Lung Radiofrequency Ablation: Post-procedure Imaging Patterns and Late Follow-up

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Abstract

Background: Radiofrequency ablation (RFA) is a safe and effective minimally invasive treatment for primary or secondary malignancies of the lung. This study aims to describe imaging features on chest computed tomography (CT) after RFA of primary and secondary lung tumors, and their frequency over the time after the procedure.

Methods: In this double-center retrospective study, we reviewed 69 patients with primary and secondary lung tumors who underwent percutaneous RFA. Patients were excluded if they had received concomitant radiation therapy or chemotherapy, and if there was no CT follow-up. The imaging features were assessed in four different time points: immediate post-procedure, <4 weeks, 5-24 weeks, 25-52 weeks and >52 weeks. Late follow-up (3 and 5 years after procedure) was assessed clinically in 48 patients.

Results: The study population consisted of 69 patients and 144 pulmonary tumors. Six out of 69 (8.7%) patients had primary lung nodules (stage I) and 63/69 (91.3%) had metastatic pulmonary nodules. Based on per patient analysis, immediately after lung RFA, the most common CT features were consolidation (56/69, 81.1%), reversed halo (55/69, 79.7%), and hyperdensity (47/69, 68.1%). Less than 4 weeks, reversed halo was demonstrated in 19/22 (86.3%) patients, and consolidation and pleural thickening in 17/22 (77.2%). Between 5-24 weeks, 25-52 weeks and after 52 weeks, the most common imaging features were parenchymal bands.

Conclusions: Our study demonstrated the expected CT features after lung RFA, a procedure which use has been progressively growing. Diagnostic and interventional radiologists should be familiar with the expected imaging features immediately after RFA and their change during follow-up in order to avoid misinterpretation and inadequate treatments.

Introduction

Surgical resection is considered the standard of care for the local treatment of primary and metastatic resectable lung tumors (1, 2). However, the minority of the patients are diagnosed in a resectable stage (3) and many patients with resectable disease are high-risk surgical candidates (4). In this scenario, image-guided minimally invasive therapies have emerged as an alternative treatment for lung malignancies either alone or in combination with other treatment modalities, including surgical resection chemotherapy and radiation therapy (1, 2).

Currently, percutaneous lung tumor ablation, which encompass ethanol ablation, laser ablation, cryoablation, irreversible electroporation, radiofrequency ablation (RFA) and microwave ablation (5, 6), is considered a safe and effective minimally invasive treatment for selected patients with primary and secondary lung tumors (7). Most of these procedures can be performed in an outpatient situation and frequently under conscious sedation, thus providing a faster recovery and discharge, when compared with surgery. Furthermore, lung tumor ablation is used as a curative treatment, symptoms relieving, and for cytoreduction purposes (8), improving the efficacy of chemotherapy and/or radiation therapy by causing
tumor cytoreduction, with a minimal impact on normal lung parenchyma and on pulmonary function. That is of key importance in patients with metastatic and/or recurrent disease, since multiple procedures are often necessary during patient’s treatment (9). From these techniques, lung RFA is one of the most commonly used methods, being specially recommended for patients with early stage lung cancer who are unfit for surgery or sublobar lung resection, or in the context of oligometastatic lung disease (10).

Computed tomography (CT) is the most used imaging modality for pre-procedural planning and in the post-ablation follow-up; however, no standard imaging protocol has been established or uniformly accepted for that. There are several imaging features that are expected after lung ablation and which are not related to tumor (4, 11). Therefore, an understanding of the expected imaging features after that procedure is essential to accurate assessment of treatment response (12) and to differentiate normal posttreatment appearances from incomplete treatments and local recurrences (13). In this context, this study aims to describe imaging features on chest CT after lung RFA and their frequency over the time after the procedure.

**Materials And Methods**

**Study population**

In this double-center retrospective study, the Institutional Review Board of both institutions approved the study and waived the requirement for patients’ informed consent. The radiology databases from both institutions were retrospectively queried from January 2007 to January 2014 to identify patients with lung tumors who underwent percutaneous RFA. Patients were excluded if they had received concomitant radiation therapy or chemotherapy, and if there was no CT follow-up.

