Disappearance of Renal Cysts Included in Iceball During Cryoablation of Renal Cell Carcinoma: A Potential Therapy for Symptomatic Renal Cysts?

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Abstract

Purpose: To retrospectively evaluate the effect of cryoablation of renal cell carcinoma on nearby renal cysts, aiming to investigate the potential for an alternative therapy to treat symptomatic renal cysts.

Materials and Methods: The study population comprised 46 cysts (mean size: 12 mm, range: 5–43 mm) that were either included in or close to the iceball during cryoablation in 22 patients. Size change of each cyst was evaluated via enhanced CT or MRI before and 1, 3, 6, and 12 months after cryoablation. Forty-one cysts were also followed after 12 months. Variables including positional relationship between the cyst and the iceball were evaluated via linear regression analysis using generalized estimating equation models to determine which factors affected cyst shrinkage rate at 12 months.

Results: Fifteen, 12, and 19 cysts were completely included in, partially included in, or excluded from the iceball, respectively. The overall shrinkage rate was 62%, and 57% (26/46) disappeared at 12 months. Only the relationship between the cyst and the iceball was significantly ($P < 0.001$) associated with cyst shrinkage rate. Cyst disappearance rates at 12 months were 100% (15/15), 67% (8/12), and 16% (3/19) for cysts in the complete inclusion, partial inclusion, and exclusion groups, respectively. Among the 22 cysts that disappeared at 12 months and then followed, none recurred after 12 months.

Conclusion: All renal cysts that were completely included in the iceball disappeared after cryoablation, demonstrating the potential utility of cryoablation as an alternative therapy for symptomatic renal cysts.

INTRODUCTION

While renal cysts are common in elderly patients, the vast majority of them are asymptomatic and clinically unimportant. However, approximately 2–4% of renal cysts may become symptomatic (1). The most common symptom is abdominal pain, followed by hypertension secondary to renal segmental ischemia (2, 3). Further, cysts may be complicated by infection (4), rupture (5), or the compression of pelvicalyceal collecting systems (6, 7). Once renal cysts become symptomatic, treatments including surgical and percutaneous interventions are required. Less invasive percutaneous interventions are usually preferred to surgical ones requiring general anesthesia. However, percutaneous simple aspiration results in recurrence in 30–80% of cases (1, 8); thus, aspiration followed by sclerotherapy is recommended. Nevertheless, recurrence rates are still 23–77% after a single session of sclerotherapy (9–11). Although multiple sessions may be more effective (12), those are time-consuming and may be associated with increased risk of leakage of sclerosing agent and additional patient discomfort (13–15). Thus, a technique to provide more powerful ablation with a single session is required.

Cryoablation for renal cell carcinoma (RCC) was first reported in 1995 (16). Recent studies showed that cryoablation is safe and highly effective, resulting in a major complication rate of 2–7% (17, 18) and local control rate of 87–97% (17–20). Therefore, it was hypothesized that cryoablation may also be effective for renal cyst treatment. However, the effect of cryoablation on renal cysts is unknown. Therefore, we investigated the effect of cryoablation on renal cysts by retrospectively evaluating subsequent size change of renal cysts close to RCCs that were treated with cryoablation.

MATERIALS AND METHODS

Approval from the institutional review board and informed consent from the patients were obtained to perform cryoablation for RCC. The ethics committee at our institution provided approval for this retrospective study (approval number: 1509-007) and did not require that patient informed consent be obtained to perform this study.

Study Population

Between May 2012 and August 2014, 109 patients with RCC underwent cryoablation at our institution. The inclusion criteria for this study were as follows: (i) the patient had renal cysts that were either involved in the iceball or located close to (<5 mm) the iceball during cryoablation; (ii) renal cysts were at least 5 mm in maximum diameter; and (iii) computed tomography (CT) or magnetic resonance imaging (MRI) images were available before and 1, 3, 6, and12 months after cryoablation. Patients who underwent other local therapies (e.g., surgery and transarterial embolization) for RCC within 6 months before or 12 months after cryoablation were excluded. A total of 46 cysts [mean maximum diameter ± standard deviation (SD), 12 mm ± 8.7] in 22 patients (19 male and 3 female; mean age ± SD, 70.1 ± 13.7) were included in this study. Characteristics of the patients and the cysts are summarized in **Table 1**.

Cryoablation Techniques

Cryoablation was always performed in an inpatient setting. Intraprocedural pain was treated using a combination of local anesthesia and conscious sedation using fentanyl. The procedure was percutaneously carried out using CT-fluoroscopy (Aquilion, Toshiba Medical Systems, Tochigi, Japan). The cryoprobe used was IceRod or IceSeed (Galil Medical, Upper Yokneam, Israel); the cryoablation system was Cryohit (Galil Medical).

After administration of local anesthesia, 2–5 cryoprobes were placed into the RCC. The number of cryoprobes used was mainly determined by tumor size. The treatment consisted of two cycles of freezing and thawing. Each freezing cycle was 10–15 min. To evaluate the iceball, CT scans were performed at the end of each cycle. Images with section thicknesses of 3–5 mm were reconstructed in the axial, coronal, and sagittal planes. Ablation was performed in an attempt to treat RCCs with at least 6-mm margins.

Pre- and Post-Ablation Imaging Follow-up

All patients underwent abdominal CT or MRI before and 1, 3, 6, and 12 months after cryoablation. After 12 months, such examination was also available in 41 cysts. For CT scans, both non-contrast and dynamic contrast-enhanced CT with 2 or 3 phases were performed; images were reconstructed in the axial plane with 5-mm thick sections and in the coronal plane with 3-mm thick sections. MRI examination included T2-weighted images (TR, 2000.0 ms; TE, 89.0 ms) with 4-mm thick sections in the axial and coronal planes.

Study Endpoint

The endpoint measurement of this study was the serial size change of the cysts after cryoablation. The shrinkage rate of each cyst was calculated at each follow-up. Further, cyst disappearance rates were estimated at each follow-up. Then, in order to determine the factors that affected cyst shrinkage rates at 12 months, several variables were evaluated: age, sex, location of the cyst (central, parenchymal, exophytic, or mixed), maximum diameter of the cyst, the number of cryoprobes used, insertion of cryoprobes through the cyst (yes or no), and the positional relationship between the cyst and the iceball.

