

Assessment of Therapeutic Response of Ablated Lesion after Radiofrequency Ablation in Patients with Unresectable Lung Malignancies by Multiphase Contrast-enhanced MRI

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Purpose : We evaluated which phase was important to recognize local progression of an ablated zone after RFA on multiphase contrast-enhanced MRI (CE-MRI) in patients with unresectable lung malignancy.

Materials and Methods : Twenty patients who had unresectable lung malignancy underwent multiphase CE-MRI examinations immediately after RFA. We evaluated the enhancement patterns of the ablated zone on multiphase CE-MRI: type I, no enhancement of the ablated zone; type II, enhancement of the ablated margin; type III, heterogeneous enhancement of the ablated zone. We evaluated the association enhancement type with local progression of the ablated zone on the follow up CT using Spearman's ranked test.

Results : In complete ablation, the enhancement pattern was types I (11.1%) or II (88.9%). In unsuccessfully treated, type II (57.1%) or III (42.9%) pattern observed in the arterial phase. However, types II (21.4%) and III (78.6%) observed in the venous, and types II (7.1%) and III (92.9%) observed equilibrium phases. Local progression of the ablated zone was associated with the enhancement pattern in equilibrium phases ($r=0.8$, $p < .05$).

Conclusion : Equilibrium phases on multiphase CE-MRI might play a more important role in evaluating an ablated zone for predicting local recurrence after RFA.

Index words : Lung neoplasms
Radiofrequency (RF) ablation
Magnetic resonance imaging (MRI)

Introduction

Lung cancer is one of the most common malignancies

and the leading cause of cancer death. The well-established therapeutic methods for a primary lung malignancy or secondary pulmonary metastatic nodules are surgery, chemotherapy, and radiation

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therapy. Unfortunately, patients with a lung malignancy or pulmonary metastatic nodules are often poor surgical or chemotherapy candidates due to chronic obstructive pulmonary disease, co-morbidity, or cardiac disease (1–5).

Most investigators have been used CT as a follow up modality after RFA (4–9). Steinke et al. (7) reported the complete absence of contrast enhancement in the ablated zones on the follow-up CT scans obtained immediately after treatment in the complete ablation group, whereas the ablated zones in the partial ablation group showed various degrees of enhancement.

MRI has been explored as an alternative imaging method for lung cancer, with the potential to provide morphological information, while being completely free from radiation hazards. To our knowledge, there were a few of the MRI findings of the ablated zones after RFA in patients with unresectable lung malignancies (10, 11). Okuma et al. (10) reported that the apparent diffusion coefficient (ADC) on DWI without local progression was significantly higher than with local progression after RFA, suggesting that the ADC can predict the response to RFA for lung tumors. However, there is no report for local progression of ablated lesion using multiphase contrast-enhanced MRI (CE-MRI).

In this study, we examined which phase was important for predicting local recurrence of an ablated zone after RFA treatment in patients with an unresectable lung malignancy on multiphase CE-MRI.

Materials and Methods

Patients

The MRI assessment of the ablated zone after RFA was retrospectively investigated with the approval of the institutional ethics committee at our institution. Sixteen patients with a primary lung malignancy and four patients with a single metastatic nodule from extrapulmonary malignancies were referred for CT-guided RFA. There were sixteen men and four women, ranging in age from 37 to 84 years (mean age, 61.5 years). All patients were diagnosed non-small cell lung cancer using percutaneous needle lung biopsy or bronchoscopic biopsy and included as follows; (a) medical inoperability (stage I - II) due to medical contraindications or strong refusal of surgery (n=5); (b)

the presence of a single metastatic nodule originating from extrapulmonary malignancy (n=4); (c) the patients want to reduce the volume of the primary tumor in patients with stage III-IV (n=11).

The tumors ranged in diameter from 1 to 5 cm (mean, 3.9 ± 1.1 cm). The tumor cell types were squamous cell carcinomas (n=10), adenocarcinomas (n=6), and metastases (n=4; colon, breast, uterus). Five patients (25%) had stage Ia or Ib lung cancer, eleven (55%) had an unresectable stage III or IV cancer, and four (20%) had metastases from an extrapulmonary malignancy (Table 1).

