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Lung radiofrequency ablation: post-procedure imaging patterns and late follow-up

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HIGHLIGHTS

- RFA is an effective minimally invasive treatment for selected patients with primary and secondary lung tumors.
- We described the expected imaging features after RFA of lung tumors, and their frequency over time after the procedure.
- Radiologists should be familiar with these features in order to avoid misinterpretation and inadequate treatments.
- These normal post-procedure imaging features must be considered in future post-ablation follow-up protocols.

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ABSTRACT

Purpose: To describe expected imaging features on chest computed tomography (CT) after percutaneous radiofrequency ablation (RFA) of lung tumors, and their frequency over time after the procedure.

Methods: In this double-center retrospective study, we reviewed CT scans from patients who underwent RFA for primary or secondary lung tumors. Patients with partial ablation or tumor recurrence during the imaging follow-up were not included. The imaging features were assessed in pre-defined 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 (9%) patients had primary lung nodules (stage I) and 63/69 (91 %) had metastatic pulmonary nodules. In a patient-level analysis, immediately after lung RFA, the most common CT features were ground glass opacities (66/69, 96 %), consolidation (56/69, 81 %), and hyperdensity within the nodule (47/69, 68 %). Less than 4 weeks, ground glass opacities (including reversed halo sign) was demonstrated in 20/22 (91 %) patients, while consolidation and pleural thickening were detected in 17/22 patients (77 %). Cavitation, pneumatocele, pneumothorax and pleural effusions were less common features. From 5 weeks onwards, the most common imaging features were parenchymal bands.

Conclusions: Our study demonstrated the expected CT features after lung RFA, a safe and effective minimally invasive treatment for selected patients with primary and secondary lung tumors. Diagnostic and interventional radiologists should be familiar with the expected imaging features immediately after RFA and their change over time in order to avoid misinterpretation and inadequate treatments.

Abbreviations: CT, Computed tomography; PET-CT, Positron emission tomography – computed tomography; RFA, Radiofrequency ablation; HU, Hounsfield units.

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1. 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 radiofrequency ablation (RFA), microwave ablation, cryoablation and irreversible electroporation [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 has been used as a curative treatment and for symptoms relieving 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 [4,11,12], whose understanding and interpretation are essential for an accurate assessment of treatment response and to differentiate normal posttreatment appearances from incomplete treatments and local recurrences [13]. In this context, this study aims to describe expected imaging features on chest CT after lung RFA and their frequency over time after the procedure.

2. Materials and methods

2.1. Study design

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 with available imaging follow-up.

From 109 patients initially selected, 40 patients were excluded if: they have received concomitant radiation therapy or chemotherapy or if they showed any imaging features suggestive of partial ablation or tumor recurrence, as previously described [12], during the imaging follow-up (0–58 weeks). Sixty-nine patients were identified with complete CT imaging follow-up in five different time points: immediate post-procedure, ≤4 weeks, 5−24 weeks, 25−52 weeks and ≥52 weeks.

In the late follow-up (3 years and 5 years after the procedure) of this sample (n = 69), only clinical follow-up was performed. 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, some patients were lost to follow-up after first year of the procedure.

2.2. 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 17 G radiofrequency electrode kits (ACT1530/ACT2030).

2.3. Image and data 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 and considered imaging features definitions based on Fleischner Society: glossary of terms for thoracic imaging [14]. The imaging features evaluated on chest CT (Fig. 1) were as following: ground glass opacity, hyperdensity within the nodule, pneumatocele, cavity, consolidation, parenchymal bands, pneumothorax, pleural effusion and pleural thickening.

Ground glass were defined by an increase in the perilesional parenchyma density preserving the bronchial and vascular margins. When the ground glass opacity was surrounded by a ring of consolidation it was considered a reversed halo sign. Consolidation was defined as an increased lung density, which obscures underlying bronchial structures and pulmonary vessels. Hyperdensity was characterized by an increase above 15 HU (Hounsfield units) 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. Pneumatocele was defined as a thin-walled, gas-filled space in the lung. 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 as a liquid in the pleural space, pneumothorax as gas within the pleural space and pleural thickening as any focal thickness of parietal or visceral pleura.

