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Original Article

Comparative safety and efficacy of single-agent chemotherapy combined with microwave ablation versus radioactive seed brachytherapy in elderly patients with advanced NSCLC: a ten-year retrospective study

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Abstract: Elderly patients with advanced non-small cell lung cancer (NSCLC) often have limited tolerance for standard therapies and experience reduced efficacy with lower-intensity treatments. This study evaluated the safety and efficacy of single-agent chemotherapy combined with either microwave ablation (MWA) or radioactive iodine-125 seed ablation brachytherapy (RSABT) as first-line treatments, aiming to establish personalized, high-efficacy, and low-toxicity options for this vulnerable population. We conducted a retrospective analysis of 128 untreated elderly patients with advanced NSCLC from November 2013 to November 2023. 71 patients received RSABT plus chemotherapy, while 55 underwent MWA plus chemotherapy, with single-agent pemetrexed, docetaxel, or gemcitabine initiated 5-7 days post-procedure. Overall outcomes, including time to local progression (TTLP), overall survival (OS), and progression-free survival (PFS), did not differ significantly between the RSABT and MWA groups. However, in patients with tumors ≥ 4 cm, the RSABT group demonstrated significantly longer TTLP (14 versus 8 months, P = 0.005) and OS (15 versus 11 months, P = 0.039). The MWA group exhibited higher rates of postoperative pectoralgia (58% versus 34%, P < 0.001) and pleural effusion (18% versus 4%, P = 0.013). Additionally, tumors located within 10 mm of the pleura in the MWA group were linked to increased pulmonary complications, including pneumothorax and bronchopleural fistula (odds ratio [OR] = 9.455, P = 0.041), whereas no such association was observed in the RSABT group (OR = 0.872, P = 0.79). In conclusion, combining single-agent chemotherapy with either MWA or RSABT is effective and safe for elderly patients with advanced NSCLC. RSABT demonstrated superior safety and efficacy compared to MWA for tumors ≥ 4 cm or those located within 10 mm of the pleura, making RSABT a more suitable first-line treatment option in these cases.

Keywords: Non-small cell lung cancer, microwave ablation, brachytherapy, single-agent chemotherapy, elderly

Introduction

Lung cancer is the most prevalent malignancy worldwide, ranking first in both incidence and mortality, with non-small cell lung cancer (NSCLC) comprising the majority of cases [1]. Despite considerable advances in treatment over the past decade, significant challenges remain in managing elderly patients with advanced-stage NSCLC, who continue to face a poor prognosis. Due to age-related declines in physical function, organ health, and increased comorbidity risks [2], elderly patients often cannot tolerate full-dose, guideline-recommended regimens. Consequently, clinicians frequently employ reduced-dose chemotherapy and palliative radiotherapy, whereas biomarker-guided targeted therapies can deliver meaningful and durable responses but are applicable to only a subset of patients. Immune-checkpoint inhibitors (ICIs) offer another treatment avenue [3]; however, real-world data show that non-squamous NSCLC with programmed death-ligand-1 (PD-L1) expression < 1% attains significantly shorter overall survival (OS) than that reported in registration trials, underscoring the

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difficulty of reproducing trial gains in routine clinical practice [4]. Age-related immunosenescence predisposes older adults to more severe immune-related adverse events and further limits treatment tolerance [5]. Accordingly, the optimal therapeutic strategy for elderly NSCLC patients who lack high PD-L1 expression or actionable driver mutations remains uncertain.

Chemotherapy remains a cornerstone for elderly NSCLC patients with adequate performance status. However, clinical trials have shown that platinum-based doublets increase grade 3-4 haematologic toxicity without improving survival compared with single-agent regimens [6, 7]. To individualize therapy and mitigate toxicity, we routinely apply the Cancer and Aging Research Group (CARG) score to guide treatment selection, stratifying patients into low (0-5), intermediate (6-9) and high (10-23) risk categories. In line with ASCO recommendations [8], intermediate-risk patients receive single-agent chemotherapy, and high-risk patients receive palliative care. To address the modest local control achieved with mono-chemotherapy in intermediate-risk patients, we supplemented systemic treatment with targeted local therapies, microwave ablation (MWA) or radioactive iodine-125 seed ablation brachytherapy (RSABT), thereby enhancing focal tumor destruction while preserving overall tolerability.

MWA is a thermal treatment modality endorsed by the National Comprehensive Cancer Network (NCCN) guidelines and supported by expert consensus for managing both primary and metastatic lung cancers. Its applications include early-stage and inoperable tumors, as well as patients who are not candidates for radiotherapy [9, 10]. In advanced NSCLC patients, combining MWA with chemotherapy has been associated with significant improvements in progression-free survival (PFS) and OS (PFS: 10.3 vs. 4.9 months, $P < 0.001$; OS: not reached vs. 12.4 months, $P < 0.001$) [11]. Similarly, RSABT has shown promising results in delivering high-dose localized radiotherapy to lung tumors, achieving excellent local control and enhancing patient quality of life compared to conventional chemotherapy and radiotherapy [12]. RSABT administers a significantly higher radiation dose (140-160 Gy), effectively eradicating targeted tumor cells while minimizing exposure to surrounding healthy tissues, thereby reducing the incidence of radiation-induced pneumonia [13]. Recent advancements in computerized three-dimensional treatment planning systems (TPS) have further enhanced the precision and safety of RSABT. For elderly NSCLC patients, percutaneous computed tomography (CT)-guided RSABT combined with single-agent chemotherapy has been validated as an effective and safe option, demonstrating superior clinical outcomes compared to chemotherapy alone [14].

An individualized treatment approach is essential, particularly for elderly patients with advanced NSCLC, and should be based on a comprehensive evaluation of individual risk factors. Determining which treatment modality offers superior quality of life outcomes and longer survival is inherently complex. This study compares the clinical outcomes of MWA and RSABT in elderly patients with advanced NSCLC, evaluating which modality is safer and more effective in improving survival. The innovation lies in directly comparing two minimally invasive local therapies combined with single-agent chemotherapy, specifically tailored to the unique needs of the elderly population.

Materials and methods

Patients

We retrospectively reviewed the medical records of elderly patients with Stage III-IV NSCLC, who were treated with CT-guided RSABT or MWA plus mono-chemotherapy in our center from November 2013 to November 2023. Inclusion criteria were: (1) age between 65 and 85 years; (2) intermediate risk based on the CARG chemotherapy risk assessment tool (score 6-9); (3) Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≤ 2; (4) pathologically confirmed NSCLC with a clinical stage of III or IV; (5) negative or unknown EGFR (epidermal growth factor receptor) mutations, ALK (anaplastic lymphoma kinase) rearrangements, and ROS1 (ROS proto-oncogene 1, receptor tyrosine kinase) fusion genes; and (6) patients ineligible for or who declined surgery, radiotherapy, and ICIs. Exclusion criteria were: (1) > 3 pulmonary tumor lesions; (2) poor coagulation function, defined as platelet count $\leq 50 \times 10^9$/L or prothrombin

time activity < 40%; (3) estimated life expectancy ≤ 3 months; (4) tumors infiltrating the pulmonary artery, aorta, trachea, or esophagus; (5) severe cardiopulmonary dysfunction (New York Heart Association class III-IV, maximum ventilation capacity < 39%); (6) severe kidney disease (stage 3 and above chronic kidney disease); and (7) severe liver disease (Child-Pugh class C).

This retrospective study was approved by the Ethics Committee of Tengzhou Central People's Hospital (2025 Ethics Review No. 59). Informed consent was waived due to the retrospective nature of the study.

