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Original Article

Pulmonary changes after single dose interstitial brachytherapy for lung tumors

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ABSTRACT

PURPOSE: The reaction of lung tissue to extreme single brachytherapy doses have not been analyzed in the past.

METHODS: Overall, 46 lung tumors were treated in 32 patients with HDR (high dose rate) brachytherapy (median dose 20Gy). Treatment planning (n = 46) and follow up CT images (n = 154) performed up to 60 months after brachytherapy were evaluated.

RESULTS: The long-term local tumor control was 81%. Pneumonitis was classified as grade 1, 2 and 3 in 26 (57%), 4 (9%) and 3 (7%). Early changes include spotted consolidation in the majority and ground glass opacity in about 40% of patients within the first six months. Partial atelectasis or pleural effusion were observed in 10–20%, respectively.

In the period after 6 months, streaky or dense consolidation were noted in the majority of follow-up images. The lung tissue consolidation progresses into retraction. Lung atelectasis occurred in about 10% of patients. Pleural effusion was noted more rarely.

CONCLUSION: As a result of high focal doses in one fraction, tissue consolidation must be expected in all patients, with progressive retraction predominantly in the second year after brachytherapy. There is a smaller risk of partial atelectasis and pleural effusion. © 2026 The Author(s). Published by Elsevier Inc. on behalf of American Brachytherapy Society. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Keywords: HDR brachytherapy; Lung tumors; Fibrosis; Radiologic changes

Introduction

Brachytherapy is a highly conformal radiotherapy technique in which a radioactive source is placed directly within or adjacent to the tumor, allowing for high-dose delivery while sparing surrounding organs (1,2). The low-dose areas are considerably lower, but extremely high-dose areas higher in comparison to external beam radiotherapy (EBRT) or stereotactic body radiotherapy (SBRT), which is the current standard technique in patients with inoperable lung tumors or metastases. Interstitial brachytherapy has emerged as a promising alternative to surgical resection or SBRT, particularly due to its favorable toxicity profile and potential for single-session treatment (2–4).

Despite encouraging local tumor control rates of up to 84% after 1 year (2), post-treatment imaging remains a diagnostic challenge. As with other local ablative therapies, radiation-induced lung changes may mimic tumor recurrence on follow-up computed tomography (CT) scans, complicating the interpretation of treatment response (5–7). While the evolution of radiologic findings after SBRT is well characterized and follows a predictable temporal pattern of an initial period of mostly normal findings, followed by acute changes such as spotted or streaky consolidations

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Abbreviations: CT, computed tomography; EBRT, external beam radiotherapy; FDG-PET, fluorodeoxyglucose-positron emission tomography; GTV, gross tumor volume; HDR, high-dose-rate; PTV, planning target volume; SBRT, stereotactic body radiotherapy.

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within months and later chronic fibrotic remodeling confined to the high-dose region (7–9), the radiologic changes after interstitial brachytherapy have not been systematically described.

This retrospective study aims to investigate the temporal evolution of CT-based pulmonary changes following interstitial brachytherapy for lung tumors. We aim to identify common imaging patterns and assess their association with clinical outcomes. The knowledge of these changes over time is important to interpret CT images receiving high-dose radiotherapy treatments.

Methods and material

Study design and patient selection

This retrospective, single center study included 32 patients who underwent CT-guided high-dose-rate (HDR) interstitial brachytherapy for malignant lung tumors or pulmonary metastases between 2014 and 2022, involving a total of 46 treated lung lesions. Indications included medically inoperable primary lung cancer (n = 9) and pulmonary metastases from other malignancies (n = 23), most commonly colorectal carcinoma (n = 8) and sarcoma (n = 4).

Brachytherapy was offered to patients with oligometastatic or oligoprogressive metastatic disease, provided that the lung lesions were accessible for CT-guided percutaneous catheter implantation. The choice of treatment modality was made considering both the referral structures, physician's clinical judgment and the patient's preferences. Important aspects were treatment duration (SBRT not used as single fraction treatment), conformality of dose distribution and limited treatment volume (needles moving with target during respiration, thus no additional safety margins needed). Patients with severely restricted lung function were excluded.