Qualitative features were assessed visually and were recorded in a binary system (present/absent). Different imaging features were assessed at 2 levels, including separate tumor-level and patient-level analyses. The categorical data were presented as absolute values and percentages. The values were expressed as mean, median, minimum and maximum values. Analyses were performed using SPSS v19.0.

3. Results

The study population consisted of 69 patients and 144 pulmonary nodules. From these, 63/69 (91 %) patients had metastatic tumor and 6/69 (9%) had primary lung tumor (stage I) according the histopathology reports. Six out of 69 (9%) patients had primary lung nodules and 63/69 (91 %) had metastatic pulmonary nodules. Thirty-seven out of 69 (54 %) patients were man and 32/69 (46 %) 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.

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 %) were followed between 5−24 weeks, 57/144 (40 %) were followed between 25−52 weeks, and 30/144 (21 %) were followed ≥ 52 weeks. Considering a per patient analysis, 22/69 (32 %) were followed ≤ 4 weeks after RFA, 45/69 (65 %) were followed between 5−24 weeks, 31/69 (45 %) were followed between 25−52 weeks, and 18/69 (26 %) were followed ≥ 52 weeks. From the 185 CT scans included, only 16 (8.6 %) were performed after contrast injection (6 between 25/52 weeks and 10 after 52 weeks).

Tables 2 and 3, and Figs. 2 and 3 demonstrate the evolution of imaging features during imaging follow-up over different time points considering tumor-level (Table 2 and Fig. 2) and patient-level (Table 3 and Fig. 3) analyses.