Technical procedures

I-125 seed implantation and dose verification: Preoperative planning is essential for optimizing RSABT by achieving precise dose distribution and minimizing radiation exposure to surrounding tissues. CT images were imported into TPS for comprehensive dosimetric analysis. Gross Tumor Volume (GTV) was delineated by experienced clinicians and radiologists. Adjacent Organs at Risk (OARs) were independently identified and precisely outlined to ensure their protection during treatment. The Clinical Target Volume (CTV) was established by uniformly expanding the GTV by 5-6 mm in all directions. Then the isocenter was selected, and optimal needle angles and depths were determined to ensure accurate seed alignment (**Figure 1A**). Finally, the quantity and activity of I-125 seeds were calculated based on the dosimetric analysis of the CTV and OARs. The prescribed dose was between 110 Gy and 160 Gy, with I-125 seed activity ranging from 0.5 to 0.8 mCi. The radiation doses to OARs, such as the main stem bronchus, spinal cord, lung tissue, esophagus, major blood vessels, and heart were calculated as necessary.

I-125 seeds (4.5 mm × 0.8 mm; emitting 27.4-31.5 keV X-rays and 35.5 keV γ-rays; half-life: 59.6 days; Beijing Atom High-Tech Pharmaceutical Company Ltd., China) were implanted under the guidance of a 64-slice spiral CT scanner using placement devices from Mick Radio-Nuclear Instruments, Inc., USA and Eckert & Ziegler BEBIG GmbH, Germany. Patients were immobilized on the CT bed with a vacuum pad, and the planned puncture sites were marked on the skin before seed placement. The quantity and activity of I-125 seeds were determined based on the dosimetric analysis of the CTV and OARs. A 3D-printed coplanar template (3D-PCT) was employed in all I-125 seed implantation procedures for lung cancer, which was installed in the navigation bracket and attached to the CT carbon fiber bedplate. The template position was calibrated by aligning the x-axis and y-axis laser lines with the positioning crosshairs of the 3D-PCT (**Figure 1B**), to ensure precise placement. 1% lidocaine and 0.25% ropivacaine were administered for local anesthesia. During the procedure, the tumor's central plane was first identified. Following the preoperative plan, several fixed puncture needles were then strategically inserted through the guide holes of the 3D-PCT into the patient's skin at precise angles (**Figure 1C**). Subsequently, metal artifacts generated by the fixed needles were used to evaluate whether the puncture path posed a risk to major blood vessels. If the path was adjacent to large vessels, such as the pulmonary artery, an intraoperative contrast agent was administered to enhance imaging and reduce bleeding risk (**Figure 1D**). Once all needles were positioned within the target lesion, I-125 seeds were implanted at 0.5-1.0 cm intervals according to the preoperative plan (**Figure 1E**). A post-implantation CT scan was performed to evaluate seed distribution, and additional seeds were placed if underdosed regions were identified (**Figure 1F**). Procedural complications, such as pneumothorax and bleeding, were monitored in real time and managed promptly. Finally, radiation detectors surveyed the treatment area and instruments for any displaced I-125 seeds; any detected seeds were promptly retrieved and secured in a lead-lined container. Follow-up CT images acquired 2-3 days after surgery were used to monitor complications and then imported into the TPS to assess GTV volume and the dosimetric indices D90 and D100 (doses to 90% and 100% of the GTV, respectively) (**Figure 1G**). Short-term treatment response was evaluated at three months postoperatively (**Figure 1H**).

Microwave ablation procedure

A preoperative CT scan was conducted to determine the tumor's location and size (**Figure 2A**). An optimal puncture plan was then formulated with attention to the following criteria: (1) the

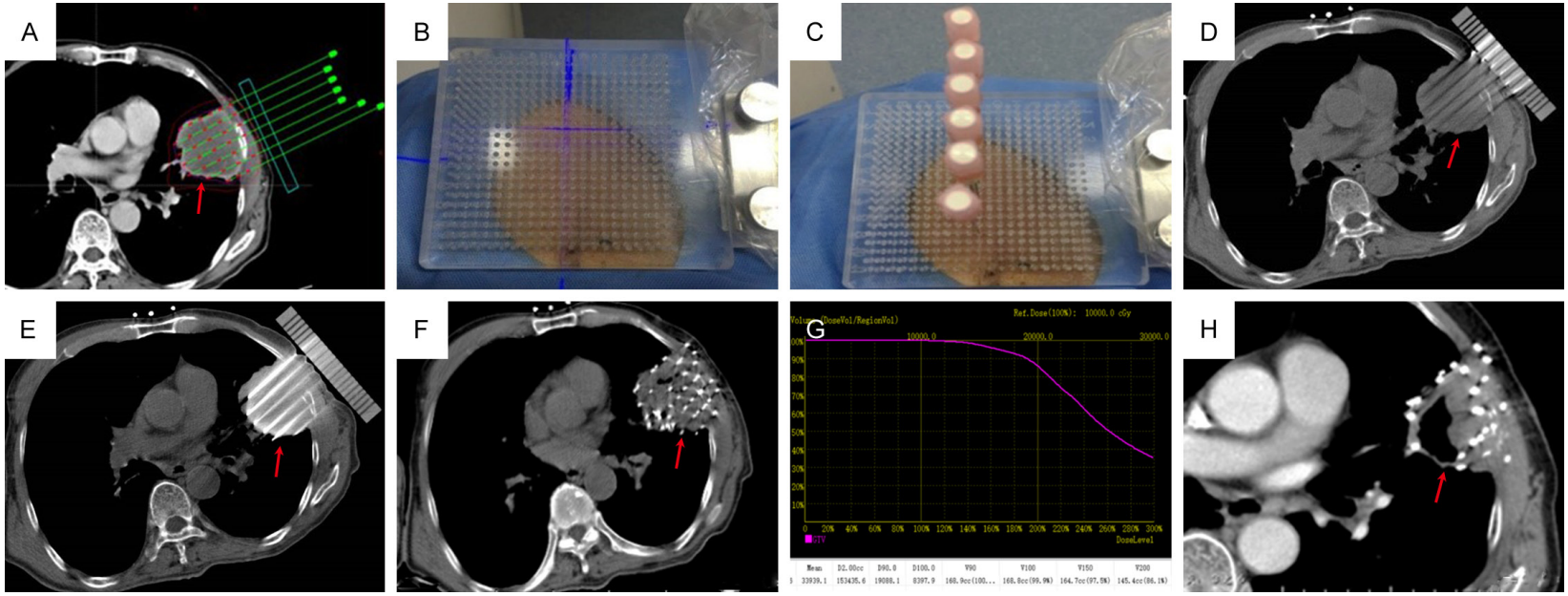

Figure 1. A case of stage IV lung adenocarcinoma treated with I-125 seed implantation. Flowchart of the implantation procedure: (A) Preoperative planning; (B) Calibration of the 3D-printed coplanar template using laser light; (C) Insertion of fixed puncture needles; (D) Assessment of puncture path safety using the metal artifacts generated by the fixed needles; (E) Insertion of all needles into the predetermined lesion; (F) Postoperative CT scan to assess I-125 seed distribution and complications; (G) Evaluation of postoperative dosimetric parameters; (H) Three-month postoperative follow-up to assess treatment efficacy. Red arrows indicate the target lesion.

