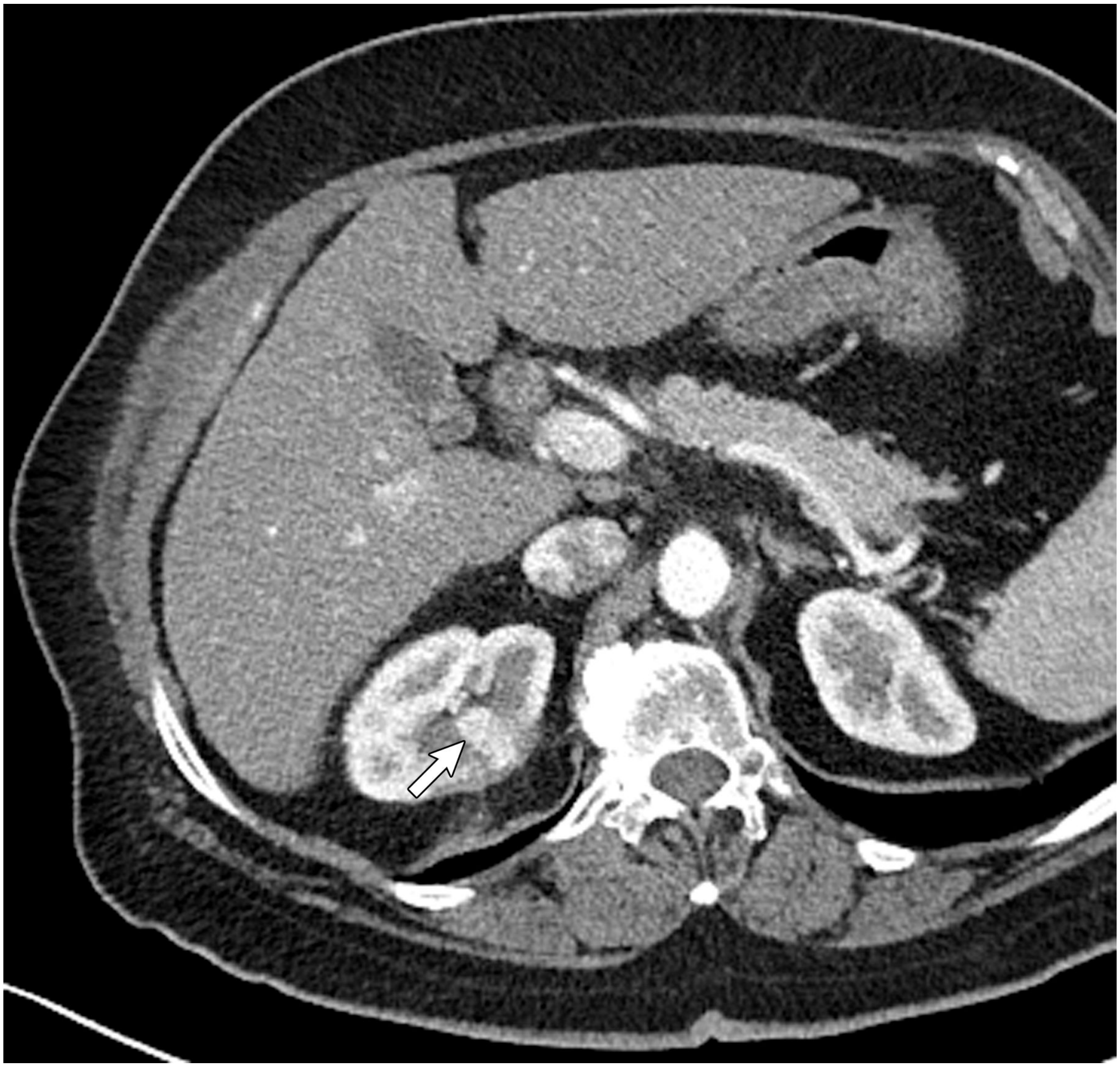


Figure 2.