The majority of patients (75%) received only a single pulmonary brachytherapy treatment for a single lesion. Five patients (16%) underwent treatment for two lesions. Two patients (6%) received treatment for three lesions. One patient (3%) underwent two sessions, each involving three lesions, resulting in a total of six treated lesions. This patient was the only patient who received a treatment for more than a single lesion on a single day.

This retrospective study was conducted in accordance with the Declaration of Helsinki. Informed consent for the treatment was obtained from all patients. Formal ethical approval was waived by the local ethics committee due to the retrospective nature of the analysis according to the local legal regulations.

Brachytherapy procedure

Under sedation with local anesthesia and CT guidance, percutaneous plastic catheters (Oncosmart ProGuide, 6F, 200 mm length, Nucletron, The Netherlands) were inserted using a rigid obturator (Onco-Smart ProGuide Obturator, Nucletron, Veenendaal, The Netherlands). The number and positioning of catheters was chosen based on tumor size and geometry. The treatment technique has been described in detail in prior publications (1,2). Treatment planning was performed using the Eclipse 15.1 system (Varian Medical Systems, Palo Alto, CA).

The prescription dose was applied in a single fraction, with a dose constraint of maximum dose $\leq$8 Gy for the heart, spinal cord, and esophagus, $\leq$20 Gy for the main bronchi, trachea and thoracic wall (ribs). The planning target volume (PTV) corresponded to the gross tumor volume (GTV) without margins.

Follow-up and imaging

CT scans were scheduled at 6, 12 weeks and 6 months post-treatment and subsequently every 6 months. The actual timing could vary slightly, depending on the individual clinical situation and other logistical factors. A total of 154 follow-up CT scans (mean 4.8 per patient) were available for analysis. The CT images were classified into different follow-up intervals: 6 weeks (n = 34), >6 weeks–3 months (n = 21), >3–6 months (n = 24), >6–12 months (n = 26), 12–18 months (n = 16), >18 months (n = 33).

Imaging analysis

Radiologic changes were categorized based on the classification described by Takeda *et al.* and later also used by Guckenberger *et al.* (7,8). Early changes included ground-glass opacities and spotted consolidation, indicative of radiation pneumonitis. Findings such as streaky or dense consolidations and evidence of lung retraction were considered late changes, typically associated with the development of pulmonary fibrosis. Local tumor control was defined as volume reduction of the irradiated lesion.

The analysis considered the development of a pneumothorax, pleural effusion, partial or complete atelectasis, inflammatory or streaky changes along the bronchial tree, acute changes in the first 6 months classified as ground glass opacity and spotted consolidation and late changes after more than 6 months classified as streaky consolidation, dense consolidation and retraction.

In case of a pneumothorax, the apical and lateral extensions were measured, defined as the distance of lung tissue to the normal lung apex and the distance of lung tissue to the lateral thoracic wall, respectively. These dimensions are relevant for the decision to place a drainage, with a pneumothorax <1 cm usually not requiring an intervention.

Lesions have been classified as central, if they were located within 2 cm of central bronchial structures. Pneumonitis after brachytherapy was classified as grade 1 (only radiographic changes), grade 2 (steroid treatment needed),

grade 3 (oxygen needed) and grade 4 (inhalation needed) according to the Southwest Oncology Group classification (10).

Results

A single fraction with a median prescribed dose of 20 Gy (range 15–30 Gy, 20 Gy in 70% and 25 Gy in 24%) to the PTV was applied using a median number of two needles (range 1–8). Median PTV was 22.5 cm^3 (range 2–423 cm^3, interquartile range 7.9–58 cm^3).