RFA Preparation and Procedure

RFA was performed on in-patients after 6 hrs fasting. The coagulation parameters were always checked before the procedure. All patients underwent a chest CT examination (Somatom Plus 4, Siemens, Erlangen, Germany) at most one week before RFA. RFA was always performed by one radiologist with CT guidance. The patients' vital signs were monitored continuously throughout the procedure. In all the patients, RF therapy was performed with the analgesia achieved by the intravenous administration of 50–100 μ g of fentanyl citrate (Myungmoon, Kyungki, Korea). RFA was carried out using a 17-gauge, single internally cooled RF electrode (Radionics, Burlington, Mass, USA). Once proper positioning was confirmed, the electrode was attached to a 500-KHz, monopolar RF generator (CC-1; Radionics, Burlington, MA, USA). At the end of each treatment, the perfusion was stopped and the maximum temperature was recorded. If the temperature exceeded 60 °C during treatment, the electrode was withdrawn in increments of 1 cm up to the length of the active-tip, while the intratumoral temperature was measured simultaneously. An additional treatment was performed at the same position if the maximum intratumoral temperature recorded after the RFA treatment did not exceed 60 °C. After treatment, the electrode was withdrawn without cauterizing the probe tract (2, 9).

MR Sequence and Analysis of the MR Findings

The chest MRI images were obtained within 24 hrs after RFA treatment to assess the immediate results. The post-RFA MRI (Magnetom Symphony, Siemens, Erlangen, Germany) was evaluated by two radiologists,

who are experienced in chest CT scans and MRI and were aware of the findings of the CT scans performed before RFA.

In all cases, MRI was performed on a 1.5-T superconducting imager using phased array multicoils. The lungs were imaged using the following sequence: contrast-enhanced T1-weighted image (volumetric interpolated breath-hold examination, VIBE). CE-MRI using VIBE was performed after administering gadopentate dimeglumine (Gd-BOPTA; MultiHance, Bracco SpA, Milan, Italy) at a dose of 0.1 mmol/kg and a rate of 3 cc/ sec using an MR-compatible power injector (Spectris®; Medrad, Pittsburgh, USA). VIBE was performed in the pre-contrast, arterial (20–35 sec), venous (45–60 sec), and equilibrium phases (3–5 min) using the following parameters: 3.4/1.5 msec; flip angle, 12°; bandwidth, 490 Hz/pixel; matrix, 256 (readout direction) × 120 (phase) × 64–72 (partition); effective

slice thickness, 2.3 mm; and field of view, 30–35 cm (12, 13). Image reconstruction was carried out using the source images taken with a slice thickness of 3 mm on an MRI workstation.

Image analysis was performed independently by two radiologists, who analyzed the CT images obtained before RFA and the MRI findings after RFA on the same patient using a picture archiving and communication system (PACS, m-view™; Marotech, Korea). The enhancement pattern on CE-MRI was also analyzed. The ablated zone was divided into the central zone (central ablated zone except for the ablated margin) and the ablated margin (peripheral ablated zone within 10 mm of the outermost margin of the ablated zone). These enhancement patterns were classified into the following three types: Type I, the ablated zone showed absolutely no enhancement; Type II, only enhancement of the ablated margin was

Table 1. Clinical Characteristics, Therapeutic Response, Types of MRI findings of the 20 Patients with Lung Malignancies Treated by Radiofrequency Ablation

N	Age/sex	Histology	Stage	TS before RFA (cm)	TS on last F/U (cm)	IF (month)	TR	Enhancement pattern (MRI)		
								arterial	venous	equilibrium
1	73/M	squamous	IA	2	2	13	CA	II	II	II
2	75/M	adeno	IB	1	1	11	CA	II	II	II
3	46/M	adeno	meta	1	0	18	CA	I	I	II
4	49/F	chorio	meta	3	1.7	18	CA	II	II	II
5	62/M	adeno	meta	4	4	20	CA	II	II	II
6	71/F	adeno	IA	2.4	2.4	20	CA	II	II	II
7	75/M	squamous	IB	5	6.5	8	UT	III	III	III
8	84/M	squamous	IB	4	5	9	UT	II	II	II
9	76/M	squamous	IIIB	2	3	25	UT	II	III	III
10	67/M	squamous	IIIA	4	5	18	UT	III	III	III
11	62/M	squamous	IIIA	5	7	8	UT	II	III	III
12	73/M	squamous	IIIB	4	6	8	UT	III	III	III
13	72/M	squamous	IIIB	5	8	4	UT	III	III	III
14	64/F	adeno	IIIB	5	7	8	UT	III	III	III
15	78/M	adeno	IV	3.5	4	24	UT	II	II	III
16	55/M	adeno	IV	3	3.5	8	UT	II	III	III
17	63/M	adeno	IV	6	10	5	UT	II	III	III
18	62/M	squamous	IV	6	9	6	UT	II	II	III
19	57/M	squamous	IV	6	9	8	UT	III	III	III
20	37/F	adeno	meta	3	3.5	22	UT	II	III	III

