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Assessment of Local Tumor Progression After Image-Guided Thermal Ablation for Renal Cell Carcinoma

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Focal enhancement typically suggests local tumor progression (LTP) after renal cell carcinoma is percutaneously ablated. However, evaluating findings that are false positive or negative of LTP is less familiar to radiologists who have little experience with renal ablation. Various imaging features are encountered during and after thermal ablation. Ablation procedures and previous follow-up imaging should be reviewed before determining if there is LTP. Previous studies have focused on detecting the presence or absence of focal enhancement within the ablation zone. Therefore, various diagnostic pitfalls can be experienced using computed tomography or magnetic resonance imaging examinations. This review aimed to assess how to read images during or after ablation procedures, recognize imaging features of LTP and determine factors that influence LTP.
Keywords: Renal cell carcinoma; Thermal ablation; Local tumor progression; Computed tomography; Magnetic resonance imaging

INTRODUCTION

Thermal ablation has been accepted as an alternative treatment for partial nephrectomy in patients who are not suitable for surgery because of a high risk of postoperative morbidity or mortality [1,2]. Accordingly, radiologists should recognize the difference between complete ablation and local tumor progression (LTP). Findings on various images following renal tumor ablation may be ambiguous for radiologists to determine whether these are consistent with LTP [3-5]. Additional thermal ablation or radical nephrectomy is recommended in the event of LTP [6,7]. Therefore, it is of considerable importance to understand the imaging features that suggest LTP [8-10]. Understanding LTP findings enables radiologists to proceed with management. In addition, they can avoid unnecessary biopsies, ablation, or surgery if post-ablation findings are not consistent with LTP. Therefore, determining the presence of LTP depends on knowledge about post-ablation imaging features on follow-up examination.

Few reports have mentioned true or false positive findings of LTP after renal tumor ablation. Most studies on post-ablation imaging features only consider localized enhancement within the ablation zone [8-11]. Furthermore, they barely mention how to estimate the extent of tumor ablation margin, the post-ablation changes that can occur, and factors that are related to LTP. This review aimed to assess how to read images during or after ablation procedures, determine the imaging features of LTP, and recognize factors that influence LTP.

Assessing the Ablation Zone

Radiologists should review the follow-up computed tomography (CT) or magnetic resonance imaging (MRI) scans to determine whether an ablation zone has completely and sufficiently covered a renal tumor during the thermal ablation procedure on three-dimensional CT or MRI [12,13]. They need to localize the renal tumor on pre-ablation images and locate it within the tumor ablation margin,

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which is not enhanced on contrast-enhanced images. Subsequently, radiologists should assess axial, sagittal, or coronal images carefully to ensure that the ablation margin covers an entire tumor. Therefore, follow-up CT or MRI should be reconstructed or scanned into a 3-dimensional axis.

When CT or MRI is obtained immediately or 1 month after renal tumor ablation, a renal cell carcinoma (RCC) should be located within the ablation zone and renal tissue to be ablated should be more than 5–10 mm from the tumor to minimize the likelihood of LTP (Figs. 1, 2) [14,15]. LTP may not be seen clearly on immediate or one-month post-ablation CT/MRI if the focal enhancement is minimal to be depicted (Fig. 1). Therefore, the first follow-up examination is recommended more than 1 month after thermal ablation [1,2,16].

Assessing Post-Ablation Enhancement

Radiologists should verify the presence of any enhancement within or around the tumor on follow-up CT or magnetic resonance (MR) images [10]. LTP frequently manifests as focal or curvilinear enhancement within the tumor. Clear cell RCC usually shows strong enhancement on cross-sectional images (Fig. 1). However, in non-clear cell RCC, LTP usually shows weak enhancement. This tumor shows dark signal intensity on T2-weighted imaging, and it is difficult to differentiate LTP from the ablation area (Fig. 2). When patients have poor renal function, they cannot be administered intravenous contrast material. Several studies have reported that diffusion-weighted imaging (DWI) can help to identify LTP that shows strong diffusion restriction [17,18]. DWI is useful in detecting incidents of LTP in cases where magnetic resonance contrast materials are not recommended because of poor renal function. However, diffusion restriction is heterogeneous, hence challenging for radiologists to frequently assess LTP according to the signal intensity on only DWI (Figs. 3, 4).

Post-ablation inflammation can cause ambiguity to radiologists in interpreting follow-up images (Figs. 4-6). It manifests as a geographic lesion showing weak or moderate