The patient population (n = 32) included 16 male and 16 female patients with a median age of 66 years with a median overall survival of 16 months after brachytherapy. The lung lesions treated were classified as central in 29 (63%) and peripheral in 17 (37%) cases. The median distance to the carina was 7.3 cm (range 0.3–13 cm), the median distance to the thoracic wall 0.5 cm (range 0–6 cm) and the median distance to the mediastinum 1.0 cm (0–9 cm).

The actual median dose in 95% of the PTV (D95%) was 20.6 Gy (interquartile range 13.6–24.0 Gy) and the median dose in 10% of the PTV (D10%) was 117 Gy (interquartile range 75–148 Gy). The median mean dose to the ipsilateral lung was 3.7 Gy (interquartile range 2.2–5.3 Gy) and the dose to 10% of the ipsilateral lung volume (V10) 5.8 Gy (interquartile range 2.8–6.8 Gy). The median maximum dose to 2% of the contoured thoracic wall (D2%) was 11 Gy (interquartile range 8.8–17 Gy).

The 2-year local tumor control was 81%, remaining at 81% until the maximum follow-up period of 62 months. The single patient who was treated with more than a single lesion at the same day was excluded from the local control analysis. He received a treatment for oligoprogression in colorectal cancer for three lesions at the same day and again for three lesions 3 months later. He developed a fulminant pulmonary tumor progression 6 months after brachytherapy.

In the treatment planning CT after the intervention, a pneumothorax was observed in 15 (33%) of cases. An apical extension was not detectable in three (7%), >0–1 cm in 10 (22%) and >1 cm in two (4%) cases (maximum 5.3 cm). The lateral extension was <1 cm in nine (20%) and >1 cm in four (9%) cases (maximum 2.9 cm). An intervention (drainage) was required in seven (15%) cases. All interventions for a pneumothorax were completed successfully.

Figures 1 and 2 demonstrate pulmonary changes in two patients with follow-up CT scans up to about 5 years after brachytherapy.

Pneumonitis in the months following brachytherapy was classified as grade 1, 2 and 3 in 26 (57%), four (9%) and three (7%) cases, respectively. In 19 cases pneumonitis was diagnosed in the first 3 months and 11 cases 3–8 months after brachytherapy. During follow-up, a pleural effusion was detected in eight (17%) of cases. No rib fractures were detected in the follow-up imaging or chronic chest pain documented clinically. Partial or complete lung atelectasis was described in 10 (22%) cases and a single (2%) case, respectively. The patient with the complete atelectasis was treated for a central sarcoma metastasis close to the carina (Fig. 3). No specific target volumes, dose levels and critical distances to the central bronchial structures were found to be statistically relevant for ≥grade 2 toxicity in this patient population.

An increasing fibrotic reaction was detected in the second year after brachytherapy in 77% of cases, thus the vast majority (Fig. 4). In 70% of cases (as also presented in Fig. 1–4), the lesion volume decreased initially (median 43% of initial volume 6–12 months after brachytherapy) and subsequently increased in the high-dose area (median 93% of initial volume >18 months after brachytherapy).

Tables 1 and 2 give a detailed overview of the pulmonary treatment-associated changes that have been detected in different follow-up intervals. Early changes (Table 1) include a spotted consolidation in the majority of patients and ground glass opacity in about 40% of patients within the first 6 months. A partial atelectasis was observed in 10–20%. A pleural effusion was diagnosed also in 10–20% of patients. The average extension of the pleural effusion above the dorsal ribs was 2.5 cm, 2.2 cm, and 3.1 cm after 6 weeks, 6 weeks–3 months and 3–6 months, respectively.

In the period after 6 months (Table 2), a streaky or dense consolidation was noted in the majority of follow-up images (>50% at each defined period). The lung tissue consolidation progresses into a retraction with increasing follow-up intervals. A lung atelectasis occurred in about 10% of patients. A pleural effusion was noted more rarely in comparison to the acute phase (<10% at all intervals; Fig. 4). The average extension of the pleural effusion above the dorsal ribs was 3.1 cm, 5.0 cm, and 3.0 cm after 6–12 months, 12–18 months and >18 months, respectively.