Note.— TS= tumor size, IF= interval of follow-up, TR= therapeutic response, CA= complete ablation, UT= unsuccessfully treated, GGO=ground glass opacity, squamous=squamous cell carcinoma, adeno=adenocarcinoma, =small cell=small cell carcinoma, chorio=choriocarcinoma, meta=metastasis, Type I, the ablated zone showed absolutely no enhancement; Type II, only enhancement of the ablated margin was observed; and Type III, irregular enhancement of the ablated zone. Complete ablation was defined as no enhancement (type I) of the ablated lesion at CE-MRI obtained within 24 hours after RFA. Also, there was decrease or no change of the size, or no enhancement of the treated lesion at last follow-up contrast-enhanced CT. Unsuccessfully treated was defined as enhanced lesion at CE-MRI (type II or III) obtained within 24 hours after RFA. Additionally, there was an increase in size of ablated lesion at last follow-up contrast-enhanced CT.

observed; and Type III, heterogeneous enhancement of the ablated zone (Fig. 1).

The tumor sizes before and after treatment were assessed in the axial plane using the maximum diameters on the pre procedural CT image taken in the axial plane and the follow-up contrast-enhanced CT, respectively.

Therapeutic Response Criteria

For the therapeutic response, complete ablation was defined as no enhancement (type I) of the ablated lesion at CE-MRI obtained within 24 hours after RFA. Also, there was decrease or no change of the size, or no enhancement of the treated lesion at last follow-up contrast-enhanced CT. Unsuccessfully treated was defined as enhanced lesion at CE-MRI (type II or III) obtained within 24 hours after RFA. Additionally, there was an increase in size of ablated lesion at last follow-up contrast-enhanced CT.

The tumor size was assessed in the transverse plane with the largest diameter and the greatest perpendicular measurement recorded on the post-RFA MRI and follow-up contrast CT. The CE-MRI obtained within 24 hours after RFA compared with baseline contrast-enhanced CT scans that obtained before the procedure, and technical success assessed. Technical success, primary effectiveness rate, and local tumor progression were defined according to the guidelines recommended by Goldberg et al. [14] Technical success was defined when tumor was treated according to protocol and completely tumor coverage can be assessed immediately after the procedure on multiphase CE-MRI. Also, primary effectiveness rate is defined as the percentage of tumors that were successfully eradicated following the initial procedure. We evaluated primary effectiveness rate and local tumor progression as performed using a contrast-enhanced CT at 1, 3 months and every 6 months after RFA.

Statistical Analysis

A κ coefficient was calculated to evaluate the degree of agreement between the two chest radiologists in evaluating lung cancer on CT and ablated lesion after RFA (less than 0.20, poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and 0.81–1.00, very good agreement).

The Spearman correlation coefficient was also used to characterize the MR features (type of ablated lesion) and local tumor progression of the ablated zone on the follow up CT. Also, we evaluated diagnostic performance of CE-MRI (arterial, venous, or equilibrium phase) for local recurrence using chi-square test when predicted local recurrence of CE-MRI was defined type III pattern. All analyses were performed using SPSS 9.0 computer software (SPSS Inc., Chicago, Ill., U.S.A). The values are expressed as a mean \pm SD. For all statistical analyses, p values < 0.05 were considered significant.