Based on tumor-level analysis, the most common CT imaging

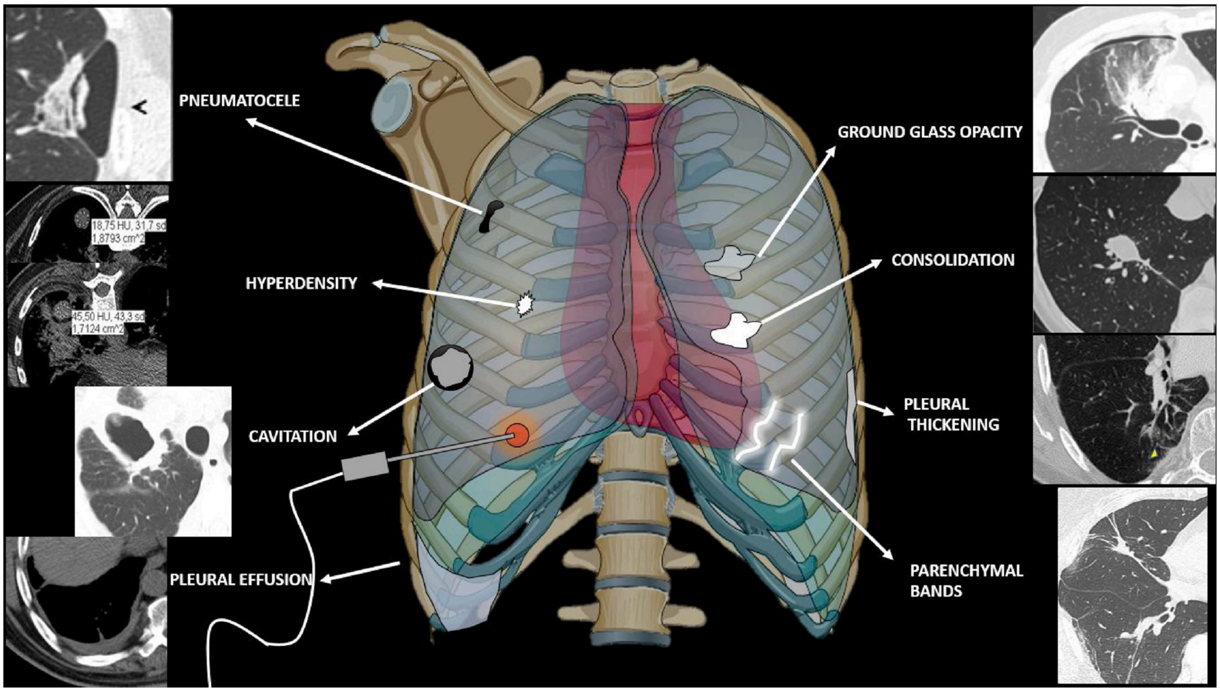

Fig. 1. Illustration with some of the computed tomography imaging features evaluated in our study: pneumatocele, hyperdensity (increase of density) within the nodule, cavitation, pleural effusion, ground glass opacity, consolidation, pleural thickening, and parenchymal bands.

Table 1
Characteristics of the nodules and patients included in the sample.

Characteristics	Values
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 in a tumor-level analysis.

CT features	Immediate (n = 144)	≤4 weeks (n = 49)	5–24 weeks (n = 90)	25–52 weeks (n = 57)	≥52 weeks (n = 30)
Consolidation	87/144 (60 %)	27/49 (55 %)	55/90 (61 %)	26/57 (46 %)	6/30 (20 %)
Ground-glass opacities	136/144 (94 %)	42/49 (86 %)	33/90 (37 %)	12/57 (21 %)	5/30 (17 %)
Hyperdensity	71/144 (49 %)	5/49 (10 %)	2/90 (2%)	0/57 (0%)	0/30 (0%)
Cavitation	4/144 (3%)	18/49 (37 %)	23/90 (25 %)	4/57 (7%)	2/30 (7%)
Pneumatocele	26/144 (18 %)	8/49 (16 %)	6/90 (7%)	2/57 (4%)	1/30 (3%)
Parenchymal Bands	27/144 (19 %)	20/49 (41 %)	70/90 (78 %)	46/57 (81 %)	25/30 (83 %)
Pleural Thickening	63/144 (44 %)	27/49 (55 %)	49/90 (54 %)	26/57 (46 %)	10/30 (33 %)

Table 3
Distribution of the imaging features among the different time points in a patient-level analysis.

CT features	Immediate (n = 69)	≤4 weeks (n = 22)	5–24 weeks (n = 45)	25–52 weeks (n = 31)	≥52 weeks (n = 18)
Consolidation	56/69 (81 %)	17/22 (77 %)	33/45 (73 %)	16/31 (52 %)	4/18 (22 %)
Ground-glass opacities	66/69 (96 %)	20/22 (91 %)	18/45 (40 %)	8/31 (26 %)	4/18 (22 %)
Hyperdensity	47/69 (68 %)	4/22 (18 %)	2/45 (4%)	0/31 (0%)	0/18 (0%)
Cavitation	4/69 (6%)	12/22 (54 %)	13/45 (29 %)	4/31 (13 %)	2/18 (11 %)
Pneumatocele	19/69 (27 %)	7/22 (32 %)	6/45 (13 %)	2/31 (6%)	1/18 (5%)
Parenchymal Bands	18/69 (26 %)	12/22 (54 %)	41/45 (91 %)	28/31 (90 %)	17/18 (94 %)
Pleural Effusion	30/69 (43 %)	7/22 (32 %)	5/45 (11 %)	3/31 (10 %)	1/18 (5%)
Pleural Thickening	43/69 (26 %)	17/22 (77 %)	29/45 (64 %)	16/31 (52 %)	7/18 (39 %)
Pneumothorax	20/69 (29 %)	6/22 (27 %)	2/45 (4%)	0/31 (0%)	0/31 (0%)