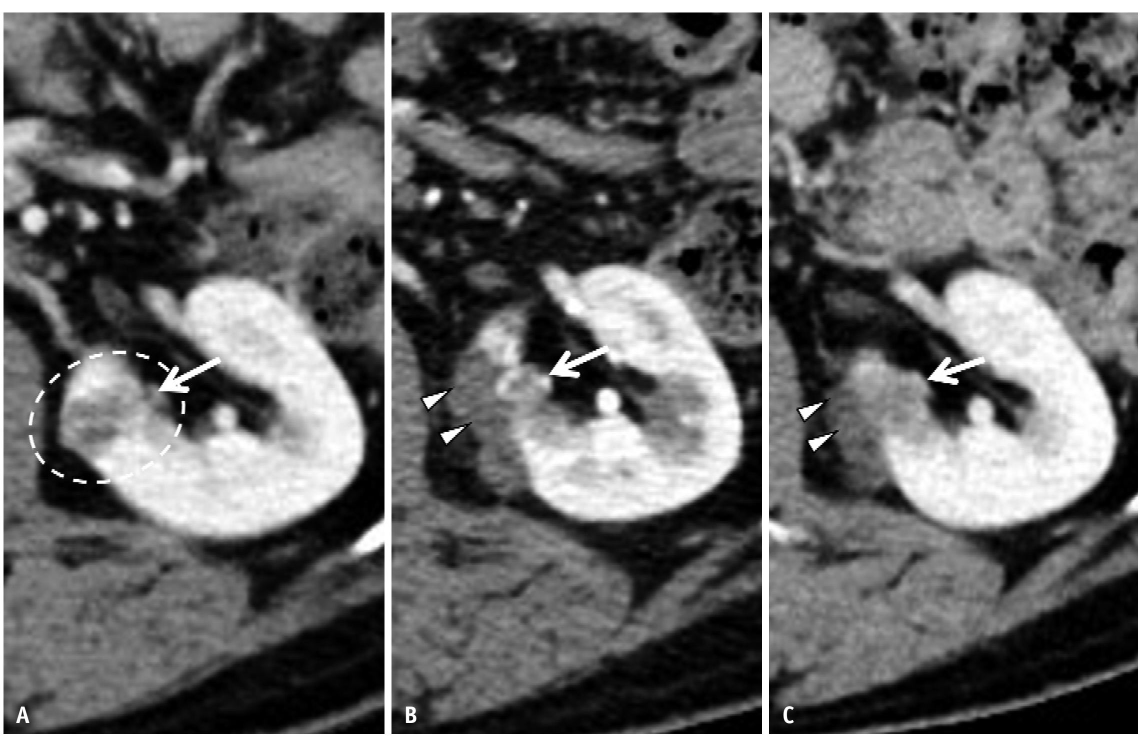

Fig. 1. Local tumor progression of clear cell RCC in a 62-year-old man. **A:** Pre-RFA CT shows a left endophytic RCC (white arrow). A white oval dashed line indicates an optimal ablation zone exceeding 5 mm from the tumor to sufficiently cover the tumor margin. Post-RFA 1-month CT does not show a focal enhancement within the tumor. **B:** Contrast-enhanced CT obtained 3 months after RFA shows that the ablation zone covers the lateral portion (white arrowheads) of the RCC, but not the medial portion (white arrow) of the tumor, suggesting local tumor progression. **C:** Contrast-enhanced CT obtained 30 months after RFA shows that the local tumor progression (white arrow) increases the original tumor size. White arrowheads indicate an ablation zone. RCC = renal cell carcinoma, RFA = radiofrequency ablation, CT = computed tomography

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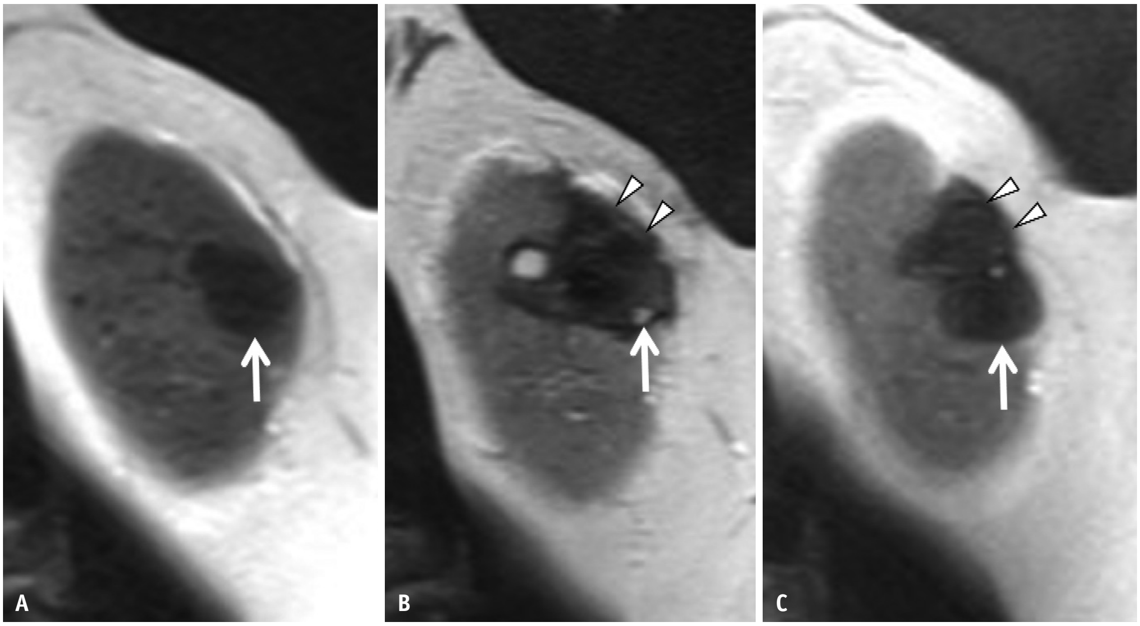