Results

All patients (n=20) treated by RFA were technical successes (100%). On follow-up CT, primary effectiveness rate were shown in 9 patients (45%) and 11 patients (55%) were shown to have local progression. The overall survival time for the patients with lung malignancy in this study were 13.1 ± 6.8 months. Of the 20 patients, nine (45%) showed a gradual decrease or no change in the diameter of the ablated zone on contrast-enhanced CT until the last follow-up (mean, 17.1 ± 5.3 months); mean size, $2.5 \pm$

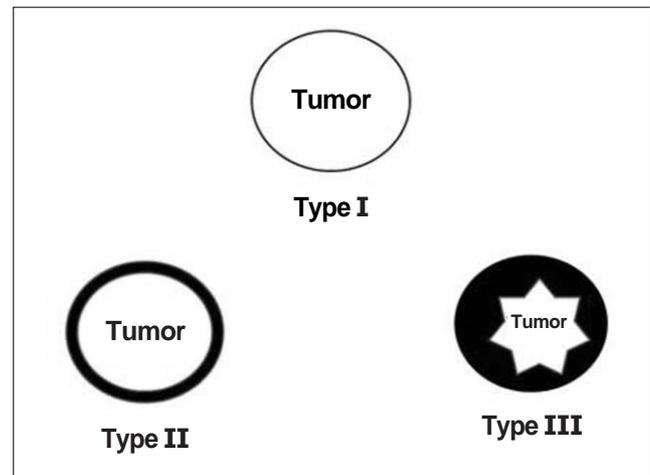


Fig. 1. Diagrams of the enhancement patterns on the contrast-enhanced MRI performed immediately after RFA: The ablation zone was divided into the central region (central ablated zone except ablated margin) and the ablated margin (peripheral ablated zone within 10 mm of the outermost margin of the ablated zone). These enhancement patterns of ablated zone are classified into the following three types: Type I, absolutely no enhancement; Type II, only enhancement of the ablated margin; and Type III, heterogeneous enhancement of the ablated zone.

1.0 cm to 2.4 ± 1.4 cm. Eleven patients (55%) showed a gradual increase in the diameter of the ablated zone on contrast-enhanced CT until the last follow-up (mean, 9.7 ± 6.2 months); mean size, 4.7 ± 1.1 cm to 6.8 ± 2.0 cm (Table 1).

In the arterial phase on CE-MRI after RFA, the enhancement of the ablated zone was categorized as types I (n=1, 5%), II (n=13, 65%), and III (n=6, 30%). In the venous phase, the enhancement of the ablated zone was categorized as types I (n=1, 5%), II (n=8, 40%), and III (n=11, 55%). In the equilibrium phase, the enhancement of the ablated zone was categorized

as types II (n=7, 35%) and III (n=13, 65%) (Figs. 2, 3). Interobserver agreement of the enhancement patterns of the lung cancers on the contrast-enhanced CT [κ (95% CI) values of 0.825 (0.650–0.934)] and the enhancement of the ablated zone on CE-MRI after RFA [κ (95% CI) values of 0.715 (0.530–0.872)] was assessed using the kappa test, which indicated a good and moderate inter-observer correlation, respectively.

Of the 20 patients, six (30%) showed a complete ablation and fourteen (70%) had unsuccessfully treated. In those with a complete ablation, the enhancement pattern was types I (11.1%) or II (88.9%) regardless of