For categorization of cyst location, a classification system used for describing the locations of renal tumors, which was proposed by Gervais et al. (21). Thus, “exophytic” was defined as cysts with a component extending into the perirenal fat but no component extending into the renal sinus fat; “parenchymal” was defined as those limited to the confines of the renal parenchyma, without extension into either the perirenal fat or the renal sinus fat; “central” was defined as those with extension into the sinus fat; and “mixed” was defined as those had components extending into both the renal sinus fat and the perirenal fat.

The positional relationship between the cyst and the iceball was evaluated on CT images obtained at the end of the second freezing cycle, and the cysts were then categorized into three groups: (i) complete inclusion, which indicated that the cyst was completely included in the iceball; (ii) partial inclusion, which indicated that the cyst was partially included in the iceball; and (iii) exclusion, which indicated that the cyst was not included in the iceball at all. The partial inclusion group was further divided into two subgroups by percentage of cyst volume included in the iceball (≥50% or <50%).

Measurement of Renal Cyst Sizes

The sizes of the cysts were evaluated based on CT or MRI images. Maximum diameter was measured on axial CT images in the last contrast-enhanced phase or on axial T2-weighted images. Shrinkage rate was calculated by the maximum diameter at any follow-up divided by that before cryoablation. When the cyst became unidentifiable on the images after cryoablation, the cyst was considered to have disappeared.

Statistical Analysis

To evaluate the factors affecting cyst shrinkage rate, uni- and multi-variate linear regression analyses using generalized estimating equation (GEE) models were used, as the cysts were nested by the patients. GEE models were estimated using an exchangeable correlation matrix with robust standard errors because correlations between cysts in the same patient were estimated to be equal. For all analyses, a *P*-value of <0.05 was considered statistically significant. GEE analyses were conducted using the statistical software package Stata14.1 (StataCorp LP, College Station, TX, USA).

RESULTS

Fifteen, 12, and 19 cysts were completely included in, partially included in, or excluded from the iceball, respectively. In the partial inclusion group, percentage of cyst volume included in the iceball was ≥50% and <50% in five and seven cysts, respectively.

Overall shrinkage rates of the 46 cysts were 30%, 51%, 61%, and 62% at 1, 3, 6, and 12 months, respectively. Overall cyst disappearance rates were 24% (11/46), 43% (20/46), 57% (26/46), and 57% (26/46) at 1, 3, 6, and 12 months, respectively.

With regard to the factors affecting the cyst shrinkage rate at 12 months, only the relationship between the cyst and the iceball was significant ($P < 0.001$) in both uni- and multi-variate analyses with GEE models (**Table 2**). Cyst shrinkage rates at each follow-up in the three types of cyst-iceball relationships are shown in **Figure 1**. Cyst shrinkage rates at 12 months were 100%, 83%, and 19% in the complete inclusion, partial inclusion, and exclusion groups, respectively. In the partial inclusion group, cyst shrinkage rates at 12 months were 94% and 75% in the subgroups of cyst volume included in the iceball of ≥50% and <50%, respectively. Cyst disappearance rates at each follow-up in the three groups are shown in **Figure 2**. All of the 15 cysts in the complete inclusion group disappeared by 6 months after cryoablation. Cyst disappearance rates at 12 months were 100% (15/15), 67% (8/12), and 16% (3/19) in the complete inclusion, partial inclusion, and exclusion groups, respectively. In the partial inclusion group, cyst disappearance rates at 12 months were 80% (4/5) and 57% (4/7) in the subgroups of cyst volume included in the iceball of ≥50% and <50%, respectively.

Although it did not reach a significant level ($P = 0.07$), there was a borderline association between larger number of cryoprobes used and larger cyst shrinkage rate at 12 months in the multi-variate analysis. Pre-ablation cyst size was not significantly associated with cyst shrinkage rate at 12 months in either uni- or multi-variate analysis. Mean cyst shrinkage rate at 12 months was 74% in the 23 cysts of smaller than 10 mm, while it was 50% in the 23 cysts of 10 mm or larger. Mean pre-ablation size of cysts that disappeared at 12 months was 11 mm (range, 5–37 mm), while the same that remained at 12 months was 14 mm (range, 5–43 mm).

During the procedure, cryoprobe was inserted through five cysts (**Table 1**). However, insertion of cryoprobes through cysts was not significantly associated with cyst shrinkage rate at 12 months by either uni- or multi-variate analysis (**Table 2**).

Follow-up results after 12 months are summarized in **Figure 3**. While five cysts were lost for follow-up, 41 cysts were followed after 12 months; the median follow-up period of the 41 cysts was 39 months (mean, 38 months; range, 23–55 months). Among the 22 cysts that disappeared at 12 months, none recurred thereafter. Among the 19 cysts that remained at 12 months, 2 cysts disappeared; 5 cysts further shrank but remained; 5 cysts unchanged; and 7 cysts enlarged.

Each case of complete inclusion, partial inclusion, and exclusion groups is shown in **Figures 4, 5, and 6**, respectively.

DISCUSSION

Simple renal cysts form when serous fluid collects and is surrounded by a cyst wall composed of simple-layered, cuboid epithelial cells (22). Epithelial cells are assumed to produce and absorb serous fluid, and the balance between the two is associated with changes in cyst size. Ethanol and other agents, such as ethanolamine oleate, tetracycline, and minocycline, have been used to treat symptomatic renal cysts (1). Such agents may ablate the epithelial cells, resulting in subsequent cyst shrinkage. However, cysts treated with sclerotherapy may recur (1) as a result of incomplete ablation of the cyst wall, leading to persistent production of fluid by residual epithelial cells.

Considering limited efficacy of the sclerotherapy, we noted cryoablation as an alternative, more powerful ablation technique. Then, this study showed that the relationship between the cyst and the iceball was the only significant factor predictive of cyst shrinkage. This result suggests that cyst shrinkage was a direct result of cryoablation. This study also showed that all cysts in the complete inclusion group disappeared by 6 months after cryoablation, and then none recurred. This indicates that cryoablation may be highly effective in ablating cysts if they are completely included in the iceball. In addition to relationship between the cyst and the iceball, the multi-variate analysis showed a borderline association between the number of cryoprobes used and cyst shrinkage. We assumed that it was resulted from synergetic effect with the use of multiple cryoprobes, which might lead to lower temperature inside the iceball.

Cellular damage by cryoablation results from a complex combination of several mechanisms (24, 25). As the temperature falls into the freezing range, ice crystals are first formed in the extracellular space, causing cellular dehydration due to osmotic shift (26). With further cooling, intracellular ice crystals form, disrupting organelles and cell membranes (24, 26). In addition, perfusion stasis and thrombosis of the microvasculature induced by cryoablation may be another indirect mechanism of cell injury (27).