The final study population consisted of 69 patients with 144 pulmonary masses, 63/69 (91.3%) patients had metastatic tumor and 6/69 (8.7%) had primary lung tumor (stage I) according the histopathology reports.

**Percutaneous lung ablation procedure**

All procedures were performed in an interventional suite with CT fluoroscopy capabilities under general endotracheal anesthesia. Radiofrequency ablation procedures used a Cool-tip™ RFA generator (Covidien, Mansfield, Massachusetts, USA) with single 17G radiofrequency electrode kits (ACT1530/ACT2030) or cluster radiofrequency electrode kits (ACCT1525).

**Image analysis**

Two board-certified radiologists with 3 and 5 years of experience as an attending radiologist reviewed the chest CT examinations and reached a consensus in all cases. The radiologists were blinded to clinical status and histopathological results. Before the beginning of CT readings, the readers were provided by hands-on instructions with the imaging features definitions based on Fleischner Society: glossary of terms for thoracic imaging (14). The imaging features evaluated on chest CT were as following: ground glass
opacity, ground glass opacity with reversed halo sign, hyperdensity, bulla, pneumatocele, pneumothorax, pleural effusion, cavity, consolidation, parenchymal bands and pleural thickening.

Ground glass were defined by increase in the lung parenchyma density preserving the bronchial and vascular margins. When the ground glass opacity was surrounded by a ring of consolidation it was called ground glass opacity with reversed halo. Consolidation was defined as an increased lung density, which obscures underlying bronchial structures and pulmonary vessels. Hyperdensity was characterized by an increase above 15 UH of nodule density in an exam without contrast. Parenchymal bands were defined as a linear opacity, usually 1-3 mm thick and up to 5 cm long, that extends to the visceral pleura. Bulla was defined as an airspace sharply demarcated by a thin wall smaller than 1 mm in thickness, while pneumatocele was defined as a round, thin-walled airspace in the lung and it was reversed for those larger than 1.0 cm. Cavity was defined a gas-filled space within pulmonary consolidation, mass, or nodule, with a wall thicker than 1 mm, and sometimes containing a fluid level. Pleural effusion was defined by a liquid in the pleural space. Others pleural reactions evaluated was pneumothorax, gas in the pleural space, and pleural thickening, focal thickness of parietal or visceral pleura. Figure 1 summarizes the imaging features that were evaluated. The imaging features were assessed in four different time points: immediate post-procedure, <4 weeks, 5-24 weeks, 25-52 weeks and >52 weeks.

Late follow-up

On late follow-up (3 years and 5 years after the procedure), clinical data were collected at each institution from electronic medical records (all medical consultations and hospital admissions were reviewed). For overall survival, time from the initial procedure to last follow-up visit or death from any cause was used. In some cases, phone calls were made to patients (or their relatives) to assess the exact time of overall survival; however, 21 patients were lost to follow-up after 1 year of the procedure.

Statistical analysis

Continuous variables were tested for normality with the Kolmogorov-Smirnov and Shapiro Wilk tests. The values are expressed as mean, median, minimum and maximum values. The categorical data are presented as absolute values and percentages.

Analyses were performed using SPSS 19.0.

Results

The study population consisted of 69 patients and 144 pulmonary masses. Six out of 69 (8.7%) patients had primary lung nodules and 63/69 (91.3%) had metastatic pulmonary nodules. Thirty-seven out of 69 (53.7%) patients were man and 32/69 (46.3%) were woman, with a mean age 56.3 years (range, 26-87). Table 1 summarizes the principal characteristics of nodules and patients included in the sample.

During follow-up after RFA, all patients underwent CT immediately after the procedure. After that, using a per nodule evaluation, 49/144 (34%) were followed < 4 weeks after procedure, 90/144 (62.5%) were
followed between 5-24 weeks, 57/144 (39.6%) were followed between 25-52 weeks, and 30/144 (20.8%) were followed > 52 weeks. Considering a per patient analysis, 22/69 (31.9%) were followed < 4 weeks after RFA, 45/69 (65.2%) were followed between 5-24 weeks, 31/69 (44.9%) were followed between 25-52 weeks, and 18/69 (26.1%) were followed > 52 weeks.