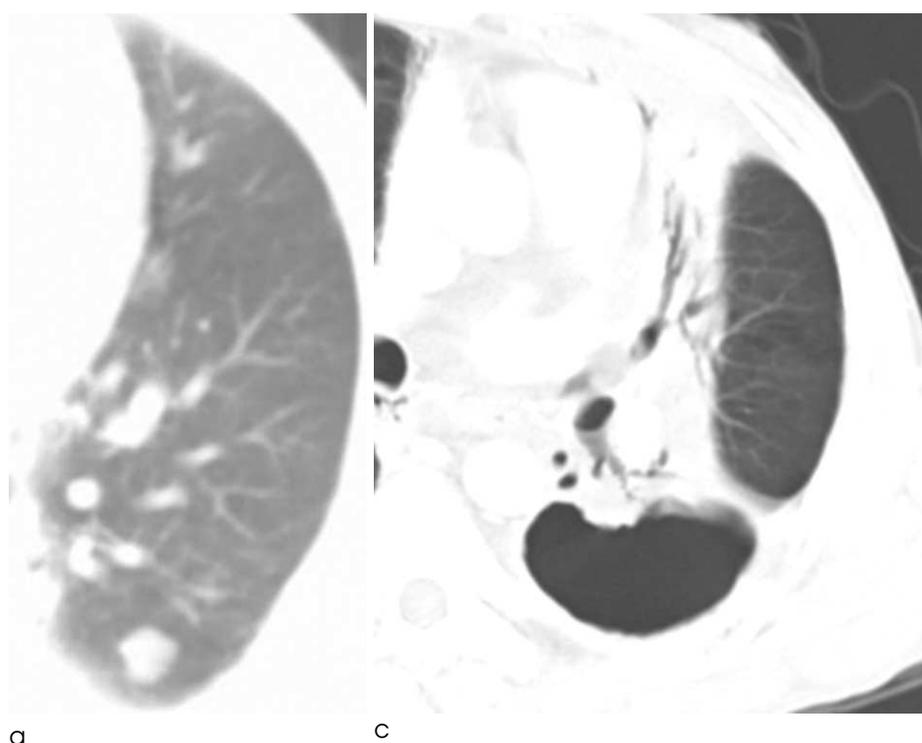
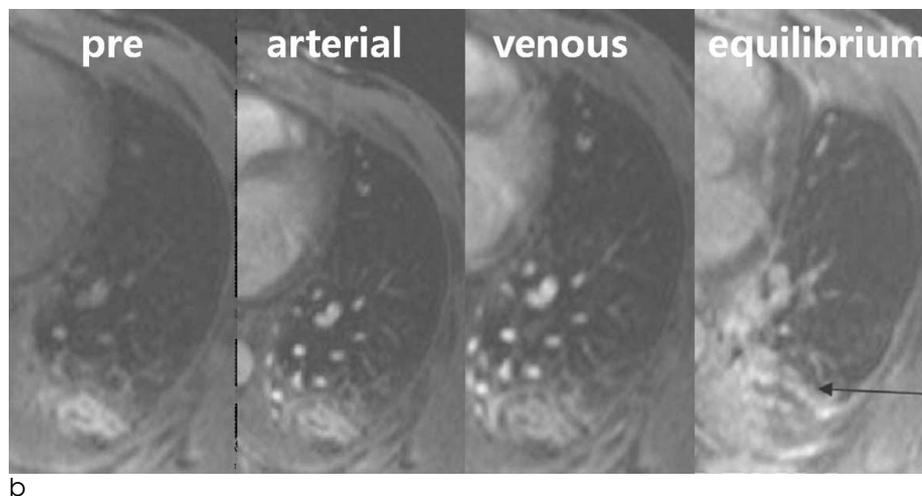


Fig. 2. 46-year-old man with a complete response. He had undergone radiation therapy due to lung malignancy. (a) Chest CT scans (lung setting) before RFA shows a 1 cm, single metastatic nodule in the left lower lobe. (b) On the CE-MRI, the enhancement pattern of the ablated zone leads it to be categorized as type I in the arterial and venous phases. In the equilibrium phase, the enhancement pattern is type II. Enhancement of the hyperemic zone is observed on the equilibrium phases (arrow). (c) Eighteen months later, the previous single metastatic nodule had disappeared completely and a large uniloculated cavity is observed as a post-RFA complication on chest CT (lung setting).