Fig. 2. Local tumor progression of papillary RCC in a 32-year-old man. **A:** Before RFA, T2-weighted coronal imaging shows a papillary RCC (white arrow) that is hypointense. **B:** T2-weighted coronal imaging obtained 1 month after RFA shows a hypointense ablation zone (white arrowheads). However, a residual RCC (white arrow) is missed because it is also hypointense. **C:** T2-weighted coronal imaging obtained 18 months after RFA shows that the size of the ablation zone (white arrowheads) decreases, whereas the size of the residual tumor (white arrow) increases. However, the local tumor progression is not recognized because it has the same signal intensity as the ablation zone. RCC = renal cell carcinoma, RFA = radiofrequency ablation

enhancement around the tumor [19-21]. This needs to be differentiated from LTP to determine if additional ablation or radical surgery is necessary. Therefore, percutaneous biopsy is recommended to obtain sample cores from it. When it is positive for RCC, the histologic diagnosis can be accepted. However, the histologic diagnosis can be a false negative due to inadequate sampling. In this clinical setting, short-term follow-up is useful to differentiate post-ablation inflammation from LTP [19-21]. The former decreases in size or disappears, but the latter increases in size.

Dystrophic calcification is a common late finding and may occur within the ablation zone [9,22] (Fig. 7). When these findings are located outside the tumor, benign calcifications are strongly suggested. However, when these findings are located inside the tumor, radiologists should review pre-ablation CT images to determine whether the renal tumor had calcification before ablation. If calcifications are not changed without tumor enhancement, these findings are not consistent with LTP. If calcifications develop in the enhanced area, these findings suggest LTP. To detect calcifications, unenhanced CT is essential during the follow-up period. If only contrast-enhanced CT images are obtained, radiologists may misdiagnose calcifications as enhanced foci. Dual-energy CT is also useful to differentiate calcifications from LTP although a single-phase contrast-enhanced CT is obtained.

An endophytic tumor is sometimes difficult to determine whether it is completely ablated or not. When weak enhancement is shown on follow-up images, radiologists need to differentiate LTP from post-ablation inflammation (Figs. 3, 4). Although an endophytic tumor is enhanced following contrast material injection, post-ablation inflammation is more likely than LTP if the size of the tumor is decreasing (Figs. 3, 4). However, if tumor enhancement is focal, LTP should be considered although the tumor does not grow (Fig. 1). Percutaneous biopsy helps to detect LTP by targeting the focally enhanced area. Follow-up images also can show focal enhancement increasing, suggestive of LTP.

Anatomical Changes during Thermal Ablation

Marginal dimpling is a good sign of a successful ablation when radiofrequency ablation (RFA) is used to treat an RCC (Table 1). This finding is encountered frequently when treating an exophytic RCC, resulting from coagulation necrosis of renal tissue around the tumor (Fig. 8). Ablating the tumor margin as well as an RCC is key for achieving complete ablation. It manifests as a focally collapsed renal