Complete loss of RCC cell viability was reported at temperatures of –25°C and colder *in vitro* (28). Another study showed that temperatures of approximately –20°C could destroy renal parenchyma (29). However, the temperature necessary to damage cyst epithelial cells was previously unknown. Interestingly, two-thirds of the cysts in the partial inclusion group disappeared by 12 months. Furthermore, cysts in the exclusion group shrank to some extent. These results might indicate that epithelial cells were more easily damaged. Another possible explanation for these results is that ischemia was induced by damage to the feeding arteries of the cysts by cryoablation. Indeed, transcatheter arterial embolization of polycystic kidneys has been reported to shrink the kidney (30).

This study suffered from some limitations, including retrospective evaluation and small sample size, and limited follow-up period. Furthermore, the population consisted of relatively small, asymptomatic cysts. Thus, the results obtained in this study may not be directly applicable to more typical, large, symptomatic cysts. The effect of cryoablation on renal cysts was not pathologically evaluated. Finally, cyst shrinkage did not result from an intended treatment of renal cysts but from incidental inclusion in the RCC treatment zone. Nevertheless, the finding that all cysts that were completely included in the iceball disappeared after cryoablation may indicate a potential use of cryoablation as an alternative therapy to treat renal cysts. Prospective clinical studies to determine the safety and effectiveness of cryoablation for symptomatic renal cysts are therefore warranted.

References

1. Skolarikos A, Laguna MP, de la Rosette JJ. Conservative and radiological management of simple renal cysts: a comprehensive review. BJU Int. 2012; 110(2):170–178.
2. Paananen I, Hellström P, Leinonen S, et al. Treatment of renal cysts with single-session percutaneous drainage and ethanol sclerotherapy: long-term outcome. Urology. 2001; 57(1):30–33.
3. Pedersen JF, Emamian SA, Nielsen MB. Significant association between simple renal cysts and arterial blood pressure. Br J Urol. 1997; 79(5):688–691.
4. Ohkawa M, Motoi I, Hirano S, et al. Biochemical and pharmacodynamic studies of simple renal cyst fluids in relation to infection. Nephron. 1991; 59(1):80–83.
5. Marques DT, Bezerra RO, de Brito Siqueira LT, et al. Spontaneous combined rupture of a pelvicalyceal cyst into the collector system and retroperitoneal space during the acquisition of computed tomography scan images: a case report. J Med Case Rep. 2012; 6:386.
6. Barloon TJ, Vince SW. Caliceal obstruction owing to a large parapelvic cyst: excretory urography, ultrasound and computerized tomography findings. J Urol. 1987; 137(2):270–271.
7. Amis ES Jr, Cronan JJ, Pfister RC. The spectrum of peripelvic cysts. Br J Urol. 1983; 55(2):150–153.
8. Hanna RM, Dahniya MH. Aspiration and sclerotherapy of symptomatic simple renal cyst: value of two injections of a sclerosing agent. AJR Am J Roentgenol. 1996; 167(3):781–783.
9. Zerem E, Imamovic G, Omervoic. Symptomatic simple renal cyst: comparison of continuous negative-pressure catheter drainage and single-session alcohol sclerotherapy. AJR Am J Roentgenol. 2008; 190:1193–1197.

10. Xu XX, Du Y, Yang HF, et al. CT-guided sclerotherapy with ethanol concentration monitoring for treatment of renal cysts. AJR Am J Roentgenol. 2011; 196:W78–W82.
11. Bas O, Nalbant I, Can Sener N, et al. Management of renal cysts. JSLS. 2015; 19(1):e2014.00097.
12. Chung BH, Kim JH, Hong CH, et al. Comparison of single and multiple sessions of percutaneous sclerotherapy for simple renal cyst. BUJ Int. 2000; 85:626–627.
13. Ham SW, Lee JH, Kim WT, et al. Comparison of multiple sessions of 99% ethanol and single-session OK-432 sclerotherapy for the treatment of simple renal cysts. J Urol. 2008; 180(6):2552–2556.
14. Gasparini D1, Sponza M, Valotto C, et al. Renal cysts: can percutaneous ethanol injections be considered an alternative to surgery? Urol Int. 2003; 71(2):197–200.
15. Okeke AA, Mitchelmorre AE, Timoney AG. Comparison of single and multiple sessions of percutaneous sclerotherapy of simple renal cysts. BJU Int. 2001; 87(3):280.
16. Uchida M, Imaide Y, Sugimoto K, et al. Percutaneous cryosurgery for renal tumors. Br J Urol. 1995; 75:132–137.
17. Buy X, Lang H, Garnon J, et al. Percutaneous renal cryoablation: prospective experience treating 120 consecutive tumors. AJR Am J Roentgenol. 2013; 201(6):1353–1361.
18. Kim EH, Tanagho YS, Bhayani SB, et al. Percutaneous cryoablation of renal masses: Washington University experience of treating 129 tumors. BJU Int. 2013; 111(6):872–879.
19. Atwell TD, Farrell MA, Leibovich BC, et al. Percutaneous renal cryoablation: experience treating 115 tumors. J Urol. 2008; 179(6):2136–2140.
20. Georgiades CS, Rodriguez R. Efficacy and safety of percutaneous cryoablation for stage 1A/B renal cell carcinoma: results of a prospective, single-arm, 5-year study. Cardiovasc Intervent Radiol. 2014; 37(6):1494–1499.

21. Gervais DA, McGovern FJ, Arellano RS, et al. Renal cell carcinoma: clinical experience and technical success with radio-frequency ablation of 42 tumors. Radiology. 2003; 226(2):417–424.
22. Clarke BG, Hurwits IS, Dubinsky E. Solitary serous cysts of the kidney: biochemical, cytologic and histologic studies. J Urol. 1956; 75(5):772–775.
23. Lee J, Darcy M. Renal cysts and urinomas. Semin Intervent Radiol. 2011; 28(4):380–391.
24. Gage AA, Baust J. Mechanisms of tissue injury in cryosurgery. Cryobiology. 1998; 37(3):171–186.
25. Hoffman NE, Bichof JC. The cryobiology of cryosurgical injury. Urology. 2002; 60 (suppl 2A):40–49.
26. Mazur P. Freezing of living cells: mechanisms and implications. Am J Physiol. 1984; 247 (3 Pt 1): C125–42.
27. Hoffmann NE, Bischof JC. Cryosurgery of normal and tumor tissue in the dorsal skin flap chamber: Part II--injury response. J Biomech Eng. 2001; 123(4):310–316.
28. Clarke DM, Robilotto AT, Rhee E, et al. Cryoablation of renal cancer: variables involved in freezing-induced cell death. Technol Cancer Res Treat. 2007; 6(2):69–79.
29. Chosy SG, Nakada SY, Lee FT Jr, et al. Monitoring renal cryosurgery: predictors of tissue necrosis in swine. J Urol. 1998; 159(4):1370–1374.
30. Sakuhara Y, Nishio S, Morita K, et al. Transcatheter arterial embolization with ethanol injection in symptomatic patients with enlarged polycystic kidneys. Radiology. 2015; 277(1):277–285.