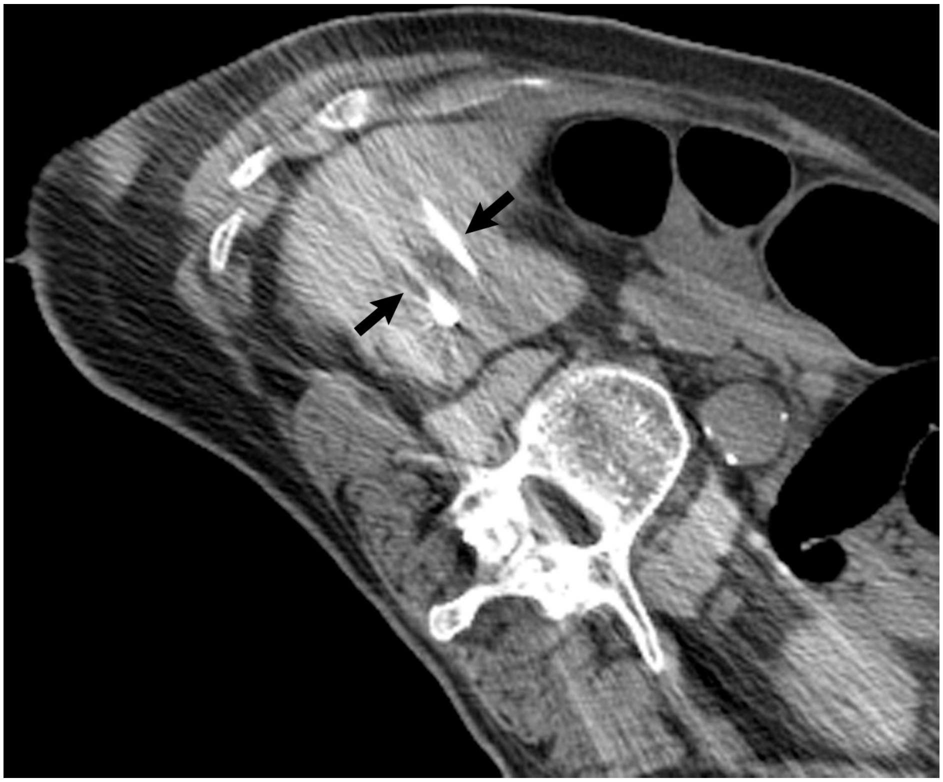
78-year-old with clear cell RCC showing failure of intra-procedural contrast enhanced CT

Figure 2A: Pre-procedure contrast enhanced CT demonstrates enhancing mass noted within the posterior aspect of the right kidney.

Figure 2B: Intra-procedural CT scan after performance of radiofrequency ablation using 2 electrodes demonstrated different areas with question of persistent enhancement (arrows).

Figure 2C: The 2 electrodes were placed in different portions of the renal mass and re-ablation was performed.

Figure 2D: 1 year follow-up contrast enhanced CT demonstrates area of residual enhancement (arrow) corresponding to residual tumor.