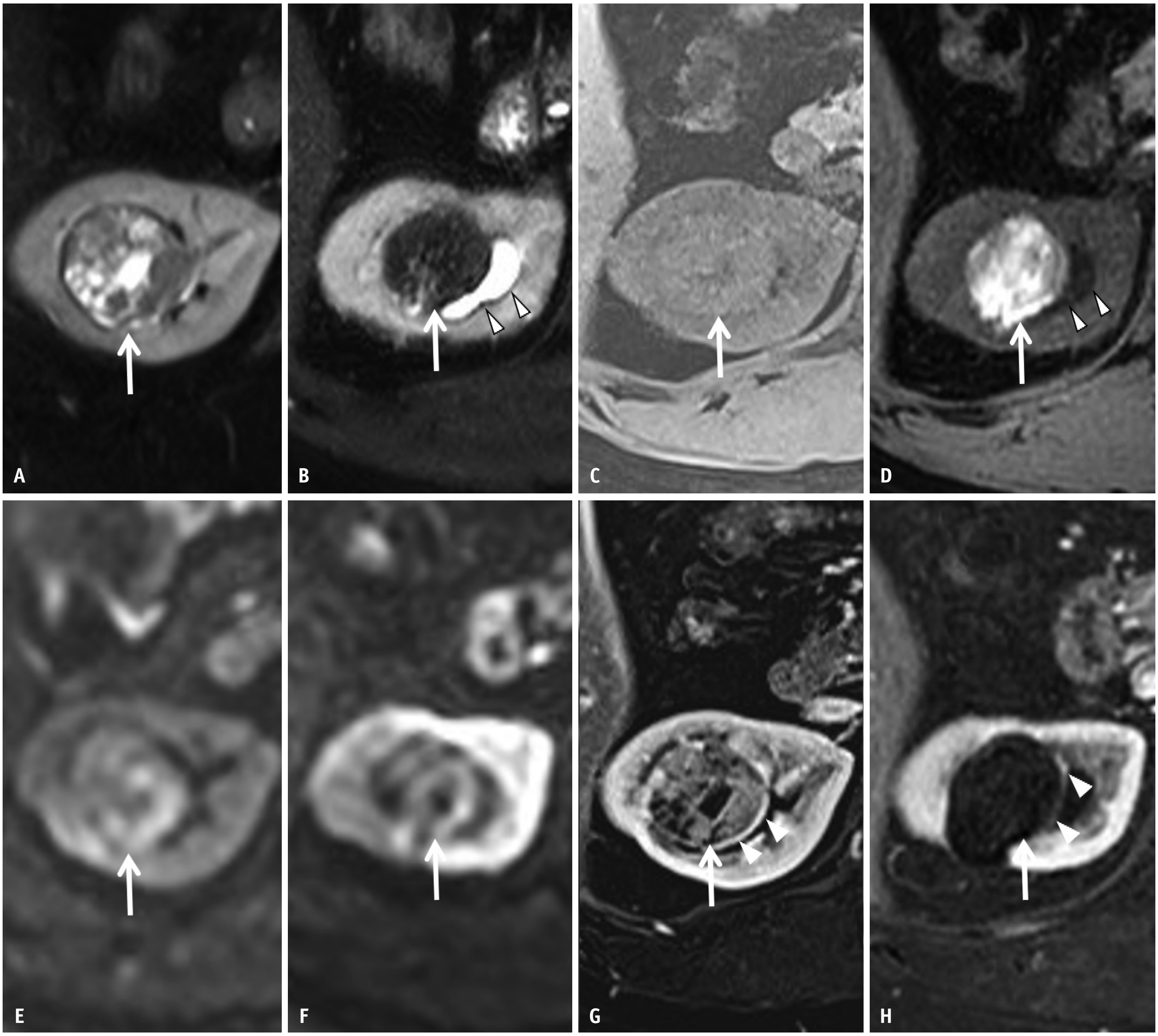

Fig. 3. Clear cell RCC in a 40-year-old man undergoing RFA. **A, B:** Before RFA, T2-weighted fat-saturated imaging **(A)** shows an endophytic RCC (white arrow) that is slightly hyperintense and heterogeneous, whereas T2-weighted fat-saturated imaging **(B)** following RFA shows that the tumor (white arrow) becomes markedly hypointense and homogenous. Arrowheads indicate dilated calyx due to heat injury. **C, D:** Before RFA, T1-weighted fat-saturated MRI **(C)** shows an endophytic RCC (white arrow) that is slightly hyperintense, whereas T1-weighted fat-saturated MRI **(D)** following RFA shows that the tumor (white arrow) becomes markedly hyperintense. Arrowheads indicate dilated calyx due to heat injury. **E, F:** Before RFA, diffusion-weighted imaging **(E)** shows an endophytic RCC (white arrow) with high signal intensity, whereas diffusion-weighted imaging **(F)** shows that the signal intensity of the tumor (white arrow) becomes weak following RFA. **G, H:** Before RFA, an endophytic RCC (white arrow) shows heterogeneous enhancement **(G)**, whereas the tumor (white arrow) shows no enhancement **(H)** following RFA. Arrowheads indicate the segmental renal artery around the tumor, which was misdiagnosed as LTP by three radiologists who did not review pre-ablation CT or MR images. RCC = renal cell carcinoma, RFA = radiofrequency ablation, MRI = magnetic resonance imaging, LTP = local tumor progression, CT = computed tomography, MR = magnetic resonance

parenchyma around the renal tumor. LTP does not occur in the marginal dimpling. If marginal dimpling is not created around the tumor, the likelihood of LTP may increase on follow-up images. In contrast, cryoablation barely induces marginal dimpling around the RCC (Fig. 8) because the freezing and thawing result in osmotic changes and mechanical damage to ablate the tumor margin as well as the RCC (Table 1).

The change in attenuation of an RCC is useful in assessing successful ablation (Table 1). Clear cell RCC, which is the