Discussion

This extended analysis refines the understanding of pulmonary tissue response after single-fraction, CT-guided interstitial high-dose-rate (HDR) brachytherapy for primary and metastatic lung tumors. By incorporating detailed longitudinal CT evaluation, the present study confirms the high efficacy and favorable safety profile of this technique while characterizing the temporal evolution of radiologic changes over a period of up to 5 years.

HDR brachytherapy achieved durable local tumor control of 81% in this study, consistent with prior reports showing local control rates of 80–90% for both primary and secondary lung lesions (1,2,11). These findings underscore the efficiency of the method across heterogeneous tumor entities and anatomical locations, as the cohort was not homogenized for specific pathologies or sites. The minimally invasive procedure was technically successful in all cases, and complications remained manage-

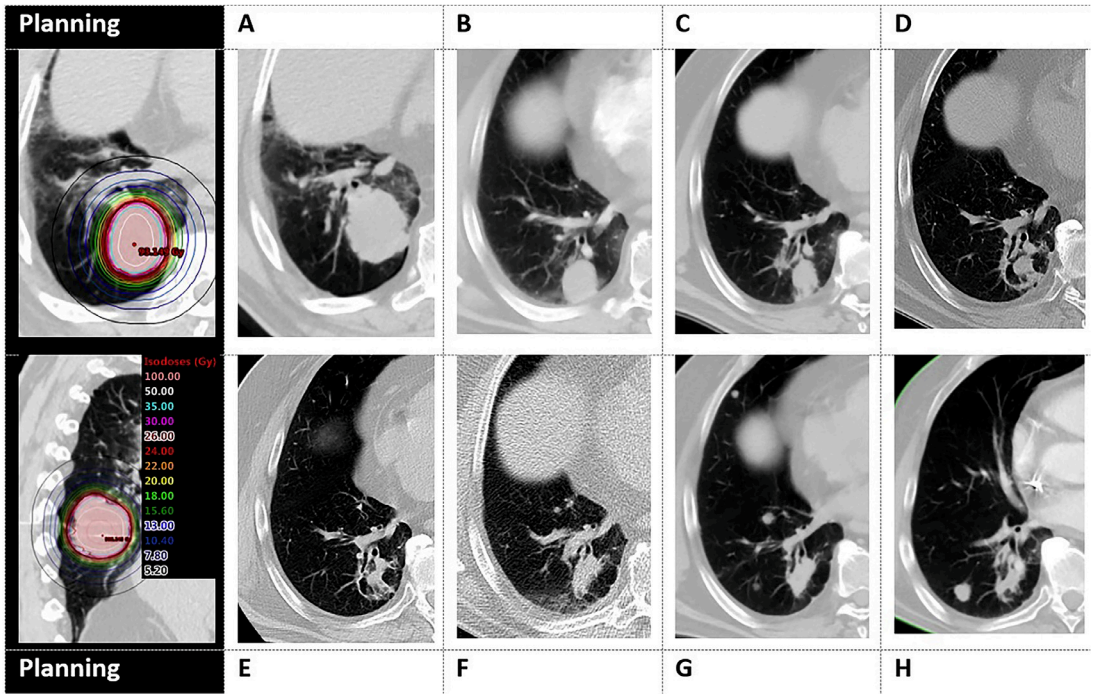


Fig. 1. Follow-up CT scans in a patient with a colorectal carcinoma lung metastasis. (a) Baseline axial CT scan. (b) 8 weeks after brachytherapy: reduction in tumor size, development of ground glass opacities. (c) 4 months: tumor shrinkage, spotted consolidation with surrounding ground glass opacities. (d) 12 months: progressive increase of dense consolidation, near complete resolution of ground glass opacities. (e) 19 months: contraction and gradual retraction of the lesion toward the hilum. (f) 34 months: dense consolidation appears thinner, continued movement of the lesion toward the hilum. (g) 37 months: further contraction. (h) 61 months: ongoing retraction toward the hilum.

