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SHORT COMMUNICATION

Assessment of cold sink effect in postulated renal cryoablation by analyzing radiographic ice ball on computed tomography

^{1,2}SUNG YOON PARK, MD, ¹JONG YUN WON, MD, ¹YOUNG TAIK OH, MD, ¹DAE CHUL JUNG, MD, ¹GYOUNG MIN KIM, MD and ¹MAN DEUK KIM, MD

¹Department of Radiology, Yonsei University College of Medicine, Seoul, South Korea

²Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

Address correspondence to: Dr Jong Yun Won

E-mail: jywon@yuhs.ac

Objective: We analyzed CT characteristics of radiographic ice ball according to anatomical location and freezing number in renal cryoablation.

Methods: 30 patients who underwent percutaneous cryoablation for renal lesions. Computed tomography (CT) was conducted at 9 min during every freezing in order to evaluate a radiographic ice ball. Software was used to reconstruct CT images of the radiographic ice ball perpendicular to cryoprobes. For each radiographic ice ball, two types of radius were measured: (a) lateral radius from epicenter to perirenal direction and (b) medial radius from epicenter to renal sinus direction. Lateral and medial radius or diameters (lateral radius plus medial radius) during the first and

second freezing were compared using paired *t*-test, respectively.

Results: Medial radius of radiographic ice ball was significantly shorter than lateral radius (first freezing, 13.8 vs 17.0 mm, $p < 0.001$; second freezing, 16.0 vs 19.3 mm, $p < 0.001$). The diameter during the second freezing was significantly longer than that during the first freezing (35.3 vs 30.8 mm, $p < 0.001$).

Conclusion: In renal cryoablation, evaluating radiographic ice ball helps identify potential postulated cold sink effect in the central portion of kidney.

Advances in knowledge: Radiologic information of postulated cold sink effect in the kidney may help secure sufficient safety margins.

INTRODUCTION

Renal cryoablation is a useful alternative approach for patients with clinical T_1 renal cell carcinoma (RCC).¹ As a minimally invasive modality, acceptable oncologic outcomes and major complications rate (<10%) can be achieved.² However, failure of primary local tumor control ranges from 1 to 15%.³ In addition, the local tumor control of cryoablation may be worse than that of surgery for larger tumors (e.g. clinical T1b).⁴

Yamanaka et al reported that deep or central location of RCC is associated with incomplete local control by percutaneous renal cryoablation.⁵ Histologically, no collecting system injury was found after renal cryoablation in a previous study with 67 patients.⁶ Conversely, an animal study demonstrated that blockage of arterial flow to the kidney increases the extent of cryoablation zone by 80%.⁷ From these data, we hypothesized that the centrally located renal vasculatures may lessen the thermal effect of cryoablation (e.g. so-called, cold sink effect), and thereby reducing the lethal area centrally.

A low attenuating, radiographic ice ball visualized on computed tomography (CT) is a useful imaging surrogate for assessing the technical success and ultimate ablation zone of cryoablation, because most of cell death occurs within 5 mm of the margin.³ Therefore, evaluating CT characteristics of the ice ball may provide radiologic clues for identifying potential cold sink effect, which can help overcome the limitation of cryoablation for centrally located renal tumors. However, it is still unclear whether the area of a radiographic ice ball differs according to the anatomical location inside ablation zone or number of freezing cycle.

The purpose of this study was to retrospectively analyze radiologic characteristics of the renal cryoablation zone according to anatomical location and number of freezing cycle by analyzing the radiographic ice ball with CT.

METHODS AND MATERIALS

Patients

This retrospective study was approved by the Institutional Review Board at our institution, and the requirement

Table 1. Characteristics of study group

Parameter	Value
Age (year)	56.4 ± 16.4 (29–83)
Sex (male:female)	19:11
Size of renal mass (mm)	22.9 ± 8.9 (11.0–45.0)
Laterality of renal mass (right:left)	17:13
Exophytic:Endophytic	16 : 14
Number of cryoprobes	2.5 ± 0.8 (1–4)

Data of age, size of renal mass, and number of cryoprobes are presented as the mean ± standard deviation (range).

for informed consent was waived. Between January 2015 and December 2015, a total of 34 consecutive patients underwent renal cryoablation. Of the patients, CT data for 4 patients were not available for image analysis because of technical failure of the data transmission. Thus, a total of 30 consecutive patients (mean age, 56.4 ± 16.4 years; range 29–83 years) were finally included in this study (Table 1). The ablated renal lesions consisted of 29 RCCs in 29 patients and one carcinoid tumor in one patient. For the 29 RCCs, 24 were confirmed by percutaneous biopsy, while 5 were radiologically diagnosed as RCC aided by a history of surgery for contralateral RCC ($n = 4$) or von Hippel Lindau disease ($n = 1$). The renal carcinoid tumor was histologically confirmed by percutaneous biopsy.