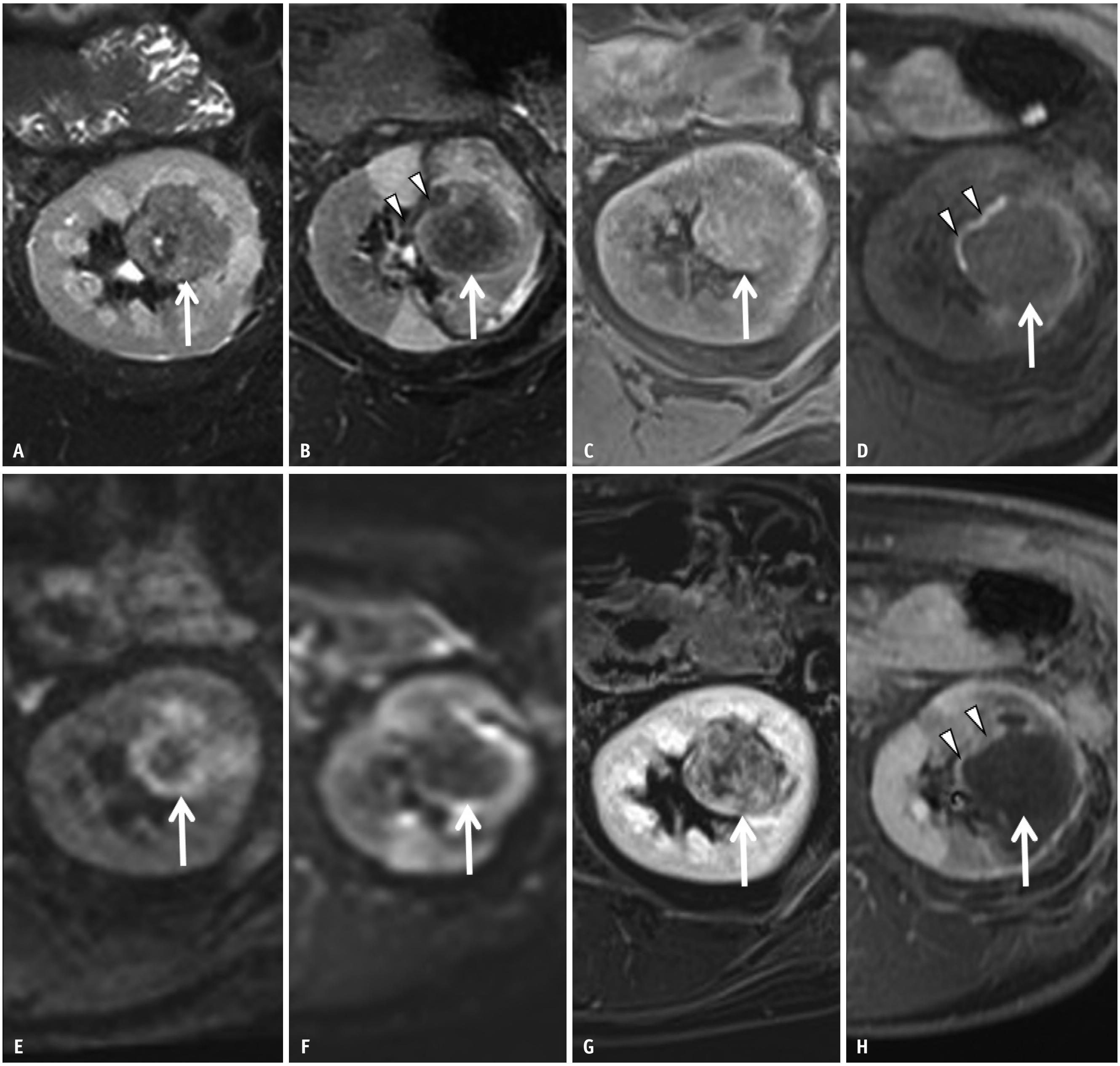

Fig. 4. Clear cell RCC in a 60-year-old man undergoing cryoablation. **A, B:** Before cryoablation, T2-weighted fat-saturated imaging **(A)** shows an endophytic RCC (white arrow) that is slightly hyperintense, whereas T2-weighted fat-saturated imaging **(B)** following cryoablation shows that the tumor (white arrow) becomes slightly hypointense. White arrowheads indicate hemorrhage around the tumor. **C, D:** Before cryoablation, T1-weighted fat-saturated MRI **(C)** shows an endophytic RCC (white arrow) that is slightly hyperintense, whereas T1-weighted fat-saturated MRI **(D)** following cryoablation shows that the tumor (white arrow) becomes slightly hyperintense. White arrowheads indicate hemorrhage around the tumor. **E, F:** Before cryoablation, diffusion-weighted imaging **(E)** shows an endophytic RCC (white arrow) with high signal intensity, whereas diffusion-weighted imaging **(F)** shows that the signal intensity of the tumor (white arrow) becomes slightly hypointense following cryoablation. **G, H:** Before cryoablation, an endophytic RCC (white arrow) shows heterogeneous enhancement **(G)**, whereas the tumor (white arrow) shows no enhancement **(H)** following cryoablation. Arrowheads indicate marginal enhancement, suggesting post-cryoablation inflammation. RCC = renal cell carcinoma, MRI = magnetic resonance imaging

most common subtype, is frequently hypoattenuating on unenhanced CT (Fig. 8). Frequently, tumor cells have enormous intra-cytoplasmic lipids, resulting in a low CT number on unenhanced CT [23]. When tumor attenuation is changed from hypoattenuation to hyperattenuation during or after RFA procedures, coagulation necrosis develops within the tumor. If hyperattenuation is detected within the entire tumor, it will suggest successful ablation. Persisting

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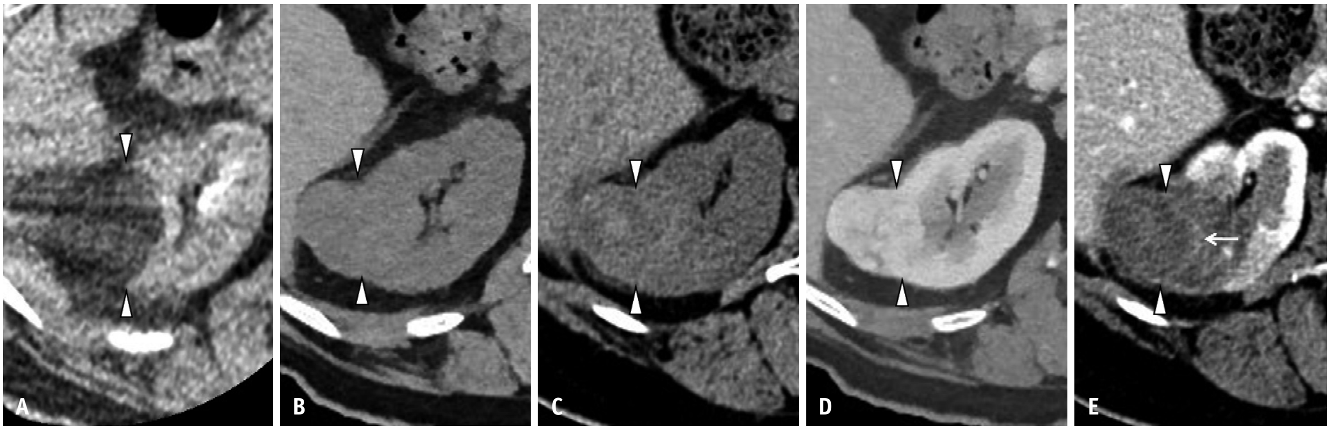