Tables 2 and 3, and Figures 2 and 3 demonstrate the evolution of imaging features during follow-up after lung RFA over different time points considering per nodule (Table 2 and Figure 2) and per patient evaluation (Table 3 and Figure 3).

Based on per nodule analysis, the most common CT imaging features immediately after lung RFA were reversed halo (111/144, 77%), consolidation (87/144, 60.4%), and hyperdensity (71/144, 49.3%). Later on (less than 4 weeks), consolidation (27/49, 55.1%), reversed halo (27/49, 55.1%) and pleural thickening (27/49, 55.1%) were commonly demonstrated in treated areas, while parenchymal bands (20/49, 40.8%), and cavitations (18/49, 36.7%) were less frequently detected. Between 5 and 24 weeks, parenchymal bands were the most common imaging feature (70/90, 77.7%), followed by consolidation (55/90, 61.1%) and pleural thickening (49/90, 54.4%). Between 25 and 52 weeks the most frequent imaging features were parenchymal bands (46/57, 80.7%), followed by consolidation and pleural thickening (26/57, 45.6%). Finally, after 52 weeks, the most common imaging features were parenchymal bands (25/30, 83.3%) and pleural thickening (10/30, 33.3%).

Based on per patient analysis, immediately after the RFA the most common CT imaging features were consolidation (56/69, 81.1%), reversed halo (55/69, 79.7%), and hyperdensity (47/69, 68.1%). Less than 4 weeks, reversed halo was demonstrated in 19/22 (86.3%) patients, and consolidation and pleural thickening in 17/22 (77.2%). Between 5 and 24 weeks, parenchymal bands were the most common imaging feature (41/45, 91.1%), followed by consolidation (33/45, 73.3%) and pleural thickening (29/45, 64.4%). Between 25 and 52 weeks, the most frequent imaging features were parenchymal bands (28/31, 90.3%), followed by consolidation and pleural thickening (16/31, 51.6%). Finally, after 52 weeks, the most common imaging features were parenchymal bands (17/19, 94.4%) and pleural thickening (7/18, 38.8%).

Regarding the long-term follow up, 48 patients were clinically followed for 5 years after procedure. Local recurrence was described in 12 cases (25%) and a repeat ablation was performed once in 4 of these patients, and twice in 1 patient. The three- and five-year overall survival rates after procedure were 54% and 33%, respectively.

**Discussion**

In our study population, we found that hyperdensity within the treated area is present predominantly immediately after lung RFA. Bulla, reversed halo with ground glass opacity, cavitation, pneumatocele, and pleural effusion were mostly detected less than 4 weeks after the procedure. Consolidation within the treated area and pleural thickening were detected from immediately after to more than 52 weeks after lung RFA, but most frequently less than 52 weeks. The frequency of parenchymal bands increased progressively over the time of follow-up.
Our results are in line with previous studies which demonstrated higher frequency of consolidation, mainly in the early follow-up, and higher frequency of fibrotic chances, such as parenchymal bands, on late follow-up CT (15, 16). Some imaging findings were almost exclusively detected on immediate post ablation CT, such as hyperdensity of the treated lesion and bulla. On the other hand, others findings including ground glass opacity with reversed halo and consolidations have a major clinical relevance, considering that their area and margins may be an early indicator of treatment success (17). Some studies have demonstrated better results when the ground glass opacity extended more than 5 mm of the treated nodule, with extremely low frequency of local recurrence (15, 18, 19). However, the area of ground glass opacity usually overestimates the genuine size of the zone of cell death induced by ablation. Besides that, ground glass opacity and consolidation may be misinterpreted as tumor recurrence and infection. Therefore, correlations with clinical symptoms, laboratorial findings and evolution during follow-up are of key importance. Furthermore, the size of the consolidation may increase during the first 3 months after RFA and should not be deemed as recurrence (12). Conversely, any enlargement after 3 months should be suspicious of recurrence and need to be investigated (20-22). When CT findings are unexpected and suggestive of tumor progression at the ablation zone or when new signs of local-regional spread are discovered during restaging, PET-CT can be used as an auxiliary imaging method (12), however, there is no sufficient evidence to support its role in the earlier recurrence detection (10).