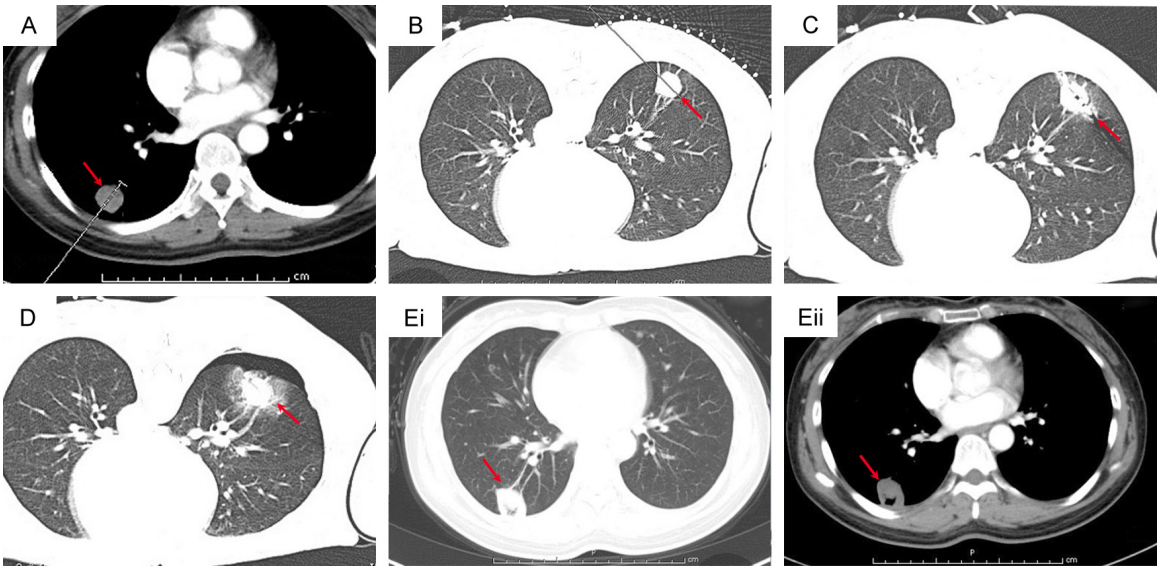

Figure 2. A case of stage IV lung adenocarcinoma treated with microwave ablation (MWA). Procedure flowchart: (A) Preoperative enhanced CT scan; (B) Preoperative planning; (C) Microwave antenna positioned along the tumor's longest axis for optimal ablation coverage; (D) Post-ablation CT showing ground-glass opacity within the ablation zone; (E) Efficacy assessment at the 3-month postoperative follow-up, with CT revealing a non-enhancing necrotic cavity within the ablation zone on (i) lung window and (ii) mediastinal window. Red arrows indicate the target lesion.

shortest possible pathway; (2) avoidance of ribs, heart, major vessels, main bronchus, bullae, chest wall, and other critical structures; and (3) alignment of the puncture pathway along the tumor's longest axis to maximize ablation coverage and ensure full encapsulation of the tumor within the thermal field (**Figure 2B**). A single ablation antenna can create an ablation zone of approximately 3.5 cm × 3 cm with a power setting of 60-80 W over a duration of 6-8 minutes [15]. For tumors larger than 3.5 cm, the use of either two or more antennae, or repositioning a single antenna, was recommended.

MWA was performed using the microwave generator (ECO Microwave Electronic Institute, Nanjing, China) under CT guidance by skilled interventional radiologists. Preoperative preparation and local anesthesia were performed in accordance with the same protocol as the RSABT group. One or more 14- or 16-gauge, 20 cm microwave antennas (ECO Microwave Electronic Institute) were then advanced into the distal aspect of the target lesion per the preoperative plan (**Figure 2C**) and coupled to a cooling system to maintain optimal antenna temperature prior to ablation. Microwave energy was delivered at a mean power of 58 W (50-70 W) for approximately 8 minutes (5-21 minutes), with real-time power and duration adjustments based on tumor size and location. Patients received subcutaneous morphine injections if severe pain occurred. Immediately post-ablation, CT was performed to confirm that the ground-glass opacity (GGO) halo completely surrounded the target lesion with a ≥ 5 mm margin (**Figure 2D**); if coverage was inadequate, the antenna was repositioned and additional ablation was applied. Short-term efficacy was assessed at 3 months by contrast-enhanced CT (**Figure 2E**).

Chemotherapy

Single-agent chemotherapy was initiated 5-7 days after MWA/RSABT, with agents selected according to tumor pathology. Agents included: (1) pemetrexed (Hansoh Pharma, 500 mg/m^2, d1); (2) docetaxel (Hengrui Medicine, 75 mg/m^2, d1); (3) gemcitabine (Hansoh Pharma, 1000 mg/m^2, d1, d8). All regimens were administered intravenously on a 21-day cycle for up to six cycles. Maintenance therapy was then individualized based on each patient's performance status and response to initial chemotherapy.

Follow-up

A CT scan was conducted within 3 days postoperatively to detect complications, including

pneumothorax, pleural effusion, pneumonitis, bronchopleural fistula and hemorrhage, with treatment provided as necessary. During chemotherapy, regular assessments were conducted each cycle, including laboratory tests (complete blood count, comprehensive metabolic profile, tumor markers), as well as evaluations of pain, quality of life, and ECOG status. During the treatment phase, enhanced chest CT scans were performed at intervals of 1 to 2 months. Following the completion of therapy, surveillance enhanced chest CT scans were conducted every 3 months to monitor for local recurrence or the emergence of new lesions. Additionally, whole-body CT and ECT/PET-CT scans were performed every 6 months to assess for distant metastasis.

Endpoints

The primary endpoint was the time to local progression (TTLP), defined as the interval from the treatment date to the radiologically confirmed progression of the target lesion. Secondary endpoints included OS, PFS, disease control rate (DCR), and treatment-related complications. In the RSABT group, treatment efficacy was evaluated by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). The DCR was calculated as the proportion of patients achieving CR, PR, or SD. In the MWA group, the post-ablation target zone typically exceeded the original tumor dimensions, reflecting both the deliberate 5 mm extension of the ablation margin to ensure complete coverage and reactive changes (e.g., oedema, haemorrhage, exudation and inflammatory infiltration). As these imaging alterations persist for 3-4 months per expert consensus and prior reports [10, 16], RECIST v1.1 is unsuitable for early response assessment [16]. Consequently, local efficacy is first judged on the 4-6-week post-ablation scan - using it as a new baseline - and classified as complete ablation (no contrast enhancement or viable tissue, manifesting as lesion disappearance, cavity formation, fibrosis or stable shrinkage), incomplete ablation (residual enhancement indicating viable tumor) or local progression (≥ 10 mm increase in maximal diameter or emergence of a new enhancing focus). After imaging stabilizes (typically by 3-4 months), RECIST v1.1 may be applied as an ancillary reference. Figures S1 and S2 illustrate the CT imaging changes associated with RSABT-induced complete response and MWA-induced complete ablation, respectively. PET within the first 3 months is confounded by inflammatory uptake and may yield false positives, whereas new or increased uptake beyond this period may signify recurrence. Treatment-related adverse events were documented and graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, along with the radiologic response criteria from the U.S. Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (RTOG/EORTC, 1987).

Statistical analysis

Statistical evaluations were performed using Statistical Product Service Solutions (SPSS) version 29.0 and R software version 4.1. Continuous variables were presented as mean ± standard deviation or median (range) according to their distribution. The Student's t-test was employed for normally distributed data, while the Mann-Whitney U test was utilized for non-normally distributed variables. Categorical data were expressed as frequencies and percentages, with comparisons made using the χ^2 test or Fisher's exact test depending on sample size and expected counts. Survival outcomes were analyzed using the Kaplan-Meier method, with univariate comparisons conducted via the log-rank test. Multivariate analyses were carried out using Cox proportional hazards regression, and logistic regression was applied to identify factors associated with postoperative complications. $P < 0.05$ was considered statistically significant.