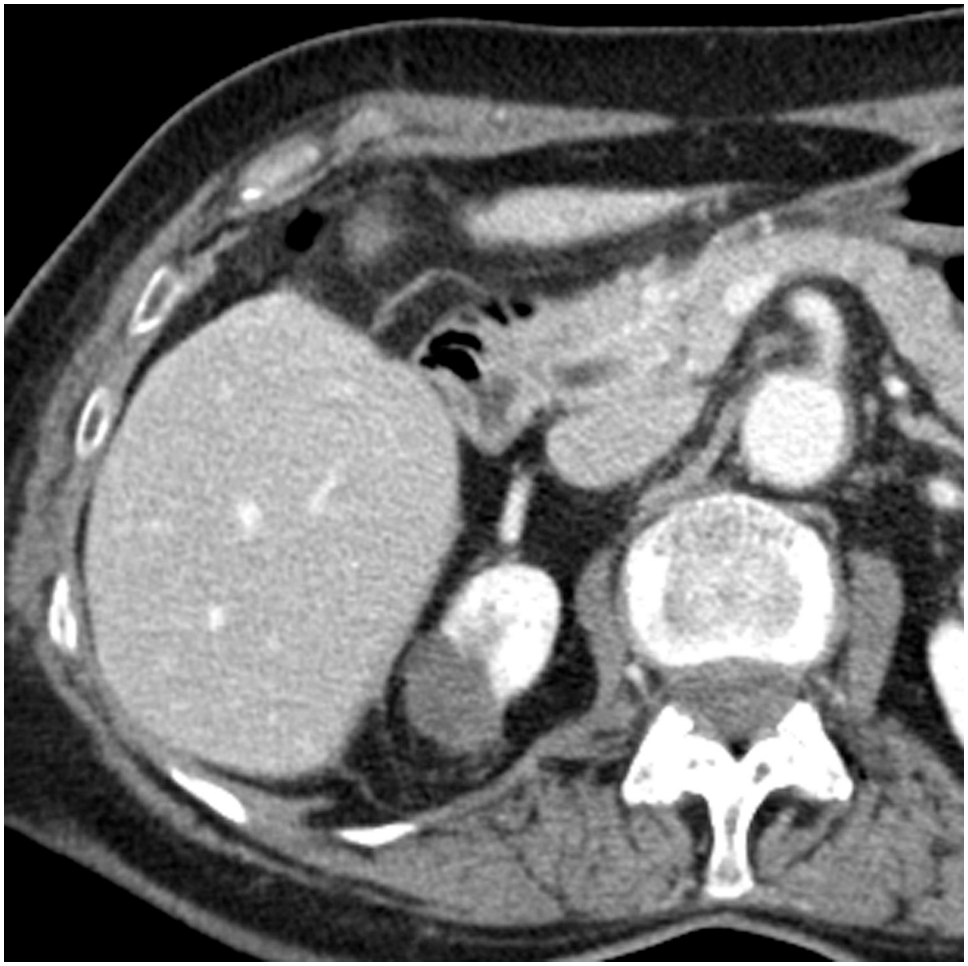


Figure 3.

80-year-old with clear cell carcinoma with initial incomplete ablation with follow-up successful intra-procedural CT performed after RFA.

Figure 3A: Contrast-enhanced CT demonstrative right renal mass corresponding to clear cell carcinoma of the right kidney.

Figure 3B: The 2 RF electrodes (arrows) were positioned under ultrasound guidance into the renal mass.

Figure 3C: Follow-up contrast enhanced CT demonstrated residual tumor (arrows).

Figure 3D: 3 month intra-procedural CT after positioning of the RF electrodes (arrows).

Figure 3E: One-year follow-up CT demonstrates complete ablation of right clear cell carcinoma.

Table 1

Patient Demographics

Baseline demographics (mean)	No intra-procedural CT (n=13)	Intra-procedural CT (n=32)
Age (years)	65	66
BMI (kg/m2)	31	30
Gender		
Female	5 (38.5%)	12 (38%)
Male	8 (61.5%)	20 (62%)

Table 2

Renal Mass Characteristics

Renal mass characteristics	No intra-procedural CT (n=13)	Intra-procedural CT (n=32)
Diameter (cm)	3.25 (*.81%)	2.88 (*.54%)
Side		
Right	10 (77%)	14 (44%)
Left	3 (23%)	18 (56%)
Location		
Superior	7 (54%)	11 (34%)
Interpole	2 (15%)	13 (41%)
Inferior	4 (30%)	8 (25%)
Position		
Anterior	8 (61.5%)	11 (34%)
Posterior	5 (38.5%)	21 (66%)
Morphology		
Exophytic	6 (46%)	23 (72%)
Endophytic	3 (23%)	1 (3%)
Mixed	4 (31%)	8 (25%)

[*] = standard deviation %

Table 3

Technical Details

Technical details	No intra-procedural CT (n=13)	Intra-procedural CT (n=32)
Repositioning	2 (14%)	12 (38%)
Hydrodissection	3 (23%)	9 (28%)