Fig. 5. Clear cell RCC in a 74-year-old woman undergoing cryoablation. The white arrowheads indicate no margin dimpling during the cryoablation. **A:** Contrast-enhanced CT shows an ice ball covering the right RCC. **B, C:** Before cryoablation, unenhanced CT shows an exophytic homogeneous RCC **(B)**, whereas unenhanced CT shows that the tumor becomes heterogeneous **(C)** following cryoablation. **D, E:** Before cryoablation, contrast-enhanced CT shows a well-enhancing RCC **(D)**, whereas contrast-enhanced CT shows no enhancement in the tumor **(E)** following cryoablation. A white arrow shows marginal enhancement, suggesting post-cryoablation inflammation. RCC = renal cell carcinoma, CT = computed tomography

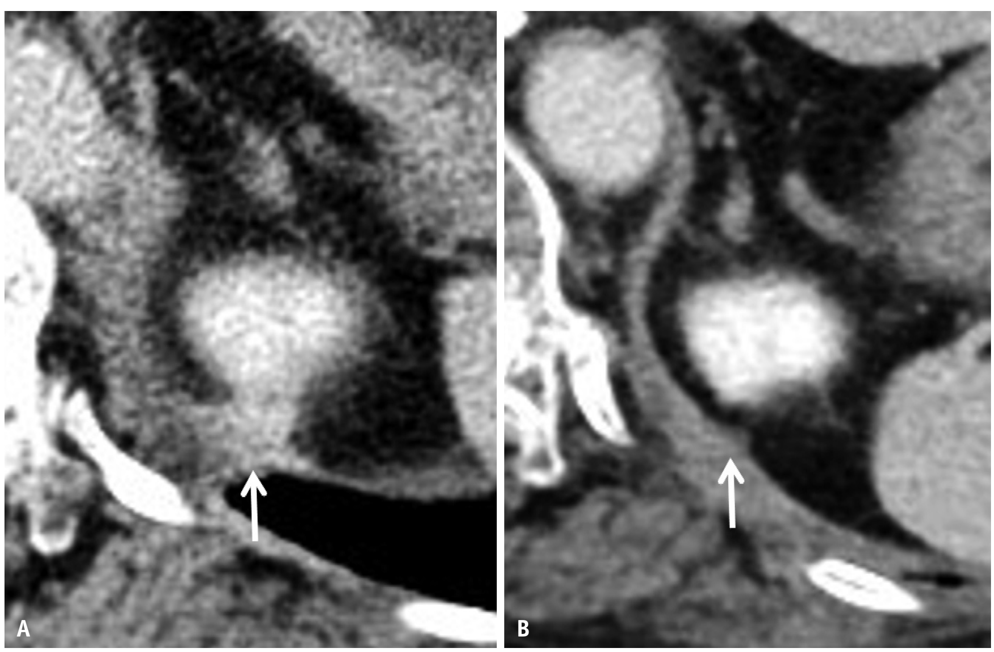

Fig. 6. Chromophobe RCC in a 76-year-old woman undergoing RFA. **A:** Contrast-enhanced CT shows an enhancing mass (white arrow) around the left kidney. It occurs 3 months after RFA is performed. **B:** The lesion (white arrow) is not visible on follow-up CT obtained 6 months later. It is considered post-RFA inflammation. RCC = renal cell carcinoma, RFA = radiofrequency ablation, CT = computed tomography

hypoattenuation of the tumor indicates incomplete ablation, suggestive of LTP on follow-up images. In contrast, non-clear cell subtypes including papillary, chromophobe, or other RCC frequently show hyperattenuation on unenhanced CT [23]. Therefore, it is challenging to identify the attenuation change of a non-clear cell RCC during RFA procedures. However, tumor attenuation changes as well as marginal dimpling are not apparent during or after cryoablation (Fig. 5) (Table 2).

RFA decreases the T2 signal intensity of the renal tumor and increases the T1 signal intensity more than cryoablation (Figs. 3, 4) (Tables 1, 2). Post-RFA tumor texture tends to be more homogeneous than post-cryoablation texture. These differences are not well understood. RFA dehydrates an RCC, leading to coagulation necrosis, whereas cryoablation promotes cell membrane rupture due to osmotic change and tissue ischemia due to hypoperfusion. Subsequently, cryoablation leads to delayed programmed cell death due to