Results

Patients and treatment

A total of 128 eligible patients were screened and enrolled in the study. Of these, 76 patients (59.4%) with stage IIIC or IV tumors were deemed unresectable, 32 patients (25%) were considered unsuitable for surgery following a multidisciplinary evaluation, and 20 patients (15.6%) declined surgery for personal reasons. The cohort included 81 males and 47 females, aged 65 to 85 years (median, 70 years), with

Table 1. Baseline characteristics of the patients

	RSABT group (N = 71)	MWA group (N = 57)	*P*-Value
Age			0.829
65-75	56 (79%)	43 (75%)	
76-85	15 (21%)	14 (25%)	
Sex			0.849
Male	46 (65%)	35 (61%)	
Female	25 (35%)	22 (39%)	
ECOG PS			0.135
0-1	46 (65%)	40 (70%)	
2	25 (35%)	17 (30%)	
Clinical stage			0.696
III	38 (53%)	28 (50%)	
IV	33 (47%)	29 (50%)	
Histology			0.133
Adenocarcinoma	31 (44%)	30 (53%)	
Squamous cell carcinoma	35 (49%)	21 (37%)	
Other NSCLC	5 (7%)	6 (10%)	
Chemotherapy			0.490
Pemetrexed	28 (39%)	27 (48%)	
Docetaxel	31 (44%)	19 (33%)	
Gemcitabine	12 (17%)	11 (19%)	
Tumor diameter (cm)			0.001
T < 4	19 (27%)	41 (72%)	
T ≥ 4	52 (73%)	16 (28%)	

Abbreviations: RSABT, radioactive iodine-125 seed ablation brachytherapy; MWA, microwave ablation; ECOG PS, Eastern Cooperative Oncology Group Performance Status; NSCLC, non-small cell lung cancer.

ECOG scores ranging from 0 to 2 (median, 1). Among these patients, 57 underwent CT-guided MWA followed by mono-chemotherapy (MWA group), while 71 received RSABT followed by mono-chemotherapy (RSABT group). All tumors in the MWA cohort were peripheral lung carcinomas. In the RSABT cohort, 23 tumors were central lung carcinomas and 48 were peripheral lung carcinomas. The median tumor diameter was 6 cm (range, 1.2-9 cm) in the RSABT group and 3 cm (range, 1-6.7 cm) in the MWA group. Many tumors in the RSABT group were either large, had irregular shapes, or were located near critical structures such as the aorta, mainstem bronchus, pericardium, or diaphragm, making them unsuitable for microwave ablation and more appropriate for seed implantation.

According to expert consensus and guidelines, MWA is primarily recommended as a curative approach for tumors ≤ 3 cm, while tumors > 5 cm are typically treated palliatively. Therefore, larger tumors in this study were more frequently managed with RSABT, resulting in a baseline difference between groups for tumors > 4 cm ($P = 0.003$), whereas no significant difference was observed for tumors ≤ 4 cm ($P = 0.183$). To account for potential survival bias due to tumor size imbalance, a stratified analysis based on tumor size will be conducted. Apart from this, other baseline characteristics were comparable between the groups, as shown in **Table 1**.

In the RSABT group, the number of iodine-125 seeds implanted varied from 10 to 210 (median, 85), with postoperative D90 doses ranging from 74 to 261 Gy (median, 143 Gy). In the MWA group, ablation power ranged from 50 to 70 W (median, 58 W), and ablation times ranged from 5 to 21 minutes (median, 8 minutes). Among patients who experienced local recurrence, 12 received secondary minimally invasive interventions: 8 patients in the MWA group underwent additional radioactive seed implantation, 2 received a second MWA session, and 2 in the RSABT group received supplemental iodine-125 seeds.

All patients underwent 1 to 12 cycles of chemotherapy (median, 6 cycles). Of these, 25 (19.5%) required second-line treatment, and 8 (6.3%) progressed to third-line. In the RSABT group, 31 patients received docetaxel, 28 received pemetrexed, and 12 received gemcitabine. In the MWA group, 18 patients received docetaxel, 31 received pemetrexed, and 8 received gemcitabine.

Efficacy

The median follow-up duration was 46.0 months (range, 3.5-121.3 months) as of January 2024. By then, 112 cases (87.4%) had died, 15 cases (11.8%) had survived, and 1 case (0.8%) was lost to follow-up. Survival analysis revealed significant differences in

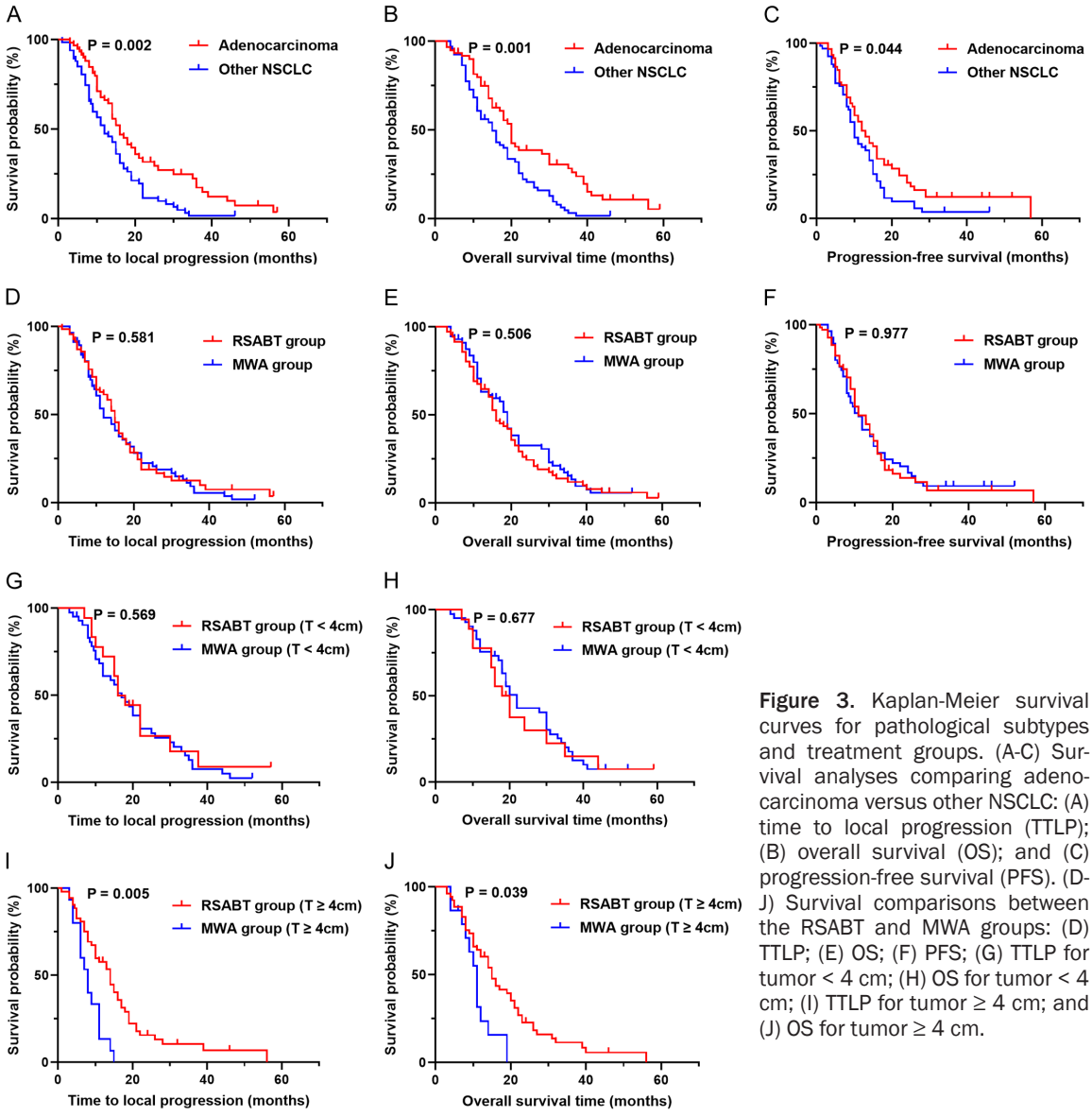

Figure 3. Kaplan-Meier survival curves for pathological subtypes and treatment groups. (A-C) Survival analyses comparing adenocarcinoma versus other NSCLC: (A) time to local progression (TTLP); (B) overall survival (OS); and (C) progression-free survival (PFS). (D-J) Survival comparisons between the RSABT and MWA groups: (D) TTLP; (E) OS; (F) PFS; (G) TTLP for tumor < 4 cm; (H) OS for tumor < 4 cm; (I) TTLP for tumor ≥ 4 cm; and (J) OS for tumor ≥ 4 cm.