Table 1. Characteristics of 46 Renal Cysts in 22 Patients.

Characteristic	Value
Age (y)	
Mean ± SD	70.1 ± 13.7
Range	39–86
Sex	
Male	19 (86%)
Female	3 (14%)
Maximum diameter of cysts (mm)	
Mean ± SD	12 ± 8.7
Range	5–43
Location of cysts	
Epiphytic	16 (35%)
Parenchymal	23 (50%)
Central	6 (13%)
Mixed	1 (2%)
Laterality	
Right	27 (59%)
Left	19 (41%)
Insertion of cryoprobes through cysts	
Yes	5 (11%)
No	41 (89%)
Relationship between cysts and iceball	
Complete inclusion	15 (33%)
Partial inclusion	12 (26%)
Exclusion	19 (41%)

SD = standard deviation

Table 2. Results of Uni- and Multi-variate Analyses of Potential Factors Affecting Cyst Shrinkage Rates at 12 Months.

	Uni-variate Analyses			Multi-variate Analyses		
	Regression Coefficient (95% CI)	*P*-value	*ρ*	Partial Regression Coefficient (95% CI)	*P*-value	*ρ*
Age (y)	0.22 (−0.51, 0.95)	0.55	−0.12	−0.36 (−1.14, 0.42)	0.37	0.23
Sex						
Male vs. Female	−18.06 (−37.12, 1.00)	0.06	−0.17	−17.33 (−49.54, 14.88)	0.29	
Location of cysts						
Exophytic vs. Central	2.15 (−40.22, 44.53)	0.92	−0.08	2.01 (−25.99, 30.01)	0.89	
Parenchymal vs. Central	10.98 (−30.16, 52.1)	0.60		1.02 (−26.05, 28.09)	0.94	
Mixed vs. Central	−57.36 (−155.19, 40.47)	0.25		−86.81 (−161.68, −11.94)	0.02	
Maximum diameter of cysts	−0.63 (−2.16, 0.90)	0.42	−0.11	0.53 (−0.94, 2.00)	0.48	
Number of cryoprobes used	0.58 (−12.96, 14.12)	0.93	−0.11	10.00 (−0.85, 20.85)	0.07	
Insertion of cryoprobes through cysts						
Yes vs. No	34.03 (−8.86, 76.91)	0.12	−0.06	3.19 (−25.76, 32.15)	0.83	
Relationship between the cyst and iceball						
Partial inclusion vs. Exclusion	64.74 (43.37, 86.10)	<0.001	0.03	63.63 (42.46, 84.81)	<0.001	
Complete inclusion vs. Exclusion	81.54 (61.46, 101.62)	<0.001		82.72 (61.26, 104.18)	<0.001	

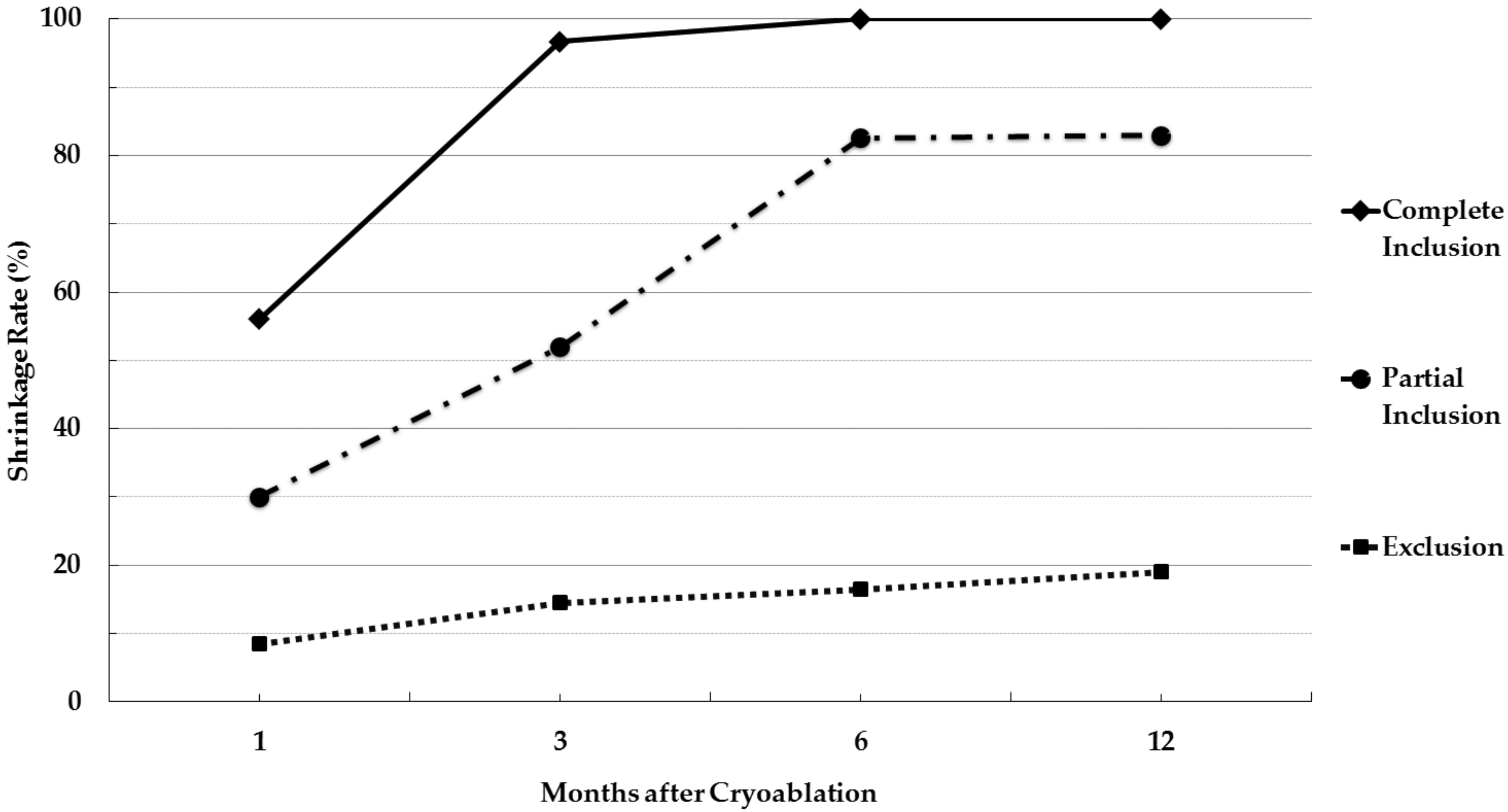


Figure 1. Cyst shrinkage rates at each follow-up in three groups.