Cryoablation and CT examination

Percutaneous renal cryoablation was performed by an experienced radiologist under the local anesthesia using 10–30 ml of 1% lidocaine. After applying local anesthesia, cryoprobes (IceRod i-Thaw 1.5 [17G], Galil Medical, Yokneam, Israel) were inserted percutaneously into the renal tumor under ultrasound guidance (LOGIQ E9, General Electric, Fairfield, CT). The number of cryoprobes (median, 3; range 1–4) was determined by an operator (S.Y.P., 4 years of experience for percutaneous renal ablation), depending on the mass size or shape. The ablation process consisted of a double freeze–thaw cycle³ as follows: 10 min freezing, 8 min active thawing, 10 min freezing, and 5 min active followed by 3 min passive thawing.

Table 2. Comparison between lateral and medial radiuses in ablation zone

Parameter	Lateral radius (cm)	Medial radius (cm)	<i>p</i> -value ^a	<i>p</i> -value ^b
First freezing	17.0 ± 3.0	13.8 ± 3.0	<0.001	<0.001
Second freezing	19.3 ± 4.0	16.0 ± 3.0	<0.001	<0.001

Data are the mean ± standard deviation.

^a*p* value between the lateral and medial radiuses.

^b*p* value of lateral or medial radius between the first and second freezing.

CT examination (INFX-8000C combined with Aquilion 128 channel CT scanner, Toshiba Medical Systems Corporation, Otawara, Japan) was conducted at 9 min during every freezing period in order to evaluate the extent of a low attenuating, radiographic ice ball. When the initial ablation of a double freezing–thawing cycle was considered insufficient to achieve optimal coverage for the tumor, additional ablation after the repositioning the cryoprobes was performed. However, we only analyzed the radiographic ice ball from the first and second freezing of the initial ablation because the size and shape of a radiographic ice ball during additional ablation might be affected by tissue changes from the initial ablation. CT data obtained during the first and second freezing were transmitted to a computer with commercial software for image reconstruction and analysis.

Image analysis

The software (Philips IntelliSpace Portal, v. 5.0; Philips Healthcare, The Netherlands) was used to generate the reconstructed CT images of a low attenuating radiographic ice ball perpendicular to the direction of cryoprobes. For reconstructed images showing the maximum radiographic ice ball, the center of cryoprobes was determined as follows: (a) for a single cryoprobe, the cryoprobe itself; (b) for two cryoprobes, the middle of an imaginary line between the two cryoprobes; (c) for three of four cryoprobes, the centroid of a polygon formed by the cryoprobes.⁸ Two types of radiuses of the radiographic ice ball were measured from the estimated center: (a) lateral radius from the estimated center to the margin of perirenal direction; (b) medial radius from the estimated center to the margin of renal sinus direction. The overall diameters of radiographic ice balls during the first and second freezing were also measured. All CT images

Figure 1. Comparison between lateral and medial radiuses.

Figure 2. Reconstructed CT images from a 36-year-old male who underwent renal cryoablation using a single cryoprobe. (A) The lateral radius (red line) of a radiographic ice ball was longer than the medial radius (blue line) during first freezing (9.4 vs 4.7 mm). (B) The lateral radius (red line) of a radiographic ice ball was also longer than medial radius (blue line) during the second freezing (9.4 vs 5.7 mm).

were analyzed by two faculty radiologists (J.Y.W. and S.Y.P.) in consensus.

Statistical analysis

Paired t-test was used to compare radiuses of the radiographic ice ball between lateral and medial directions or diameters of the radiographic ice ball between first and second freezing, respectively. MedCalc (v. 13.0, MedCalc Software, Mariakerke, Belgium) was utilized for the statistical analysis. A p value < 0.05 was considered statistically significant.

RESULTS

Lateral and medial radius

The medial radius of the radiographic ice ball was significantly shorter than the lateral radius in the first freezing (13.8 ± 3.0 mm vs 17.0 ± 3.0 mm, $p < 0.001$) (Table 2 and Figure 1). Also, the medial radius of ablation zone was significantly shorter than the lateral radius during the second freezing (16.0 ± 3.0 mm vs 19.3 ± 4.0 mm, $p < 0.001$) (Figures 2–4).

Figure 3. Reconstructed CT images from a 75-year-old male who underwent renal cryoablation using two cryoprobes. (A) The lateral radius (red line) of a radiographic ice ball was longer than the medial radius (blue line) during the first freezing (16.4 mm vs 13.5 mm). (B) The lateral radius (red line) of a radiographic ice ball was also longer than the medial radius (blue line) during the second freezing (18.3 vs 13.7 mm).