Cavitation and pneumatocele were imaging features found predominantly during early follow-up and there was a tendency to not be demonstrated after 6 months. In this scenario, cavitation should not be misinterpreted as an abscess and, again, the correlation with clinical and laboratorial findings is essential. Nevertheless, fungus ball (aspergilloma) within the cavitation was described after RFA (23).

Pleural reactions such as effusion and thickening were also common findings. Pleural effusion mainly during early follow-up and pleural thickening in all time points. If loculated pleural effusion, persistent and large volumes are present aseptic pleuritis should be considered. Kashima et al found that 2.3% of patients after RFA had aseptic pleuritis as a complication (20). Parenchymal bands were predominantly found on late follow-up and suggest a successful treated nodule.

Regarding the clinical late follow-up, our local recurrence and overall survival rates are aligned with the recent literature (24-28), endorsing the current understanding that RFA is a safe and effective treatment with a survival benefit for selected patients with primary and secondary lung tumors (29, 30). Unfortunately, after the first-year procedure, CT imaging follow-up was not available in the electronic medical records of many of the patients in our sample and, for this reason, the frequency of the CT findings was not evaluated.

There are some limitations in our retrospective study, such as a small sample size and the CT during the follow-up was not performed at the same time points. Moreover, two radiologists evaluated the imaging features in consensus and, therefore, inter-reader agreement was not evaluated. Besides that, a sub analysis comparing the CT findings in primary versus secondary tumors was not performed, considering the unbalanced number of each group. Also, clinical and pathological correlations are beyond the scope of
this study. Further prospective studies, integrating multimodal imaging and artificial intelligence tools are needed to overcome these limitations and to provide a better generalization of our results.

In conclusion, our study demonstrated the expected imaging features on CT after RFA. Diagnostic and interventional radiologists should be familiar with the expected imaging features immediately after RFA and their change during follow-up in order to avoid misinterpretation and inadequate treatment.

List Of Abbreviations

CT: Computed tomography
RFA: Radiofrequency ablation

Declarations

- Ethics approval and consent to participate: The Institutional Review Board of both institutions approved the study and waived the requirement for patients’ informed consent.
- Consent for publication: Not applicable.
- Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
- Competing interests: The authors declare that they have no competing interests.
- Funding: No funding.
- Authors' contributions: RSAM and JABA contributed equally to this study, contributed to all aspects of research process and wrote the manuscript. PSBP, JPJB and RSD performed data collection and analysis. MRM and JPJB performed the percutaneous lung ablation procedures. NH and BCO performed statistical analysis and revised the paper. All authors read and approved the final manuscript.
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**Tables**

**Table 1.** Characteristics of the nodules and patients included in the sample.
| Age (years) mean (SD) | 56.3 (± 23.4) |
|-----------------------|---------------|
| Gender                |               |
| Woman                 | 32 (46.3%)    |
| Man                   | 37 (53.7%)    |
| Histopathologic diagnosis |         |
| Primary lung cancer   | 6 (8.7%)      |
| Metastasis            | 63 (91.3%)    |
| Number of nodules     | 144           |
| Tumor diameter (cm) mean (SD) | 2.1 (± 1.3) |
| Nodule location       |               |
| Central               | 51 (35.4%)    |
| Peripheral with pleural base | 51 (35.4%) |
| Peripheral without pleural base | 42 (29.2%) |