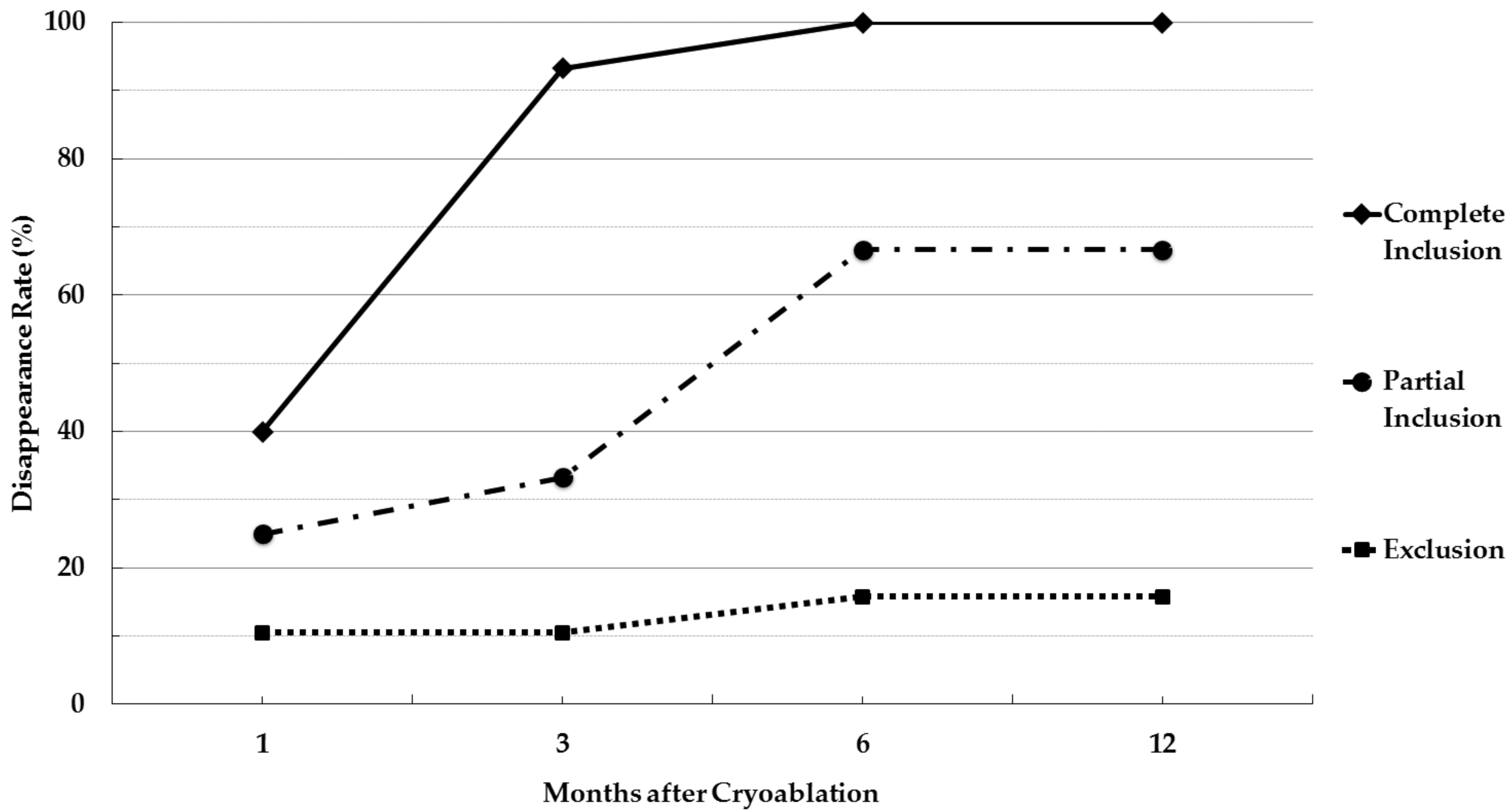


Figure 2. Cyst disappearance rates at each follow-up in three groups.