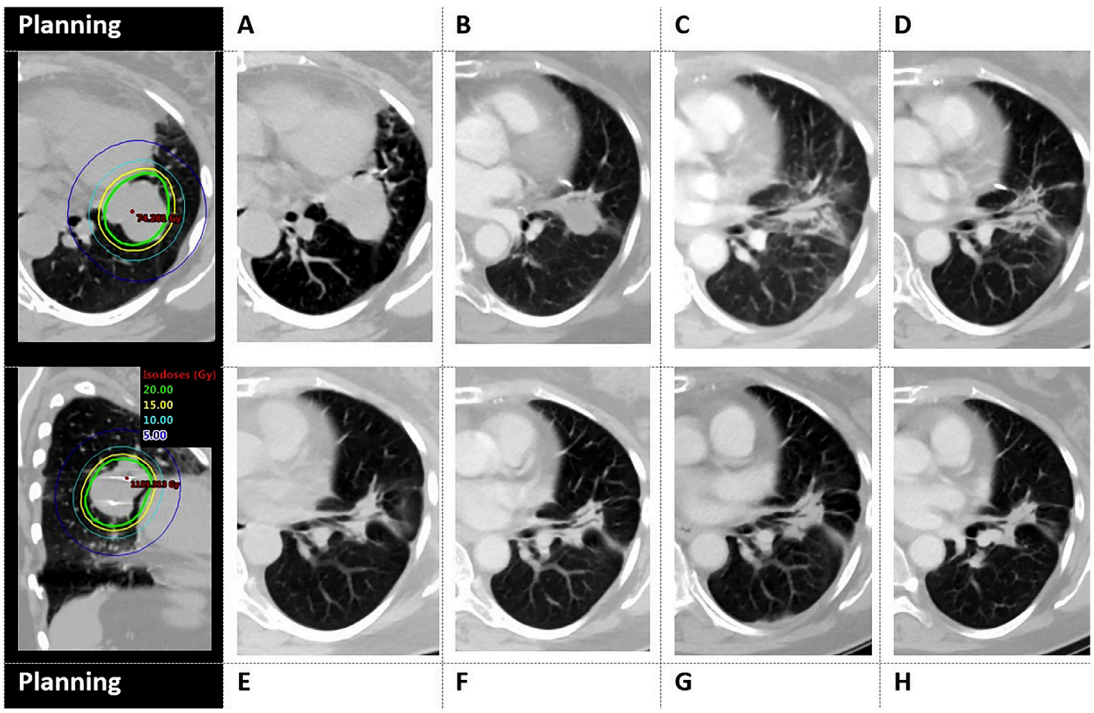


Fig. 2. Follow-up CT scans of a patient with a leiomyosarcoma lung metastasis. (a) Baseline axial CT scan. (b) 6 weeks after brachytherapy: decrease in tumor size, development of ground-glass opacities. (c) 4 months: further tumor regression, spotted consolidation and ground-glass opacities. (d) 7 months: dense consolidation, ground-glass opacities begin to resolve. (e) 13 months: further formation of dense consolidation. (f) 19 months: consolidation decreases, early retraction toward the hilum; ground-glass opacities resolved. (g and h) 29 to 56 months: progressive contraction, mass-like fibrotic scarring with retraction.