features immediately after lung RFA were perilesional ground-glass opacities (136/144, 94 %), consolidation (87/144, 60 %), and hyperdensity (71/144, 49 %). Later on (less than 4 weeks), ground glass opacities (42/49, 86 %; including reversed halo in 16 nodules) consolidation (27/49, 55 %), and adjacent pleural thickening (27/49, 55 %) were commonly demonstrated in treated areas; while parenchymal bands (20/49, 41 %), and cavitations (18/49, 37 %) were less frequently detected. Between 5 and 24 weeks, parenchymal bands were the most common imaging feature (70/90, 78 %), followed by consolidation (55/90, 61 %) and pleural thickening (49/90, 54 %). Between 25 and 52 weeks the most frequent imaging features were parenchymal bands (46/57, 81 %), followed by consolidation and pleural thickening (26/57, 45 %). Finally, after 52 weeks, the most common imaging features were parenchymal bands (25/30, 83 %) and pleural thickening (10/30, 33

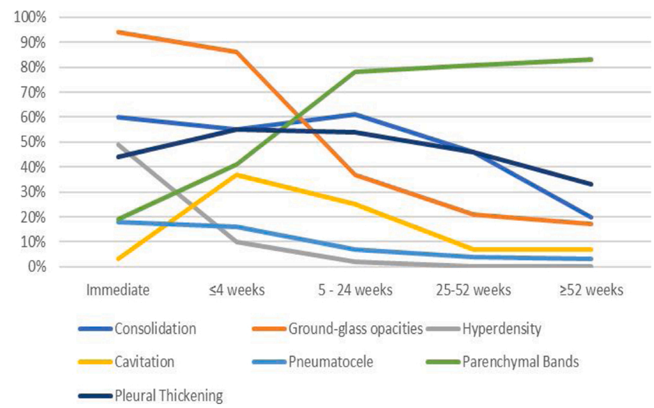

Fig. 2. Graphic demonstrating the frequency of the imaging features on chest computed tomography after lung radiofrequency tumor ablation on different time points using per nodule evaluation.

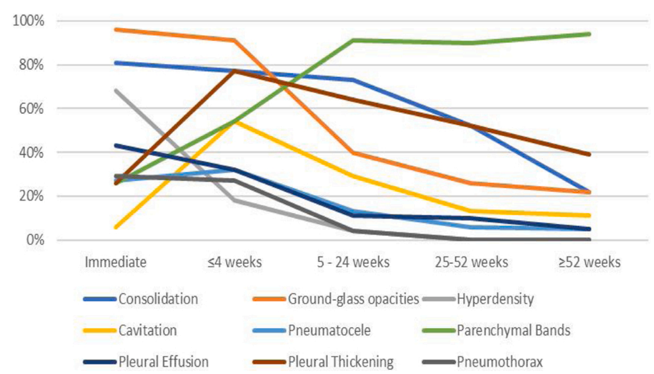

Fig. 3. Graphic demonstrating the frequency of the imaging features on chest computed tomography after lung radiofrequency tumor ablation on different time points using per patient evaluation.

%).

Based on patient-level analysis, immediately after the RFA the most common CT imaging features were ground glass opacities (66/69, 96 %), consolidation (56/69, 81 %) and hyperdensity (47/69, 68 %). Of note, pleural effusion and pneumothorax were detected in 30 (43 %) and 20 (27 %) patients, respectively. Only small pneumothoraxes / pleural effusions were detected. Less than 4 weeks, ground glass opacities (including reversed halo) was demonstrated in 20/22 (91 %) patients, and consolidation and pleural thickening in 17/22 (77 %). Between 5 and 24 weeks, parenchymal bands were the most common imaging feature (41/45, 91 %), followed by consolidation (33/45, 73 %) and pleural thickening (29/45, 64 %). Between 25 and 52 weeks, the most frequent imaging features were parenchymal bands (28/31 90 %), followed by consolidation and pleural thickening (16/31, 52 %). Finally, after 52 weeks, the most common imaging features were parenchymal bands (17/18, 94 %) and pleural thickening (7/18, 39 %).