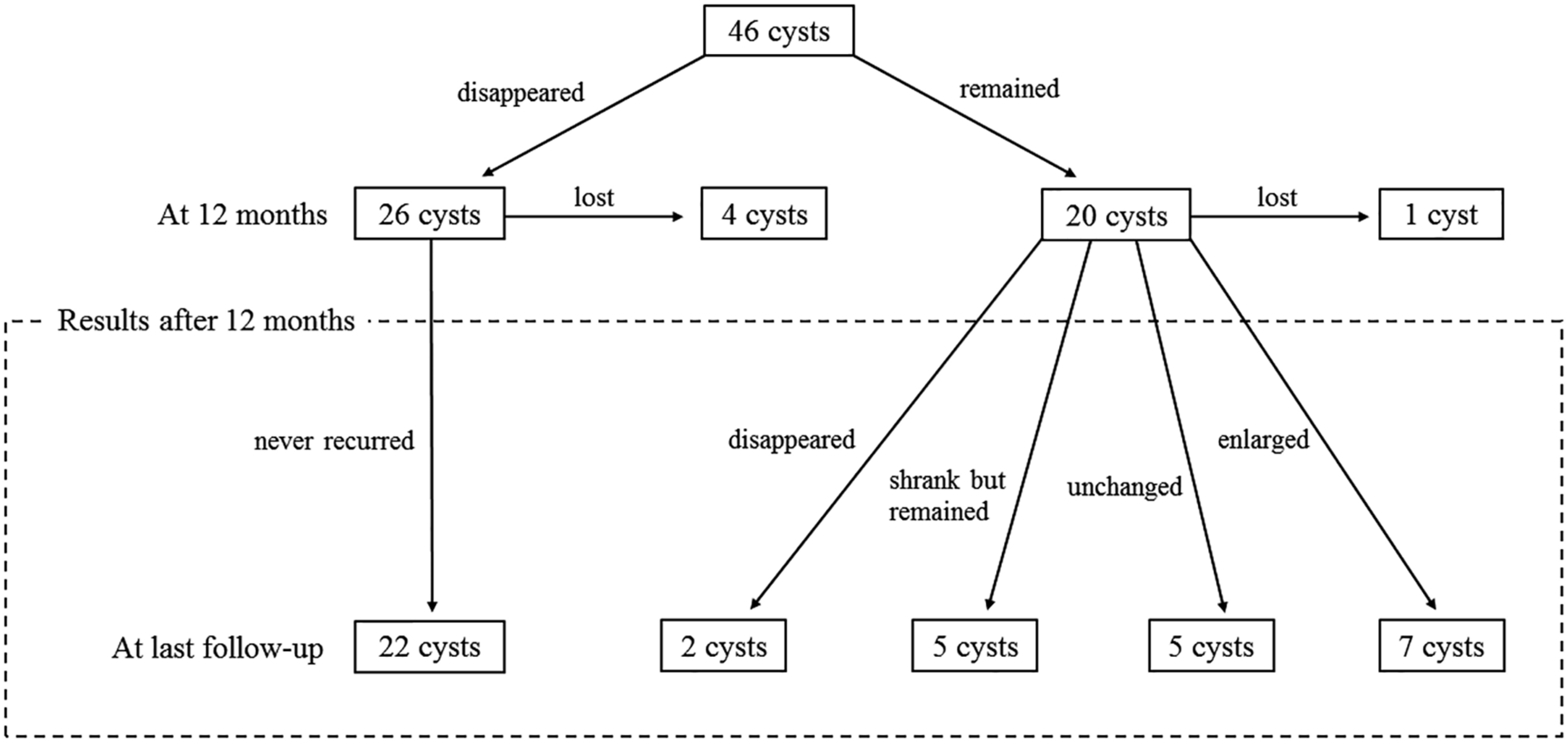
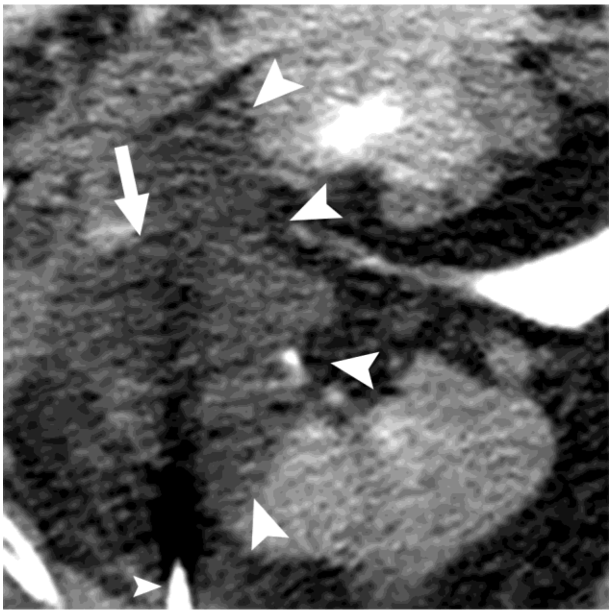


Figure 3. Summary of follow-up results of 46 cysts.


(Figure 4a)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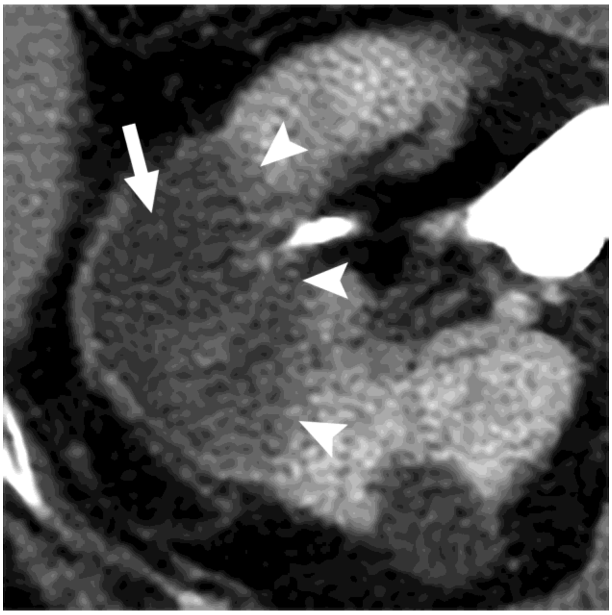
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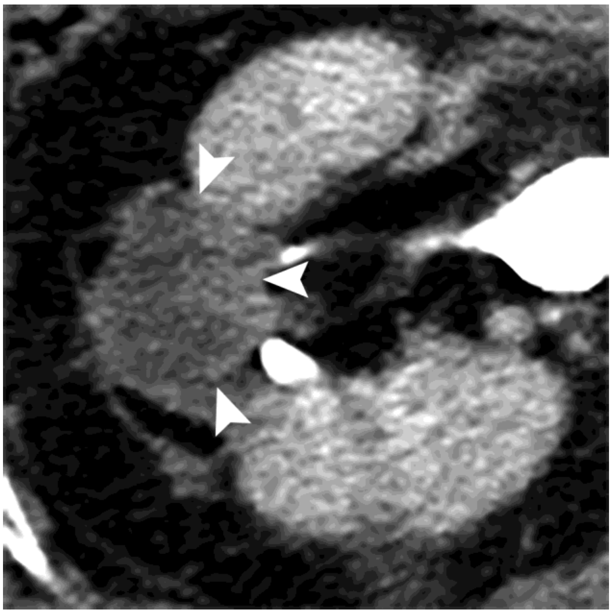
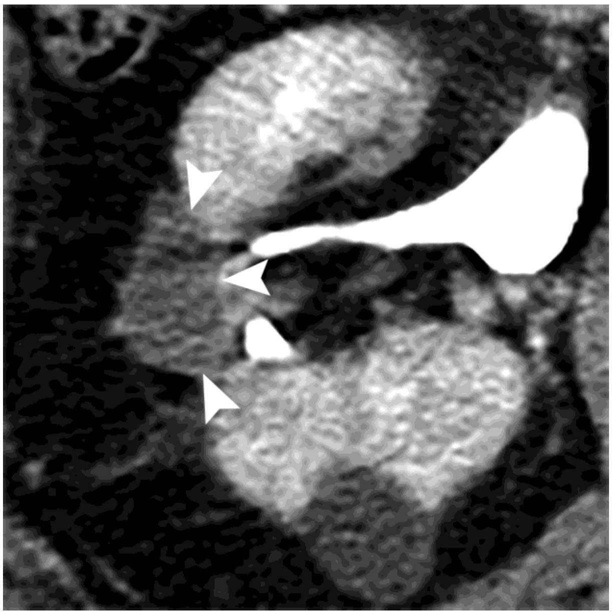
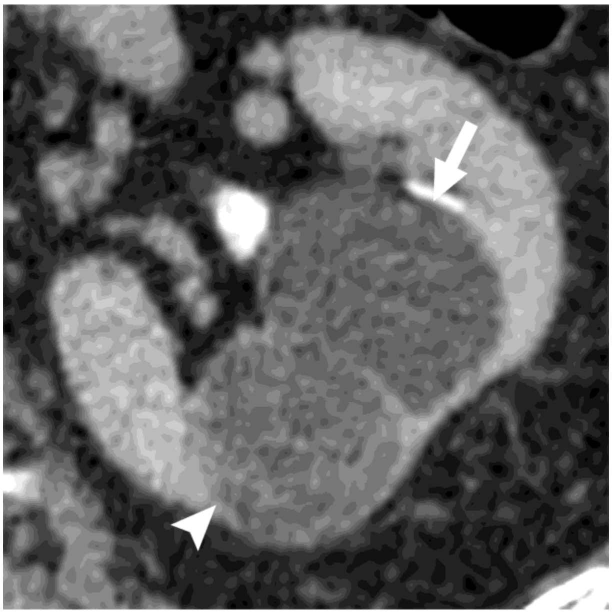