survival outcomes across pathological types. Patients with adenocarcinoma exhibited significantly longer TTLP, OS, and PFS compared to those with other NSCLC subtypes, such as squamous cell carcinoma. Median TTLP was 16.0 vs. 12.0 months (χ^2 = 9.28, *P* = 0.002; **Figure 3A**), OS was 20.0 vs. 15.0 months (χ^2 = 10.59, *P* = 0.001; **Figure 3B**), and PFS was 13.0 vs. 10.0 months (χ^2 = 4.06, *P* = 0.044; **Figure 3C**). The short-term efficacy of the target lesion was assessed 3 months post-operation. In the RSABT group, 21 cases (29.6%) achieved CR, 39 cases (54.9%) achieved PR, 8 cases (11.3%) exhibited SD, and 3 cases (4.2%) exhibited PD. In the MWA group, 41 cases (73.7%) had complete ablation, 12 cases (21.1%) had incomplete ablation, and 4 cases (5.3%) had PD. The DCR was 95.8% in the RSABT group and 93% in the MWA group (*P* = 0.709). The median TTLP was 15 months (95% confidence interval [CI], 13.1-16.9) in the RSABT group and 14 months (95% CI, 10.4-17.6) in the MWA group (hazard ratio [HR] = 0.91, 95% CI, 0.63-1.32; *P* = 0.636) (**Figure 3D**). The median OS was 16 months (95% CI, 13.2-18.9) in the RSABT group and 19 months (95% CI, 17.0-21.0) in the MWA group (HR = 1.17, 95% CI, 0.80-1.70; *P* = 0.417) (**Figure 3E**).

The median PFS was 11 months (95% CI, 8.5-13.5) in the RSABT group and 11 months (95% CI, 8.3-13.7) in the MWA group (HR = 1.01, 95% CI, 0.68-1.48; P = 0.977) (**Figure 3F**). Overall, these results indicate that the therapeutic efficacy, as measured by TTLP, OS, and PFS, was similar between the RSABT group and the MWA group.

A subgroup analysis was conducted to assess the impact of tumor size on survival outcomes. Among patients with a tumor base diameter < 4 cm, both TTLP and OS were longer than those in patients with tumors ≥ 4 cm (TTLP: χ^2 = 7.86, P = 0.005; OS: χ^2 = 9.04, P = 0.003). There were no significant differences in TTLP or OS between the RSABT and the MWA group for tumors less than 4 cm in diameter (P > 0.05, **Figure 3G**, **3H**). However, for tumors with a base diameter ≥ 4 cm, the RSABT group showed longer TTLP and OS than the MWA group. The median TTLP was 14 months (95% CI: 11.8-20.2) in the RSABT group, compared to 8 months (95% CI: 5.5-10.5) in the MWA group (HR = 0.57, 95% CI: 0.32-0.97; χ^2 = 8.04, P = 0.005, **Figure 3I**). Similarly, the median OS was 15 months (95% CI: 14.2-22) in the RSABT group versus 11 months (95% CI: 8.4-13.3) in the MWA group (HR = 0.73, 95% CI: 0.4-1.35; χ^2 = 4.28, P = 0.039, **Figure 3J**).

Further analysis in the RSABT group examined the impact of dose on survival. It was found that higher doses (D90 ≥ 140 Gy) were associated with significantly longer TTLP and OS compared to lower doses (D90 < 140 Gy) (TTLP: χ^2 = 9.8, P = 0.002; OS: χ^2 = 6.05, P = 0.014).

The forest plot compares the effects of RSABT and MWA combined with mono-chemotherapy on TTLP and OS in elderly patients with advanced NSCLC, stratified by clinical characteristics. No significant differences were observed between the RSABT and MWA groups across most subgroups (P > 0.05), indicating similar efficacy between the two treatments. However, in patients with tumor diameters ≥ 4 cm, RSABT was associated with a significantly longer OS (HR = 0.31, 95% CI: 0.13-0.72; P = 0.039) and TTLP (HR = 0.23, 95% CI: 0.10-0.54; P = 0.005), suggesting a survival benefit in this specific subgroup (**Figure 4**).

Complications

The main chemotherapy-related complications included hematologic toxicity, manifesting as neutropenia, thrombocytopenia, and anemia, along with gastrointestinal reactions and hepatic and renal dysfunction. No significant differences in these adverse reactions were observed between the RSABT and MWA groups (**Table 2**, P > 0.05). Procedure-related complications included pneumothorax, needle bleeding, and pectoralgia caused by needle puncture, as well as subsequent hemoptysis, pleural effusion, pneumonitis, and even bronchopleural fistula. Among patients who experienced at least one of these complications, the overall complication rate was similar between the RSABT and MWA groups (P > 0.05). But the incidence of pectoralgia and pleural effusion in the MWA group was significantly higher than in the RSABT group (pectoralgia, 58% vs. 34%, P < 0.001; pleural effusion, 18% vs. 4%, P = 0.013). The RSABT group exhibited a higher incidence of needle bleeding compared to the MWA group (27% vs. 9%, P = 0.031). Severe complications of grade 4 or higher were not observed in either group (**Table 2**).

The regression analysis incorporating pleural proximity (less than 10 mm) and postoperative pulmonary complications (including pneumothorax, pleural effusion, pectoralgia, and bronchopleural fistula) demonstrated a significant positive correlation in the MWA group (OR = 9.455, P = 0.041). However, no such association was observed in the RSABT group (OR = 0.872, P = 0.79). These findings suggest that pleural proximity of less than 10 mm may increase the risk of complications specifically in patients undergoing MWA. In contrast, RSABT does not appear to significantly elevate this risk. For lesions located close to the pleura, a notable increase in complications is observed following microwave ablation, underscoring the need for careful patient selection and meticulous procedural planning when performing MWA.