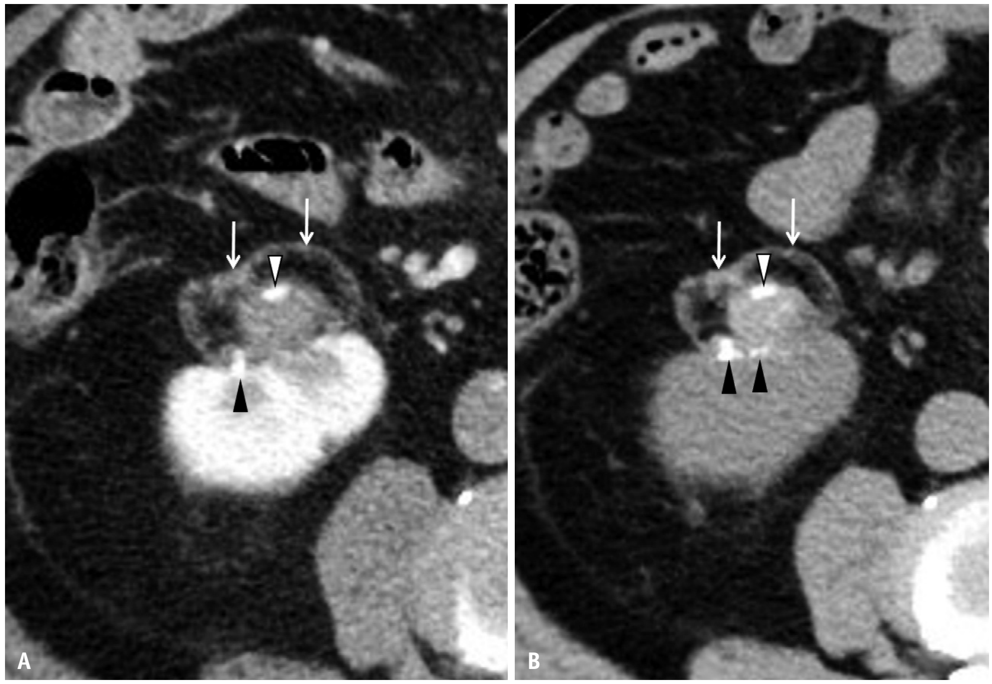

Fig. 7. Clear cell RCC in a 73-year-old man undergoing RFA. **A:** Contrast-enhanced CT obtained 4 years after RFA shows hyperattenuating foci (white and black arrowhead) in the RCC and neighboring tumor margin. A radiologist diagnosed it as a local tumor progression. White arrows indicate the ablation margin in which the RCC is located. **B:** Unenhanced CT obtained 10 days later shows dystrophic calcifications (white and black arrowheads) in the RCC and tumor base. White arrows indicate the ablation margin (Bull's eye appearance) in which the RCC is located. RCC = renal cell carcinoma, RFA = radiofrequency ablation, CT = computed tomography

Table 1. Comparison of RFA and cryoablation using post-ablation CT features

Post-ablation CT features	Thermal ablation modalities	
	RFA	Cryoablation
Tumor texture	More homogeneous	More heterogeneous
Tumor size change	More decreased	Less decreased
Tumor attenuation change	Stronger	Weaker
Marginal dimpling	Positive	Negative
Transient enhancement	Less frequent	More frequent

RFA = radiofrequency ablation, CT = computed tomography

apoptosis [24]. Therefore, post-ablation enhancement seems to be more frequent in cryoablation and is frequently seen until 1 month after the ablation [16].

The size change of an RCC during thermal ablation helps to predict the likelihood of LTP. As an RCC becomes shrunken, the number of viable tumor cells decreases. Thus, a decrease in tumor size can lead to a decrease in the frequency of LTP. RFA or microwave ablation (MWA) using heating energy induces the reduction of tumor size during the ablation. However, the size reduction occurs during cryoablation but is not so apparent compared to RFA or MWA. Accordingly, cell death increases according to the reduction of tumor size. The frequency of LTP becomes lower proportionally according to the size reduction of the renal tumor. Therefore, interventional radiologists attempt to shrink the RCC as much as possible, minimizing the likelihood of LTP when using RFA or MWA (Fig. 8).

The appearance of a bull's eye is frequently seen as a round or oval shape in the peri-nephric fat neighboring an RCC (Fig. 7). It manifests as a thin ablation line and is created at the boundary of the thermal energy during ablation. It occurs following any thermal ablation. The size of the bull's eye tends to decrease when the follow-up period increases. Tumor ablation is considered complete if the tumor is located within the bull's eye. It is a late imaging feature suggesting shrinkage of the complete ablation zone. If an RCC is included within the bull's eye, LTP is extremely rare during the follow-up. Therefore, it is a good sign representing a good long-term outcome.

Other Factors Influencing LTP

Guiding Modality

CT or MRI is a useful modality to guide ablation procedures [1-3,25]. This imaging modality can show a clear tumor margin, ablation area, and neighboring organs.

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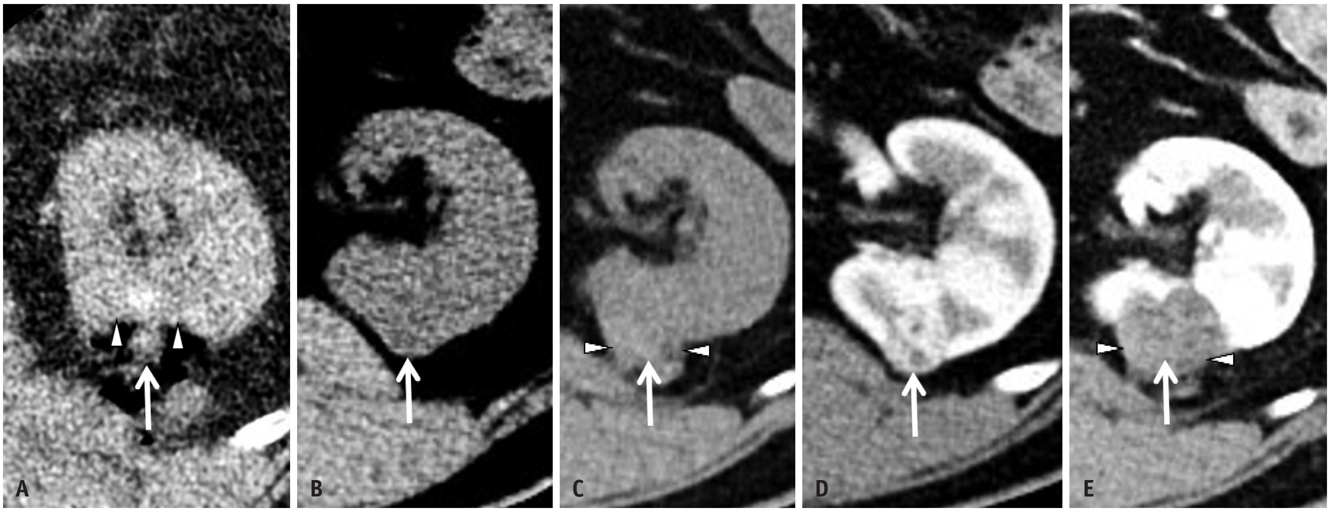