(Figure 4d)

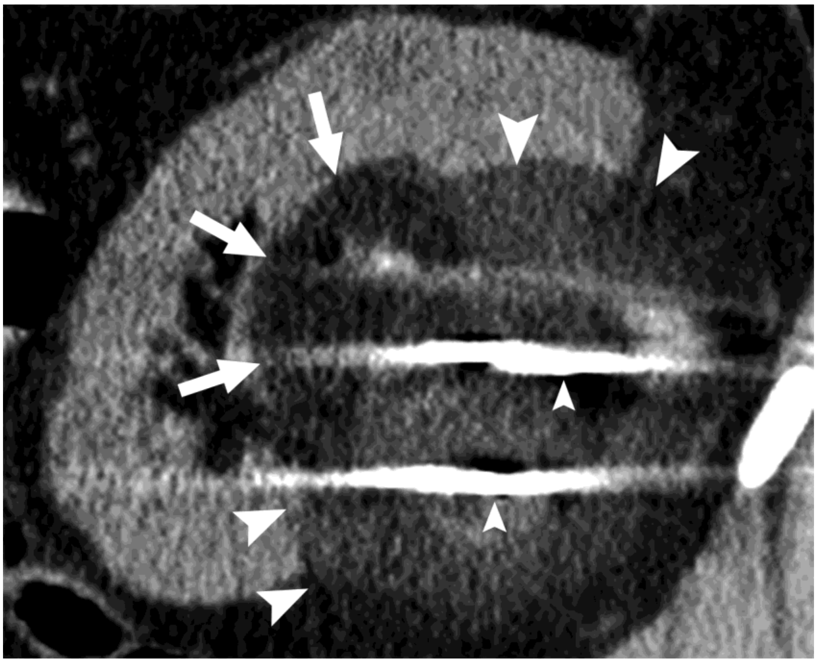


(Figure 4e)

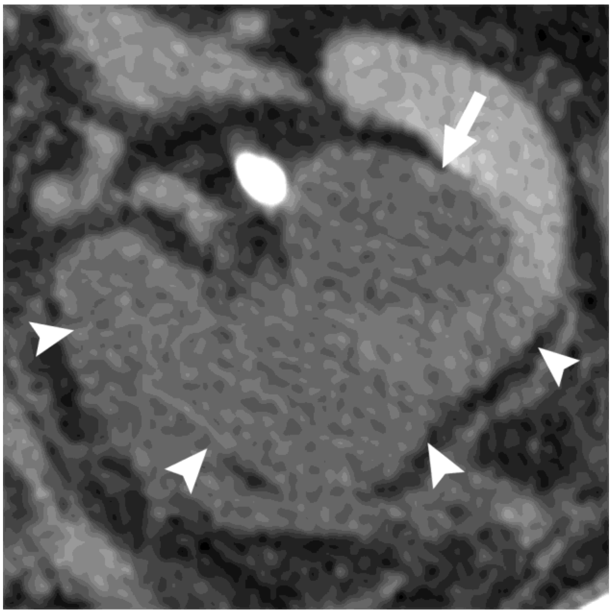
Figure 4. A case of complete inclusion group. Axial CT images of a cyst in the complete inclusion group. **(a)** Cyst shown before cryoablation (arrow). **(b)** During cryoablation, the cyst (arrow) is completely included in the ice ball (large arrowheads). Small arrowhead indicates a cryoprobe. **(c)** Image at 1 month shows the cyst (arrow) surrounded by ablation zone (arrowheads). **(d)** Image at 6 months shows that the ablation zone has shrunk (arrowheads), and the cyst is no longer identifiable. **(e)** Image at 12 months shows that the ablation zone (arrowheads) has shrunk further.