Factors affecting outcomes

In elderly NSCLC patients, univariate analysis demonstrated that an ECOG PS of 2, non-adenocarcinoma histology, Stage IV disease, and tumor diameter ≥ 4 cm were significantly associated with reduced OS and shorter TTLP (all P < 0.05). Multivariate Cox regression confirmed these variables as independent prognostic indicators, with impaired functional status, advanced stage, non-adenocarcinoma histolo-

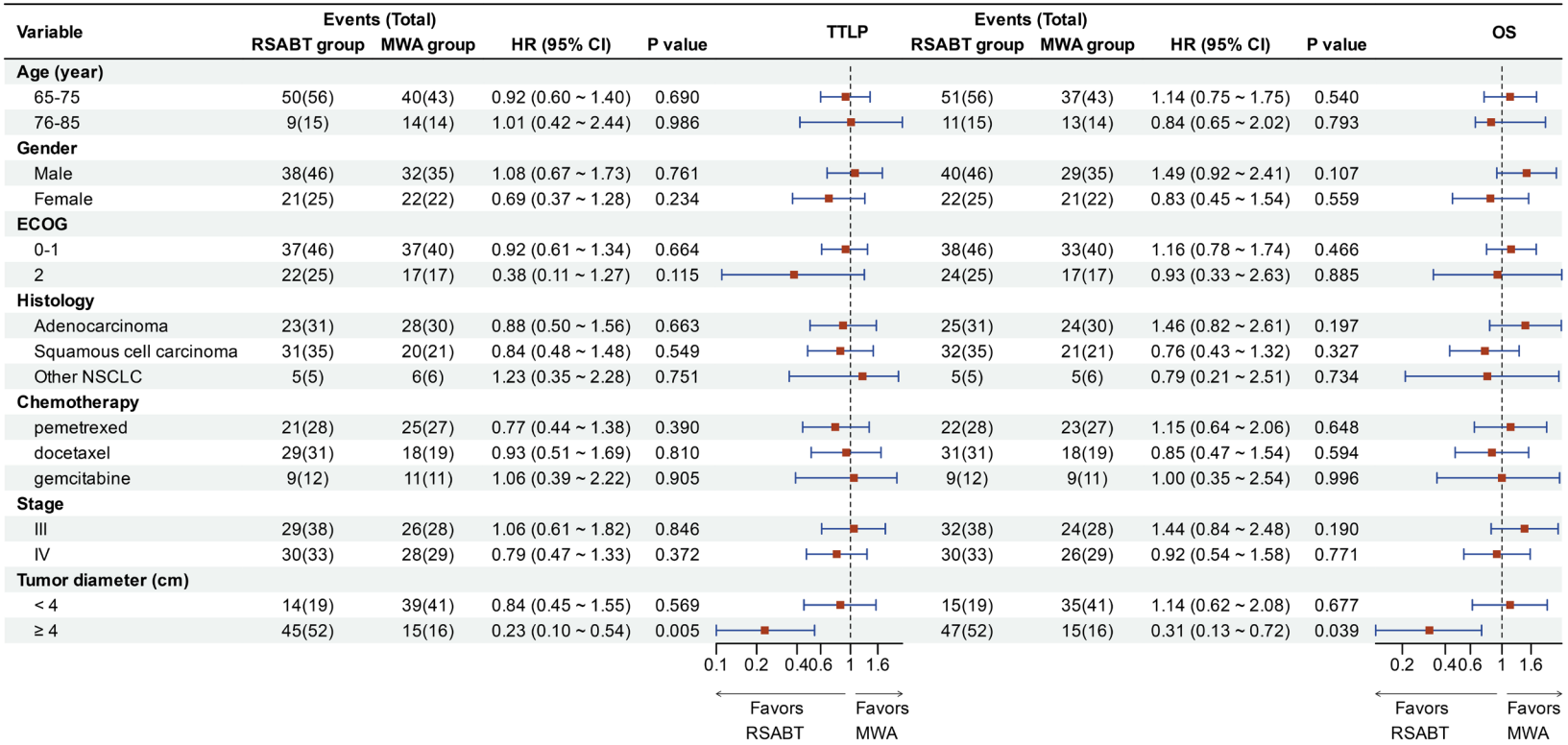

Figure 4. Forest plot comparing time to local progression (TTLP) and overall survival (OS) for RSABT group versus MWA group. In patients with tumor diameters ≥ 4 cm, RSABT showed significantly better outcomes.

Table 2. Comparison of complications between the RSABT and MWA groups

Complications	RSABT group (N = 71)					MWA group (N = 57)					*P*-value
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4-5	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4-5	
Neutropenia	42	17	7	5	0	40	8	7	2	0	0.316
Anemia	45	20	5	1	0	38	11	8	0	0	0.766
Thrombocytopenia	54	15	2	0	0	49	7	1	0	0	0.747
Gastrointestinal reactions	57	12	2	0	0	45	10	2	0	0	0.819
Hepatic and renal dysfunction	66	5	0	0	0	51	6	0	0	0	0.488
Pneumonitis	56	12	3	0	0	46	9	2	0	0	0.303
Pneumothorax	57	8	4	2	0	44	9	3	1	0	0.78
Pleural effusion	68	2	1	0	0	47	8	2	0	0	0.013
Hemoptysis	51	18	2	0	0	46	8	3	0	0	0.097
Pectoralgia	47	20	4	0	0	24	25	6	2	0	< 0.001
Bronchopleural fistula	71	0	0	0	0	55	1	1	0	0	0.196
Needle bleeding	52	18	1	0	0	52	4	1	0	0	0.031

Abbreviations: RSABT, radioactive iodine-125 seed ablation brachytherapy; MWA, microwave ablation.

gy, and increased tumor burden significantly predicting inferior outcomes. Detailed HR, 95% CI, and *P* values are presented in **Table 3**.

Discussion

Age-related frailty and comorbidity often limit tolerance to standard regimens in elderly NSCLC patients, prompting widespread adoption of comprehensive geriatric assessment. In particular, the CARG score has proven highly predictive of chemotherapy adverse events [17]. In a prospective cohort of 500 patients aged ≥ 65 years (29% with lung cancer), CARG stratified grade 3-5 chemotherapy toxicity rates at 30%, 52% and 83% in low-, intermediate- and high-risk groups, respectively ($P < 0.001$). Based on these findings and ASCO guidelines, we tailor treatment intensity: platinum-doublet chemotherapy for low-risk patients (CARG 0-5), single-agent therapy for intermediate-risk patients (CARG 6-9) and palliative care for high-risk patients (CARG 10-23). This risk-adapted approach optimizes therapeutic benefit while minimizing toxicity in this vulnerable population.

Local control remained suboptimal in intermediate-risk patients receiving systemic monotherapy alone. To address this, we introduced focal ablative modalities, MWA or RSABT, alongside single-agent chemotherapy. In our cohort, this combined approach achieved high DCR at three months (95.8% for RSABT and 93.0% for MWA; $P = 0.709$) while maintaining a low incidence of grade ≥ 3 toxicity, underscoring its efficacy and tolerability. Systemic monotherapy and focal ablation act via distinct but complementary mechanisms. Systemic chemotherapy addresses occult micrometastases, while image-guided local treatments focus destructive energy or radiation directly on the primary lesion. Advances in these minimally invasive techniques now allow precise tumor targeting, preservation of healthy lung tissue, faster post-procedure recovery and low complication rates. These therapies complement traditional treatments, serving as valuable adjuncts that enhance overall patient management. In addition to improving local control rates, these local treatment options can also prolong survival. An increasing number of clinical trials have demonstrated the efficacy of ablation in improving OS and PFS in lung cancer patients, even showing survival outcomes comparable to surgical resection and stereotactic body radiotherapy (SBRT) in early-stage lung cancer patients, with less impact on pulmonary function [18-20]. Encouraging results have also been reported for stage III and IV NSCLC; many experts have confirmed that MWA can effectively reduce tumor burden and, when combined with chemotherapy, improve disease control rates and prolong patient survival [15, 21].