Fig. 8. Clear cell RCC in a 59-year-old man undergoing RFA. **A:** Contrast-enhanced CT image, which is obtained during RFA procedures, shows a markedly decreased RCC (white arrow). It is not enhanced but appears hyperattenuating on an unenhanced CT image, which is obtained during RFA procedures. Contrast material is seen in the renal parenchyma but is delayed to be excreted after it is intravenously injected before beginning ablation for tumor localization. White arrowheads indicate margin dimpling in which the tumor margin is completely ablated. **B, C:** An exophytic RCC (white arrow) is hypoattenuating on pre-RFA CT **(B)** whereas the tumor (white arrow) is hyperattenuating on post-RFA CT **(C)**. Minimal hemorrhage (arrowheads) is seen around the tumor following RFA. **D, E:** Pre-RFA CT shows a well-enhancing RCC (white arrow) with heterogeneous texture **(D)**, whereas post-RFA CT shows no enhancement and homogeneous texture in the RCC (white arrow) **(E)**. Little hemorrhage (arrowheads) is seen around the tumor following RFA. RCC = renal cell carcinoma, RFA = radiofrequency ablation, CT = computed tomography

Table 2. Comparison of RFA and cryoablation using post-ablation MRI features

Post-ablation MRI sequence and features	Thermal ablation modalities	
	RFA	Cryoablation
Tumor texture	More homogeneous	More heterogeneous
T2WI	More hypointense	Less hypointense
T1WI	More hyperintense	Less hyperintense
DWI	Weaker	Weaker
Transient enhancement	Less frequent	More frequent

RFA = radiofrequency ablation, MRI = magnetic resonance imaging, T2WI = T2-weighted imaging, T1WI = T1-weighted imaging, DWI = diffusion-weighted imaging

However, ultrasound (US) is not a good modality to monitor the ablation margin. Because an ablation area becomes hyperechoic, it can produce a shadowing posterior.

Ablation Modality

Cryoablation shows a clearer ablation margin, which is hypoattenuating or hypointense on CT or MRI due to ice ball formation compared to RFA (Figs. 2, 5) [26,27]. Subsequently, interventional radiologists can easily identify where additional ablation is needed during cryoablation.

Type of Anesthesia

The type of anesthesia for thermal ablation includes conscious sedation, monitored anesthesia care (MAC), and general anesthesia [28]. RFA and MWA frequently are more painful during the ablation procedures compared to cryoablation. Subsequently, MAC or general anesthesia can control the pain well under RFA and MWA, resulting in better treatment compared to conscious sedation. Moreover, it takes two or more hours to treat an RCC with thermal ablation. Most patients were older than those undergoing partial nephrectomy. They tend to experience many problems because they lie on a small CT or MRI table and are asked not to move from the same position for a long time. These situations may oblige interventional radiologists to rush over procedures, leading to insufficient ablation.

Tumor Location

Tumor locations include endophytic and exophytic RCCs. Exophytic tumors contact a smaller area of renal parenchyma than endophytic tumors [12]. Therefore, the volume of the ablation area is smaller and the likelihood of LTP is lower than that of endophytic tumors (Figs. 1, 2, 7, 8). In contrast, more attention is necessary to ablate every tumor margin and interventional radiologists should not lose their concentration during the procedures. Every time, they need to check if the ablation area covers the tumor margin sufficiently as well as an endophytic tumor. However, endophytic tumors are frequently close to vessels in the renal sinus. Therefore, the heat sink effect is stronger in endophytic tumors, leading to increasing LTP (Figs. 1, 2).

Tumor Size and Number

One of the parameters influencing the frequency of LTP is the size or number of RCCs [12]. As it increases, the ablation area increases. Thermal ablation does not produce treatment outcomes of T1b as good as that of T1a. Even though increasing the number of applicators can ablate a larger area, insufficient ablation may occur in the tumor or margin, resulting in LTP. Two or more sessions are necessary when treating a large RCC [12].

CONCLUSION

Various imaging features are encountered during ablation procedures and on follow-up CT or MR images. Understanding them enables radiologists to perform thermal ablation and interpret follow-up images. Accordingly, they can do appropriate ablation procedures and detect the presence of LTP early to take the next steps.

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

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