First and second freezing

The difference in diameter for radiographic ice balls between the first and second freezing ranged from 0.2 to 10.3 mm (mean, 4.4 mm) (Figure 5). The diameter during the second freezing was significantly longer than that of the first freezing (35.3 ± 6.6 mm vs 30.8 ± 5.3 mm, $p < 0.001$). Likewise, each of the lateral or medial radiuses of the second freezing was longer than that of the respective radius of first freezing ($p < 0.001$).

DISCUSSION

The heat sink effect is a well-established phenomenon in radiofrequency ablation (RFA), in which tumors adjacent to large vessels are sometimes insufficiently ablated because perfusion-mediated tissue cooling reduces coagulation necrosis by heat energy.⁹ In our study, the length of CT-visualized ice ball was significantly different between lateral and medial sides ($p < 0.001$). A possible explanation for this observation was that centrally located renal vasculatures might have induced tissue warming and lessened cooling effect via blood perfusion, subsequently limiting thermal energy transfer of cryoablation medially. Therefore, in renal cryoablation, the cold sink effect may also exist at the medial portion of kidney due to its anatomical characteristics. Indeed, this may explain the results of previous studies showing that radiographic ice balls involving the renal sinus do not cause injury to the intrarenal collecting system or vessels.⁶

Hinshaw et al reported that the cold sink effect should be considered during the placement of cryoprobes for hepatic tumors adjacent to large hepatic vessels.¹⁰ Specifically, they recommended that some of the cryoprobes should be positioned closer to the tumor edge (e.g. 5 mm or less) when the tumor is adjacent to large hepatic vessels in order to overcome the cold sink effect. Likewise, we recommend that locating the cryoprobe slightly medially from the mass center may be an effective method to secure sufficient safety margins in renal cryoablation. When multiple cryoprobes are required to ablate a large renal tumor, the placement of a greater number or thicker cryoprobes in the medial portion or near the large renal vessels may be effective (e.g. two for medial and one for lateral rather than one for medial and two for lateral).¹¹ Because local tumor

Figure 4. Reconstructed CT images from a 77-year-old female who underwent renal cryoablation using three cryoprobes. (A) The lateral radius (red line) of a radiographic ice ball was longer than the medial radius (blue line) during the first freezing (17.4 mm vs 14.5 mm). (B) The lateral radius (red line) of a radiographic ice ball was also longer than the medial radius (blue line) during the second freezing (19.0 vs 16.4 mm).

progression frequently occurs at the periphery of the ablation zone,³ these considerations may be helpful for designing optimal placement of the cryoprobes to secure sufficient safety margins in the renal sinus.

In our study, the mean diameter of ice ball on CT was greater during the second freezing than that the first freezing (35.3 ± 6.6 mm vs 30.8 ± 5.3 mm, $p < 0.001$). Basically, cryoablation results in direct and indirect cellular damage with microvascular occlusion in a focal area during a cycle of freezing and thawing.¹² This may lessen the cold sink effect of warm viable tissues (e.g. partly damaged tissues) to a certain degree, such that additional freezing may produce better cooling effect. Thus, before repositioning the cryoprobes, operators may need to wait and observe the final extent of the second ablation zone when the ablation zone of the first freezing does not secure sufficient safety margins. However, operators should also consider the degree of increase in the radiographic ice ball diameter is approximately 5 mm.

Figure 5. Changes in diameters for radiographic ice balls between the first and second freezing period.

Our data suggest the presence and degree of postulated cold sink effect can be assessed radiologically during the freezing period. In clinical practice, determining the technical success is usually left to the operator, who must decide whether to conduct additional ablation depending on CT findings for the radiographic ice ball. Thus, current results may support further radiologic investigations in terms of the optimal selection or placement of cryoprobes in order to reduce the risk of local tumor progression. In addition, CT characteristics of the radiographic ice ball may explain previous clinical findings.⁵

This study had some limitations. First, the ablation zone was not analyzed with pathologic specimens. Thus, information about the actual ablated area is still uncertain. However, histological verification of the actual ablation zone by surgery is practically impossible after successful renal cryoablation. Reportedly, the area of the radiographic ice ball is well correlated with the actual extent of cell death,¹³ and it is usually monitored to assess the technical success or potential risk of adjacent organ injury in clinical practice.³ Accordingly, we obtained CT images at the late stage during each freezing period (e.g. at 9 min during every 10 min freezing) in order to indirectly assess the maximal ablation zone. Second, the number of patients was relatively small. The present preliminary results warrant further validation studies with large population and long-term follow-up data.

CONCLUSION

Thermal energy transfer appears to be limited at the central portion of the kidney in renal cryoablation. This may indicate the presence of cold-sink effect due to the abundant, centrally located renal vasculatures. Thus, evaluation of the radiographic ice ball can be used to identify a postulated cold sink effect in the central portion of the kidney, and repeat ablation may slightly increase the ablation zone.

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