(Figure 5a)



(Figure 5b)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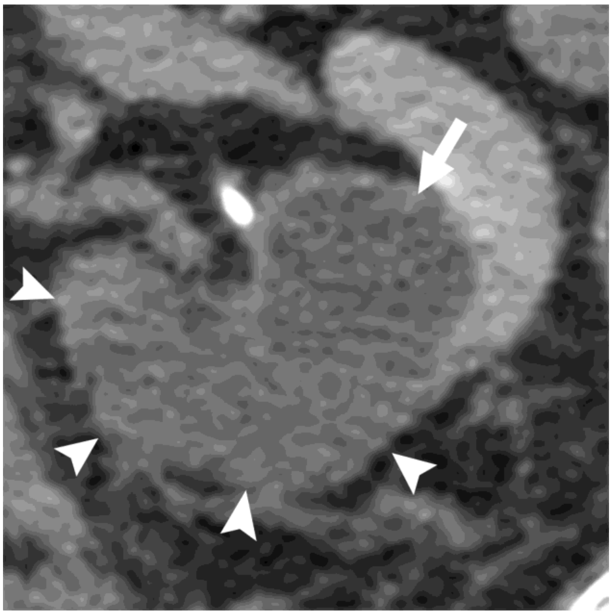
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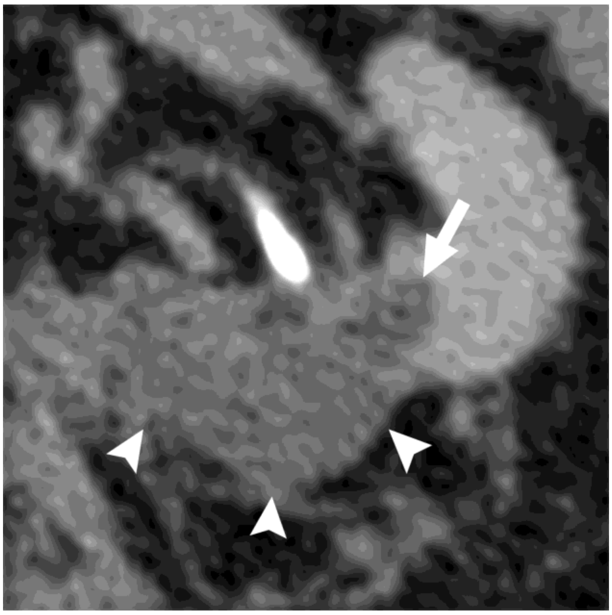
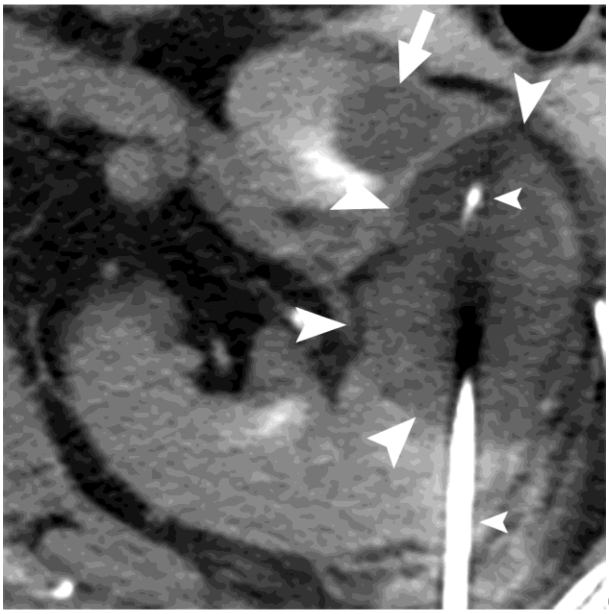
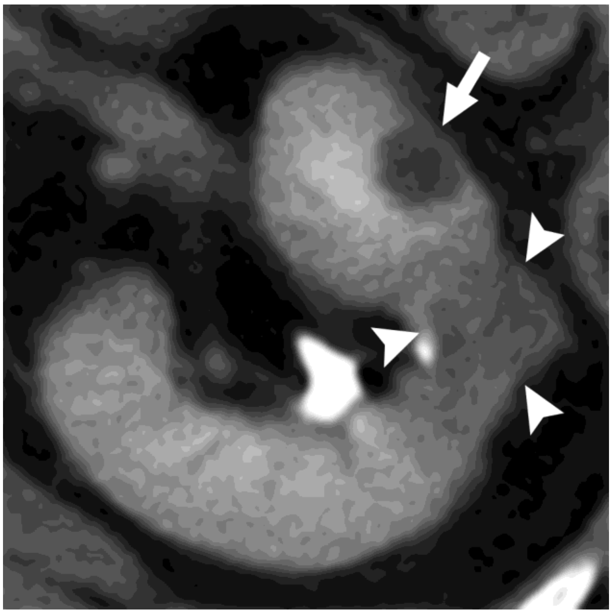

(Figure 5e)

Figure 5. A case of partial inclusion group. CT images showing a cyst in the partial inclusion group. **(a)** Axial image before cryoablation shows the cyst (arrow) in contact with renal cell carcinoma (arrowhead). **(b)** Sagittal image during cryoablation shows that the cyst is partially included in the iceball (large arrowheads). Arrows indicate a part of the cyst that is not included in the iceball. Small arrowheads indicate cryoprobes. **(c, d, e)** Axial images at 1 month (c), 3 months (d), and 12 months (e) show that the cyst, in contact with the ablation zone (arrowheads), continues to shrink with time but remains after 12 months.


(Figure 6a)


(Figure 6b)


(Figure 6c)

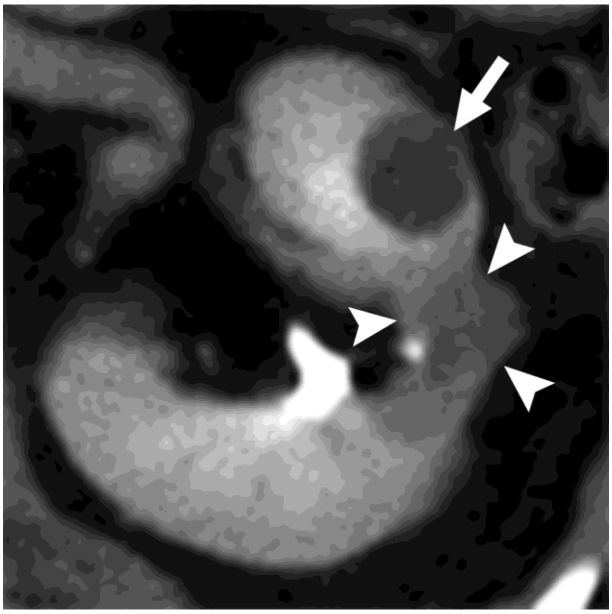

(Figure 6d)

Figure 6. A case of exclusion group. Axial CT images of a cyst in the exclusion group. **(a)** Image during cryoablation shows that the cyst is close to but excluded from the iceball (large arrowheads). Small arrowheads indicate cryoprobes. **(b, c)** Images at 1 month (b) and 6 months (c) show that the cyst (arrow) shrinks with time. Arrowheads indicate ablation zone. **(d)** Image at 12 months shows that the cyst has enlarged. Arrowheads indicate ablation zone.