Regarding the long-term follow up, 48 patients were clinically followed for 5 years. After the first-year procedure, local recurrence was described in 12 cases (25 %) and a repeated 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.

4. Discussion

We described the most common expected imaging features on chest CT imaging after RFA of primary and secondary lung tumors, including a late clinical follow-up longer the average of previous studies, corroborating the clinical safety of this procedure. The frequency of perilesional ground-glass opacities decreased progressively over time of follow-up, while parenchymal bands presented the inverse behavior. Other imaging features as hyperdensity, cavitation, pneumatocele, and pleural effusion were mostly detected less than 4 weeks after the procedure, while consolidation within the treated area and pleural thickening were detected from immediately after to more than 52 weeks after lung RFA.

Our results are in line with previous studies which demonstrated higher frequency of ground-glass opacities and consolidations, mainly in the early follow-up, and higher frequency of fibrotic chances, such as parenchymal bands, on late follow-up CT [15,16]. In the first week after procedure (early phase), perilesional ground grass opacities are considered an early indicator of treatment success [17], in correlation with coagulation necrosis of tumor within the ablation zone [18]. 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 [15,19,20]. However, the area of ground glass opacity can overestimate the genuine size of the zone of cell death induced by ablation, as detected in animal models [12,21], which can be misinterpreted as tumor recurrence and infection. Therefore, correlations with clinical symptoms, laboratorial findings and evolution during follow-up are of key importance. Noteworthily, the size of the consolidation may increase during the first 3 months after RFA and should not be deemed as recurrence [22]. Conversely, any enlargement after 3 months should be suspicious of recurrence and need to be investigated [12,23,24]. 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 (Positron emission tomography – computed tomography) can be considered as an auxiliary (not mandatory) imaging method [22], however, there is no sufficient evidence to support its role in the earlier recurrence detection [10].

In our sample, cavitation and pneumatocele were transitory imaging features found predominantly during early follow-up and there was a tendency to not be demonstrated after 6 months. While pneumatocele could be associated with intense tumor ablation and favorable initial local tumor control, cavitation should not be misinterpreted as an abscess and, again, the correlation with clinical and laboratorial findings is essential. In current literature, fungus ball (aspergilloma) within the cavitation was rarely described after RFA, when the characteristic central soft-tissue attenuating content (frequently surrounded by a crescent of air) is considered essential for the diagnosis [25].

Pleural reactions were also common findings, being pleural effusion mainly detected during early follow-up and pleural thickening in all time points. Of note, only small pleural effusions were identified. It's important to emphasize that 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 rare complication [23]. Pneumothorax was detected almost exclusively in the first 4 weeks after procedure and its incidence was slightly smaller than previous studies [12].

Regarding the clinical late follow-up, our local recurrence and overall survival rates are aligned with the recent literature [26–30], 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 [31,32]. 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 this descriptive retrospective study, such as a small sample size and the lack of standardization in the timepoints during imaging follow-up, based in large intervals. 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.

Of note, local recurrence features 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 changes during follow-up in order to avoid misinterpretation and inadequate treatments. These normal post-procedure imaging features and their changes over time must be considered in future post-ablation follow-up protocols.

Ethical approval

The Institutional Review Board of both institutions approved the study and waived the requirement for patients' informed consent.

Funding sources

No fundings were related to this study.

CRediT authorship contribution statement

Jose de Arimateia Batista Araujo-Filho: Writing - original draft, Data curation. **Raonne Souza Almeida Alves Menezes:** Writing - original draft, Data curation. **Natally Horvat:** Methodology, Writing - review & editing. **Pedro Sergio Brito Panizza:** Visualization, Investigation. **João Paulo Giacomini Bernardes:** Visualization, Investigation. **Rodrigo Sanford Damasceno:** Visualization, Investigation. **Brunna Clemente Oliveira:** Data curation, Writing - review & editing. **Marcos Roberto Menezes:** Conceptualization, Investigation, Supervision.

Declaration of Competing Interest

The authors have no competing interests to declare.

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