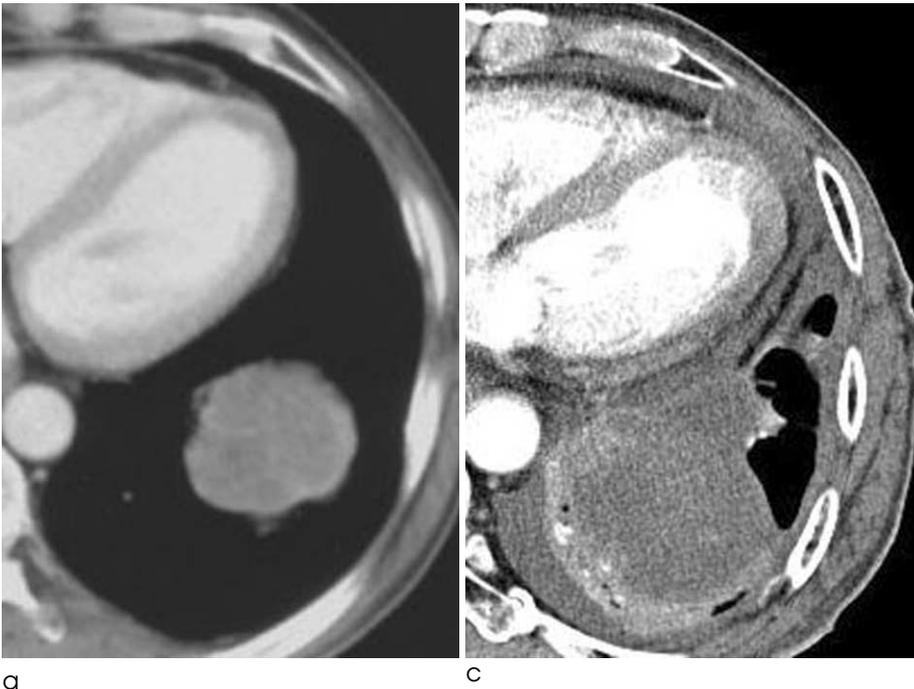
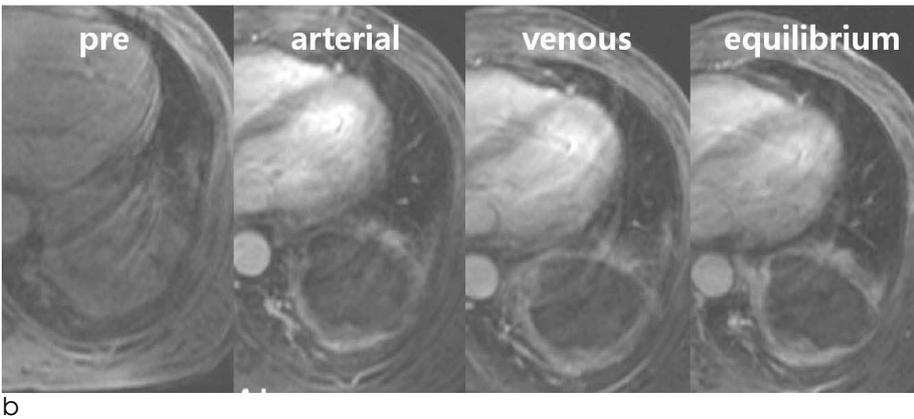


Fig. 3. 62-year-old man with progressive disease. (a) Contrast-enhanced chest CT scans before RFA shows a 6 cm mass in the left lower lobe. (b) On CE-MRI, the enhancement pattern of the ablated zone leads it to be categorized as type II in the arterial and venous phase but the enhancement pattern in the equilibrium phase changes to type III. (c) Eight months later, the tumor size increase approximately 9 cm and completely obstructed the bronchus of the left lower lobe on contrast-enhanced CT.



the enhancement time. In the case of unsuccessfully treated, type II (57.1%) or III (42.9%) pattern observed in the arterial phase. However, types II (21.4%) and III (78.6%) observed in the venous, and types II (7.1%) and III (92.9%) observed equilibrium phases. Sensitivity, specificity, PPV, NPV, and accuracy of local recurrence of ablated lesion on arterial phases of CE-MRI were 100%, 42.9%, 42.9%, 100%, and 60%, respectively. Sensitivity, specificity, PPV, NPV, and accuracy of local recurrence of ablated lesion on venous phases of CE-MRI were 100%, 66.7%, 78.6%, 100%, and 85%, respectively. Sensitivity, specificity, PPV, NPV, and accuracy of local recurrence of ablated lesion on equilibrium phases of CE-MRI were 100%, 85.7%, 92.9%, 100%, and 95%, respectively. The Spearman's

ranked test showed a correlation between local progression and the enhancement pattern of the ablated zone in the arterial, venous, and equilibrium phases, respectively ($r = 0.7$, $r = 0.72$, $r = 0.8$, $p < .05$). Base on these results, we suggested that the equilibrium phase is important in predicting the recurrence after RFA in patients with a lung malignancy than the arterial and venous phase on the CE-MRI.

Discussion

CT is still the main imaging technique for evaluating the treatment response of a lung malignancy after RFA. As another modality for a follow-up post-RFA image,

some authors (15–19) reported that post RFA PET showed virtually no FDG activity in the previous positive areas. In addition, they stated that MRI or dynamic MRI revealed reduced or no enhancement of the ablated zone. These findings corresponded to the early changes in coagulative necrosis on the histopathologic examination in the acute phase after RFA. In this study, although the enhancement pattern of ablated zone in all phase correlated therapeutic response, equilibrium phase CE-MRI provided more information whether the ablated zone would be recurrent lung cancer or not. When type III was observed in the equilibrium phase on multiphase CE-MRI, all patients have been recurred lung malignancy on follow-up CT.