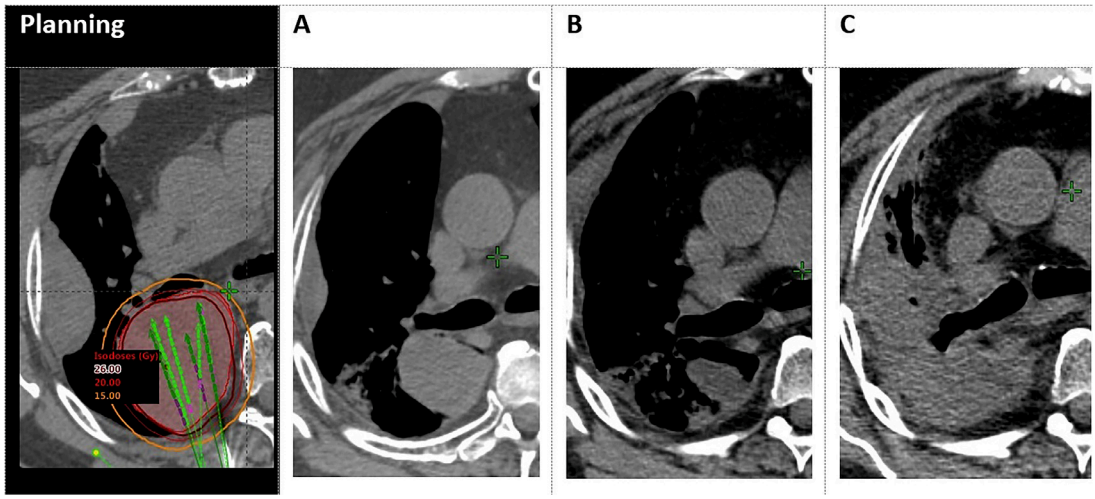


Fig. 3. Lung atelectasis in a patient with a central sarcoma lung metastasis. Reduction in tumor volume after 3 weeks (a), further significant reduction with spotted consolidation after 3 months (b) and total lung atelectasis after 8 months (c).

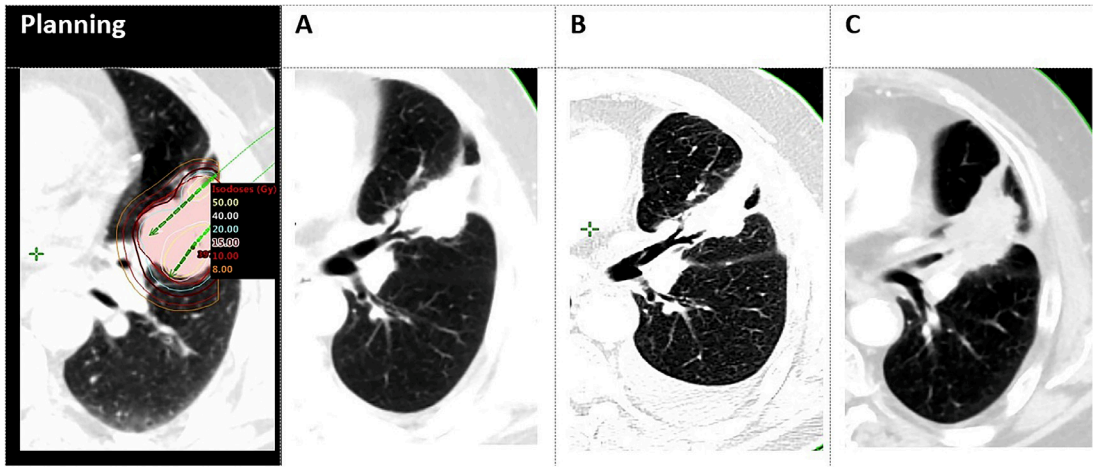


Fig. 4. Pleural effusion and fibrotic reaction in a patient with non-small cell lung cancer. Reduction in tumor volume after 6 weeks (a), further reduction with development of a pleural effusion after 3 months (b) and consolidation with increasing fibrotic reaction and retraction after 14 months (c).

Table 1
Early pulmonary changes after different follow-up intervals.