*SD: standard deviation*

**Table 2.** Distribution of the imaging features among the different time points using per nodule evaluation.
|                  | Immediate (n=144) | <4 weeks (n=49) | 5-24 weeks (n=90) | 25-52 weeks (n=57) | >52 weeks (n=30) |
|------------------|------------------|-----------------|-------------------|-------------------|-----------------|
| Bulla            | 52/144 (36.1%)   | 13/49 (26.5%)   | 11/90 (12.2%)     | 1/57 (1.7%)       | 0/30 (0%)       |
| Consolidation    | 87/144 (60.4%)   | 27/49 (55.1%)   | 55/90 (61.1%)     | 26/57 (45.6%)     | 6/30 (20%)      |
| Reversed Halo    | 111/144 (77.0%)  | 27/49 (55.1%)   | 5/90 (5.5%)       | 0/57 (0%)         | 0/30 (0%)       |
| Hyperdensity     | 71/144 (49.3%)   | 5/49 (10.2%)    | 2/90 (2.2%)       | 0/57 (0%)         | 1/30 (3.3%)     |
| Cavitation       | 4/144 (2.7%)     | 18/49 (36.7%)   | 23/90 (25.5%)     | 4/57 (7.0%)       | 2/30 (6.6%)     |
| Pneumatocele     | 26/144 (18.0%)   | 8/49 (16.3%)    | 6/90 (6.6%)       | 2/57 (3.5%)       | 1/30 (3.3%)     |
| Parenchymal Bands| 27/144 (18.7%)   | 20/49 (40.8%)   | 70/90 (77.7%)     | 46/57 (80.7%)     | 25/30 (83.3%)   |
| Pleural Effusion | 40/144 (27.7%)   | 10/49 (20.4%)   | 5/90 (5.5%)       | 3/57 (5.2%)       | 1/30 (3.3%)     |
| Pleural Thickening| 63/144 (43.7%)  | 27/49 (55.1%)   | 49/90 (54.4%)     | 26/57 (45.6%)     | 10/30 (33.3%)   |

**Table 3.** Distribution of the imaging features among the different time points using per patient evaluation.
|                          | Immediate (n=69) | <4 weeks (n=22) | 5-24 weeks (n=45) | 25-52 weeks (n=31) | >52 weeks (n=18) |
|--------------------------|------------------|-----------------|-------------------|-------------------|----------------|
| Bulla                    | 41/69 (59.4%)    | 14/22 (63.4%)   | 10/45 (12.2%)     | 1/31 (3.2%)       | 0/18 (0%)      |
| Consolidation            | 56/69 (81.1%)    | 17/22 (77.2%)   | 33/45 (73.3%)     | 16/31 (51.6%)     | 4/18 (22.2%)   |
| Reversed Halo            | 55/69 (79.7%)    | 19/22 (86.3%)   | 4/45 (8.8%)       | 0/31 (0%)         | 0/18 (0%)      |
| Hyperdensity             | 47/69 (68.1%)    | 4/22 (18.1%)    | 2/45 (4.4%)       | 0/31 (0%)         | 1/18 (5.5%)    |
| Cavitation               | 4/69 (5.8%)      | 12/22 (54.5%)   | 13/45 (28.8%)     | 4/31 (12.9%)      | 2/18 (11.1%)   |
| Pneumatocele             | 19/69 (27.5%)    | 7/22 (31.8%)    | 6/45 (13.3%)      | 2/31 (6.4%)       | 1/18 (5.5%)    |
| Parenchymal Bands        | 18/69 (26.0%)    | 12/22 (54.5%)   | 41/45 (91.1%)     | 28/31 (90.3%)     | 17/18 (94.4%)  |
| Pleural Effusion         | 30/69 (43.4%)    | 7/22 (31.8%)    | 5/45 (11.1%)      | 3/31 (9.6%)       | 1/18 (5.5%)    |
| Pleural Thickening       | 43/69 (26.0%)    | 17/22 (77.2%)   | 29/45 (64.4%)     | 16/31 (51.6%)     | 7/18 (38.8%)   |

**Figures**
Illustration with some of the computed tomography imaging features evaluated in our study: bulla, pneumatocele, hyperdensity (increase of density) within the nodule, cavitation, pleural effusion, consolidation, pleural thickening, and parenchymal bands.
Figure 2

Graphic demonstrating the frequency of the imaging features on chest computed tomography after lung radiofrequency tumor ablation on different time points using per nodule evaluation.
Figure 3

Graphic demonstrating the frequency of the imaging features on chest computed tomography after lung radiofrequency tumor ablation on different time points using per patient evaluation.