As described above, the efficacy of MWA has been clearly established, but most procedures have been performed on peripheral lung cancers, with relatively limited data available for

Table 3. Univariate and multivariate analyses of factors associated with TTLP and OS

Factor	TTLP						OS					
	Median survival months (95% CI)		Univariate analyses		Multivariate analyses		Median survival months (95% CI)		Univariate analyses		Multivariate analyses	
	RSABT group	MWA group	χ^2	*P*-value	HR (95% CI)	*P*-value	RSABT group	MWA group	χ^2	*P*-value	HR (95% CI)	*P*-value
Age (years)			0.082	0.775					0.045	0.832		
65-75	15.0 (13.3-16.7)	14.0 (10.4-17.6)					16.0 (14.4-17.6)	19.0 (17.3-20.7)				
76-85	16.0 (7.3-24.7)	11.0 (4.9-17.1)					20.0 (13.6-26.4)	20.0 (7.1-32.9)				
Gender			0.538	0.463					0.578	0.447		
Male	13.0 (8.2-17.8)	15.0 (10.4-19.6)					14.0 (10.2-17.8)	19.0 (16.9-21.1)				
Female	16.0 (14.4-17.6)	11.0 (8.1-13.9)					20.0 (17.6-22.4)	12.0 (9.2-14.8)				
ECOG PS			11.744	0.001					12.879	< 0.001		
0-1	15.0 (12.9-17.1)	15.0 (11.1-18.9)			0.49 (0.28-0.88)	0.017	16.0 (12.4-19.6)	19.0 (15.7-22.3)			0.43 (0.25-0.76)	0.004
2	14.0 (6.3-21.7)	8.0 (5.7-10.3)			Reference		14.0 (9.4-18.6)	9.0 (4.2-13.8)			Reference	
Histology			10.586	0.001					9.206	0.002		
Adenocarcinoma	18.0 (13.9-22.1)	14.0 (10.0-18.0)			0.60 (0.40-0.89)	0.012	20.0 (15.9-24.1)	20.0 (7.5-32.5)			0.60 (0.40-0.90)	0.013
Other NSCLC	13.0 (8.8-17.2)	11.0 (7.2-14.8)			Reference		15.0 (11.7-18.3)	18.0 (12.3-23.7)			Reference	
Chemotherapy			4.704	0.095					4.884	0.087		
Pemetrexed	16.0 (12.5-19.5)	14.0 (10.8-17.2)					17.0 (9.8-24.2)	20.0 (10.9-29.1)				
Docetaxel	15.0 (10.0-20.0)	11.0 (6.2-15.8)					16.0 (11.0-21.0)	17.0 (9.5-24.5)				
Gemcitabine	12.0 (6.9-17.1)	15.0 (7.3-22.7)					14.0 (7.2-20.8)	19.0 (16.4-21.6)				
Stage			13.693	< 0.001					13.877	< 0.001		
III	17.0 (13.0-21.0)	19.0 (7.2-30.8)			0.48 (0.32-0.72)	< 0.001	20.0 (13.6-26.4)	30.0 (24.9-35.1)			0.47 (0.31-0.72)	< 0.001
IV	13.0 (9.0-17.0)	11.0 (9.0-13.0)			Reference		15.0 (11.9-18.1)	15.0 (7.5-22.5)			Reference	
Tumor diameter (cm)			7.86	0.005					9.04	0.003		
< 4	16.0 (11.8-20.2)	17.0 (12.1-21.9)			0.42 (0.25-0.72)	0.001	18.0 (12.9-23.1)	22.0 (18.4-25.6)			0.53 (0.32-0.89)	0.015
≥ 4	14.0 (10.8-17.2)	8.0 (5.5-10.5)			Reference		15.0 (11.7-18.3)	11.0 (9.9-12.1)			Reference	

Abbreviations: TTLP, time to local progression; OS, overall survival; RSABT, radioactive iodine-125 seed ablation brachytherapy; MWA, microwave ablation; ECOG PS, Eastern Cooperative Oncology Group Performance Status; NSCLC, non-small cell lung cancer.

central lung cancers. This is because central lung cancers are located near critical structures, such as the cardiovascular system, bronchi, and esophagus, making MWA more likely to cause serious complications or incomplete ablation, which can lead to tumor recurrence. Some researchers [22] have aimed to reduce complications and improve ablation success rates by lowering ablation power, shortening ablation time, creating an artificial pneumothorax, or strictly adhering to specific indications. Conversely, other scholars have argued that percutaneous ablation for central lung cancers often requires a longer puncture path, increasing the risk of injuring major blood vessels or bronchi and potentially resulting in severe complications, such as major vascular hemorrhage and bronchopleural fistula. Consequently, many experts recommend that central lung cancer should be considered a contraindication for thermal ablation. This view is supported by the Standards of Practice of the Cardiovascular and Interventional Radiological Society of Europe (CIRSE), which designated lesions located less than 1 cm from central thoracic structures - including the hilum, large vessels, trachea, and esophagus - as contraindications for thermal ablation due to the significantly elevated risk of adverse events [23]. Reflecting these concerns, patients with central lung cancer in our study were excluded from the MWA group but were predominantly included in the RSABT group. RSABT is generally considered a low-risk procedure due to the minimal risk of severe hemorrhage, with most bleeding limited to needle hemorrhage resulting from the need for multiple fine needle punctures [16]. Our study also confirmed this, as no significant hemorrhages requiring intervention were observed. However, to ensure both safety and efficacy, RSABT requires a safe margin from organs at risk; therefore, lesions infiltrating the esophagus, trachea, pulmonary artery or aorta were excluded. The close proximity to these vital structures increases the risk of severe complications, such as hemorrhage, airway obstruction, or perforation, which outweigh the potential therapeutic benefits and thus make the procedure contraindicated in such cases.

Upon reviewing surgical complications, we found that the incidences of pectoralgia and pleural effusion were significantly higher in the MWA group than in the RSABT group ($P < 0.05$). Subsequent subgroup analysis indicated that tumors located within 10 mm of the pleura were associated with a markedly higher incidence of postoperative complications in the MWA group (OR = 9.455, $P = 0.041$). In contrast, pleural proximity did not significantly increase the complication rate in the RSABT group (OR = 0.872, $P = 0.79$). This finding suggests that RSABT may be a safer therapeutic option for tumors near the pleura compared to MWA. The increased complication rate in the MWA group is likely due to thermal damage caused by microwave ablation, which can affect surrounding structures, including the pleura, when the tumor is in close proximity. This thermal injury may contribute to a higher incidence of complications such as pectoralgia and pleural effusion, which were significantly more common in the MWA group than in the RSABT group (pectoralgia: 58% vs. 34%, $P < 0.001$; pleural effusion: 18% vs. 4%, $P = 0.013$). By contrast, RSABT delivers localized radiation with minimal collateral damage to adjacent tissues [24], even for tumors close to the pleura. This key difference suggests that RSABT may be a safer and more suitable treatment option for tumors located near the pleura.

To assess the impact of tumor size on the efficacy of minimally invasive therapy, this study performed a subgroup analysis using a maximum tumor diameter of 4 cm as the cutoff. This threshold was selected based on guidelines and expert consensus for MWA, which recommend curative ablation for tumors ≤ 3 cm and palliative ablation for those ≥ 5 cm [10, 23]. The 4 cm cutoff serves as an intermediate reference to evaluate the influence of tumor size on treatment outcomes. The comparative analysis revealed that TTLP and OS were similar between the RSABT group and the MWA group for tumors < 4 cm. However, for tumors ≥ 4 cm, the RSABT group showed significantly better TTLP and OS, providing greater survival benefits compared to MWA. These results suggest that RSABT may be a more effective option for larger tumors, offering enhanced survival outcomes for patients with advanced disease. The observed differences in treatment efficacy between RSABT and MWA align with previous studies. Zhong et al. [25] reported that tumors exceeding 3 cm in diam-