Time after brachytherapy		6 weeks (n = 34)	>6 weeks–3 months (n = 21)	>3–6 months (n = 24)
Early changes	Ground glass opacity	32%	43%	38%
	Spotted consolidation	56%	43%	63%
Changes along bronchial tree	Inflammatory	24%	33%	29%
	Streaky	6%	19%	21%
Atelectasis	Partial	18%	10%	13%
	Complete	3%	5%	4%
Pleural effusion		12%	10%	17%

able. Pneumothorax requiring drainage occurred in 15% of implantations, which is comparable to other methods of radiotherapy-associated interventions of the lung. Yoon *et al.* reported a rate of 10% for drainage-requiring pneumothorax following CT-guided HDR brachytherapy (11), while Jung *et al.* observed a rate of 17% in association with fiducial placements before CyberKnife stereotactic radiotherapy (12). Other studies reported markedly higher complication rates, such as Khadige *et al.*, who found up to 66% of patients experiencing complications including intra-alveolar bleeding or pneumothorax after CyberKnife associated gold marker placement (13). The incidence of symptomatic pneumonitis (Grade II or higher) in our cohort was 16%, aligning well with SBRT data (7,14).

Table 2
Late pulmonary changes after different follow-up intervals.

Time after brachytherapy		6–12 months (n = 26)	>12–18 months (n = 26)	>18 months (n = 33)
Late changes	Streaky consolidation	27%	19%	23%
	Dense consolidation	33%	50%	31%
	Retraction	9%	31%	46%
Changes along bronchial tree	Inflammatory	23%	25%	8%
	Streaky	27%	31%	54%
Atelectasis	Partial	15%	13%	7%
	Complete	4%	6%	2%
Pleural effusion		8%	6%	7%

In principle, different forms of energy can be delivered to organs to specifically destroy cancer cells. Two key characteristics determine the efficiency and safety of the procedures used. These are lesion-specific characteristics (volume, shape, vascularization, cell density) and tissue- or parenchyma-specific characteristics (thermal impedance and electrical impedance). Compared to the liver, the lung exhibits significantly higher thermal and electrical impedances. Consequently, therapies that rely on a homogeneous spread of electrical current (electrical impedance) or a homogeneous spread of the thermal front (thermal impedance) are more suitable for liver than for lung tumors. In the case of radiofrequency ablation in particular, there is a risk of a heat sink effect in the vicinity of vessels with a diameter >3 mm. A further limitation in the lung is the rapid formation of cavitation, which causes a sudden increase in tissue impedance. Brachytherapy allows a dose shaping after catheter implantation that takes into account the radiation sensitivity of different structures. The tumor destruction is not associated with a cavitation.

The radiologic analysis revealed a predictable sequence of lung parenchymal changes following HDR brachytherapy. Early changes (first weeks to 6 months) consisted of focal ground-glass opacities and spotted consolidations restricted to the high-dose region, reflecting a localized inflammatory response. By 6–12 months, these findings transitioned into denser, streaky-like consolidations with emerging parenchymal contraction. After 1 year, most lung lesions developed limited fibrosis with retraction, typically stabilizing in the second post-implantation year. With increasing time after irradiation, the prevalence of streaky changes along the bronchial tree progressively increased, reaching its highest reported level of 54% at 18 months post-treatment. This temporal trajectory parallels established SBRT data but is markedly more confined, underscoring the steep dose fall-off of HDR brachytherapy and its capacity to spare surrounding lung parenchyma (11).

Early alterations within the first 6 months consisted predominantly of spotted consolidations and ground-glass opacities. Most of these findings appeared in the first follow-up CT scan 6 weeks after irradiation, with 88% of scans at this timepoint showing early radiologic changes. This differs substantially from SBRT, where early changes typically occur between 2 and 6 months. In a study by Trovo *et al.* 54.4% of patients showed no visible changes at 6 weeks after SBRT (15), and Guckenberger *et al.* reported no changes in 76% of patients at this interval (7). The earlier onset of radiologic alterations after brachytherapy is likely attributable to the significantly higher mean and focal dose at the target area as well as the single-fraction treatment format (3,16).