Multiphase CE-MRI has two advantages in evaluating the ablated zone after a RFA treatment for a lung malignancy over contrast-enhanced CT. First, CE-MRI might be superior to contrast-enhanced CT for evaluating the ablated margin and ablated zone because MRI shows superior tissue contrast to CT. The second advantage is that CE-MRI may be useful for evaluating patients who cannot tolerate iodinated contrast agents (10, 11). If contrast-enhanced CT cannot be performed after RFA, there might be some hesitation in using RFA to treat lung malignancies because of the consequent inability to evaluate the therapeutic response. Although PET or PET/CT can provide more detailed information on the ablated zone, this modality is more expensive than CT or MRI. As a result, CE-MRI is recommended as a follow-up image modality for evaluating the ablated zone after RFA in patients with renal failure or an allergy to the CT contrast agent.

An evaluation of the ablated margin and discrimination between the hyperemic zone and remnant tumor using CT, MRI or PET/CT is very important because it is closely associated with the degree of ablation after RFA (3). Hence, attempts should be made to identify any remnant tumor with an ablated margin using imaging modalities. In this study, the important factor for predicting of therapeutic response after RFA was found to be the enhancement patterns on CE-MRI. If the size of the ablated zone was larger than the original tumor, the enhanced region outside of the enveloped low signal rim must be a hyperemic region. Enhancement of the hyperemic region was categorized as type II in this study. In the venous phase on CE-MRI,

patients who showed a type II pattern became complete ablation (62.5%) or unsuccessful treated (37.5%) at the last follow-up CT. Of these patients, 25% patients changed the enhanced pattern to type III on the equilibrium phase CE-MRI, and the tumor size increased on the last follow-up CT. As a result, it is possible to include the remnant tumor within the ablated zone if the enhancement pattern changed from type II to type III on multiphase CE-MRI.

This study had a limitation. There was no comparison of the enhancement pattern of the ablated zone on MRI before and after RFA because pre-RFA MRI was not performed. Therefore, such a comparison will be needed to accurately evaluate the ablated margin and access the therapeutic efficacy after RFA in the future.

In conclusion, CE-MRI is a useful imaging modality for evaluating the ablated zone after RFA. In addition, the equilibrium phase can play a more important role in predicting the recurrence after RFA in patients with a lung malignancy than the arterial or venous phase on the CE-MRI.

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고주파 소작술을 받은 수술이 불가능한 폐암 환자에서 다중위상 조영증강 자기 공명 영상을 이용한 소작 병변의 치료 효과 판정

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목적: 수술이 불가능한 폐암 환자에서 고주파 소작술을 시행한 후 소작 병변의 재발을 예측하기 위해 조영증강 자기 공명 영상상 어떤 시기가 중요한지 알아 보고자 하였다.

대상 및 방법: 수술이 불가능한 폐암 환자 20명에게 고주파 소작술을 시행한 후 조영증강 자기공명 영상을 시행하였다. 소작 병변의 조영 증강 형태는 3가지로 분류했다: type I, 병변이 조영증강이 안됨; type II, 병변의 가장 자리만 조영증강 됨; type III, 병변이 불균일하게 조영증강 됨. Spearman's ranked test를 이용하여 조영증강 형태와 재발 유무와의 관계를 알아 보았다.

결과: 완전 소작 군에서는 type I (11.1%) 또는 type II (88.9%)를 보였다. 성공적으로 치료하지 못한 군에서는 동맥기에 types II (57.1%)와 III (42.9%)를 보였다. 정맥기에는 types II (21.4%)와 III (78.6%)를 보였다. 그러나 평형기에는 types II (7.1%)와 III (92.9%)를 보였다. 평형기의 조영증강 형태가 소작 병변의 재발과 통계적으로 유의하였다 ($r=0.8, p < .05$).

결론: 조영증강 자기공명영상에서 평형기가 소작 병변의 재발 예측에 중요한 역할을 할 것이다.