Beyond 6 months, inflammatory changes began to change into dense or streaky consolidations, often accompanied by parenchymal volume contraction. These opacities typically reflected the geometry of the original isodose distribution. In several cases, consolidations extended along bronchovascular structures toward the pleura, resulting in subtle traction or early linear scarring, while maintaining a distinct boundary to adjacent normal lung tissue. Pleural effusions and partial atelectasis were occasionally present but decreased compared with the acute phase (Table 2).

After 1 year, the parenchymal reaction evolved into fibrotic consolidation with retraction, frequently producing distortion or displacement of adjacent bronchi, consistent with localized scarring. The fibrosis remained limited to the high-dose area and typically stabilized after the second year, with minimal further progression and, in some cases, a reduction in size on long-term follow-up. This chronic stage corresponds to the "modified conventional pattern" or "scar-like fibrosis" described in long-term SBRT analyses (7,9). Importantly, no diffuse or multilobar fibrosis was observed.

The biological progression from acute alveolitis to fibroblast-driven matrix deposition is well supported by radiobiological principles and underpins the imaging trajectory (from ground glass opacity to consolidation and finally fibrosis with retraction), which is also known after SBRT (7,8,16–18). Critically, it is the extent rather than the existence of these changes that differentiates interstitial brachytherapy from external-beam techniques. Researchers identified the irradiated lung volume as one of the most important risk factor for radiation-induced pneumonitis and lung injury (19,20). In our cohort, PTV (median 22.5 cm^3), mean ipsilateral lung dose (median 3.7 Gy) and V20 (median <1%) were low in comparison, corresponding to the limited long-term fibrosis and the absence of diffuse spread

acute or chronic lung changes. No signs of necrosis or formation of cavities in the lung were found in all follow up intervals, comparable to results found in other studies evaluating CT-guided interstitial brachytherapy (21,22). Other studies focusing on SBRT and thermoablative procedures described formation of cavities seen in the follow-up (18,23–26).

A clinically important implication of this radiologic evolution is the potential misinterpretation of benign post-therapeutic fibrosis as tumor recurrence (15). In this study, transient increases in opacity size or density were observed in approximately 70% of lung lesions, predominantly within the first 2 years. Similar "pseudoprogression" has been frequently reported after SBRT, where ongoing fibroblast activity can mimic tumor regrowth (6,7). Morphologic features suggesting benign post-treatment evolution include the absence of bulging margins, increasing parenchymal retraction over time, and confinement to the high-dose region (6,27). Metabolic imaging with FDG-PET can aid differentiation, as fibrosis typically shows decreasing uptake over time, whereas recurrent disease shows rising metabolic activity (14,15).

A time-stamped framework supports confident CT interpretation. Within the first 6 months after interstitial brachytherapy: ground glass opacity and/or spotty consolidation in the high-dose zone, corresponding to an expected radiation pneumonitis; after 6–24 months: increasing consolidation with fibrotic retraction; modest interval enlargement expected; after >24 months: stabilization expected. New mass-like growth, bulging margins, or expanding solid components warrant evaluation for recurrence (PET-CT or biopsy if clinically relevant).

Limitations of this study are the retrospective analysis of follow-up imaging in a limited number of patients, a heterogeneous study population with a variety of primary tumors and prior systemic treatments. Though the maximum follow-up is very long, the median overall survival was only 16 months, as patients were most frequently treated with a metastatic disease and palliative intention. Target volumes varied in volume and location. Dose prescriptions and distributions could be adapted and were adapted to the individual target location. Patient selection was based on the specific referral to our center and patient preferences.

Conclusion

A single dose interstitial brachytherapy is an extremely conformal treatment with a high-dose to a very small volume of the lung and an excellent local tumor control. As the treatment is invasive, it is associated with a risk of a pneumothorax. As a result of high focal doses (median PTV D10% >100 Gy) in a single fraction, a tissue consolidation must be expected in all patients, with a progressive retraction predominantly in the second year after brachytherapy. There is a smaller risk of a partial atelectasis and pleural effusion. The risk of a pleural effusion decreases with increasing follow-up.

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