eter treated with MWA showed a significantly higher likelihood of recurrence compared to smaller tumors. In contrast, RSABT has demonstrated superior efficacy in managing large tumors. Wei et al. [12] further showed that iodine-125 seed brachytherapy outperformed conventional radiotherapy in large, non-resectable NSCLC tumors (5-10 cm), achieving better tumor control and improved survival outcomes. These findings highlight RSABT's therapeutic advantages in treating large tumors, where its precise and sustained dose delivery enables comprehensive tumor ablation and improved survival outcomes for patients with advanced NSCLC. RSABT's continuous low-dose radiation provides sustained, localized treatment, effectively targeting residual tumor cells and reducing recurrence, and has been widely applied in the treatment of various solid tumors. This mechanism compensates for the limitations of MWA, such as incomplete ablation caused by uneven energy distribution or the heat-sink effect. This advantage is especially pronounced in larger tumors, where MWA's efficacy diminishes due to limited energy penetration and increased recurrence rates. Moreover, larger tumors are often more heterogeneous and hypoxic, which further reduces the effectiveness of heat-based therapies like MWA. In contrast, RSABT leverages non-thermal mechanisms that are less affected by tumor vascularity or microenvironmental challenges, making it a more suitable option for advanced-stage disease. Although MWA can utilize techniques such as multiple probe ablations or adjusted probe positioning to manage larger tumors [26], these approaches increase treatment complexity and the risk of complications, particularly when tumors are near critical structures such as blood vessels and the pleura. Clinical studies further highlight the limitations of MWA in larger tumors. Additionally, microwave ablation may be less effective for tumors with irregular characteristics due to the spherical shape of the ablation zone and the uncertain ablation range. RSABT, by contrast, enables precise dose delivery tailored to large or irregular tumor geometries, particularly when guided by accurate preoperative planning, which facilitates optimal intratumoral dose distribution and enhances therapeutic efficacy in anatomically complex settings [12, 27]. Moreover, these results highlight the importance of careful patient selection and personalized treatment planning, particularly for elderly patients, to optimize therapeutic outcomes and minimize risks.

Although both MWA and RSABT demonstrated strong local efficacy, their limitations in addressing micrometastatic disease and preventing systemic recurrence highlight the need for combined approaches, especially in advanced NSCLC. To overcome these challenges, combining single-agent chemotherapy with local therapy provided essential systemic coverage, targeting residual tumor cells and complementing the localized effects of minimally invasive interventions. In elderly NSCLC patients, evidence indicated that mono-chemotherapy is better tolerated than platinum-based regimens, delivering comparable survival benefits with fewer side effects, which was crucial for patients with comorbidities and diminished physiological reserve [7, 8]. Thus, the integration of minimally invasive local therapy with single-agent chemotherapy achieved a dual approach, enhancing both local control and systemic management. This tailored strategy was particularly advantageous for elderly NSCLC patients, offering an optimal balance between efficacy and safety to maintain quality of life while achieving durable treatment outcomes.

Building on our efficacy analyses of the combined minimally invasive ablation and single-agent chemotherapy regimen, we evaluated prognostic factors and identified baseline ECOG PS, disease stage and tumor size as key predictors of TTLP and OS in elderly NSCLC patients. Patients with ECOG PS 0-1, stage III disease or tumors < 4 cm experienced significantly longer TTLP and OS. These findings, consistent with prior reports [28], underscore the need to factor functional status and disease burden into treatment selection, especially given the limited physiological reserve and higher comorbidity load in this population. Moreover, smaller, localized tumors are more amenable to targeted treatments and associated with better outcomes. Integrating these predictors into personalized protocols - such as combining local therapy with systemic mono-chemotherapy or immunotherapy - may optimize both efficacy and tolerability in elderly patients.

Conclusion

For elderly NSCLC patients, minimally invasive therapies combined with single-agent chemotherapy provide expanded treatment options. Our findings suggest that MWA is particularly well-suited for tumors < 4 cm, while RSABT offers comparable efficacy for these tumors. RSABT, with a relatively broader range of indications, is also an appropriate option for certain cases of central lung cancer, as well as for tumors ≥ 4 cm, those with irregular morphology, or those located near critical structures such as the pleura. In these cases, RSABT combined with mono-chemotherapy appears to provide superior local control and survival compared to MWA, making it the preferred approach. These findings provide a valuable foundation for refining individualized treatment strategies in elderly patients with advanced NSCLC, highlighting the selective use of minimally invasive techniques based on tumor size, morphology, and location.

Disclosure of conflict of interest

None.

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References

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I and Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024; 74: 229-263.

[2] Chen Q, Ying S, Qin J and Zhang L. Optimization of treatment strategies for elderly patients with advanced non-small cell lung cancer. Front Oncol 2024; 14: 1384906.

[3] Baladi A, Tafenzi HA, Zouiten O, Afani L, Essaadi I, El Fadli M and Belbaraka R. Immunotherapy for elderly patients with advanced non-small cell lung cancer: challenges and perspectives. Int J Mol Sci 2025; 26: 2120.

[4] Verschueren MV, Peters BJ, Bloem LT, Kruik VR, Uitvlugt EB, Bijsmans AR, Egberts AC and van de Garde EM. Pembrolizumab plus chemotherapy per PD-L1 stratum in patients with metastatic non-small cell lung cancer: real-world effectiveness versus trial efficacy. Clin Lung Cancer 2024; 25: 119-127, e1.

[5] Naltet C and Besse B. Immune checkpoint inhibitors in elderly patients treated for a lung cancer: a narrative review. Transl Lung Cancer Res 2021; 10: 3014-3028.

[6] Abe T, Takeda K, Ohe Y, Kudoh S, Ichinose Y, Okamoto H, Yamamoto N, Yoshioka H, Minato K, Sawa T, Iwamoto Y, Saka H, Mizusawa J, Shibata T, Nakamura S, Ando M, Yokoyama A, Nakagawa K, Saijo N and Tamura T. Randomized phase III trial comparing weekly docetaxel plus cisplatin versus docetaxel monotherapy every 3 weeks in elderly patients with advanced non-small-cell lung cancer: the intergroup trial JCOG0803/WJOG4307L. J Clin Oncol 2015; 33: 575-581.

[7] Pelizzari G, Cortiula F, Giavarra M, Bartoletti M, Lisanti C, Buoro V, Cattaneo M, Rossetto C, Rizzato S, Puglisi F, Macerelli M, Fasola G and Follador A. Platinum-based chemotherapy in older patients with non-small cell lung cancer: what to expect in the real world. Drugs Aging 2020; 37: 677-689.

[8] Williams GR, Hopkins JO, Klepin HD, Lowenstein LM, Mackenzie A, Mohile SG, Somerfield MR and Dale W. Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO guideline questions and answers. JCO Oncol Pract 2023; 19: 718-723.

[9] National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: non-small cell lung cancer (Version 1.2024). NCCN 2024. Retrieved from https://www.nccn.org.

[10] Ye X, Fan W, Wang Z, Wang J, Wang H, Niu L, Fang Y, Gu S, Liu L, Liu B, Zhuang Y, Wei Z, Li X, Li X, Li Y, Li C, Yang X, Yang W, Yang P, Lin Z, Meng Z, Hu K, Liu C, Huang Y, Huang G, Huang K, Peng Z, Han Y, Jin Y, Lei G, Zhai B, Li H, Pan J, Filippiadis D, Kelekis A, Pua U, Futacsi B, Yumchinserchin N, Iezzi R, Tang A and Roy SH. Clinical practice guidelines on image-guided thermal ablation of primary and metastatic lung tumors (2022 edition). J Cancer Res Ther 2022; 18: 1213-1230.

[11] Wei Z, Yang X, Ye X, Feng Q, Xu Y, Zhang L, Sun W, Dong Y, Meng Q, Li T, Wang C, Li G, Zhang K, Li P, Bi J, Xue G, Sun Y, Sheng L, Liu B, Yu G, Ren H, Wang J, Sun L, Chen S, Geng D, Zhang B, Xu X, Zhang L, Sun D, Xu X, Diao C, Huang G, Li W, Han X, Wang J, Meng M, Ni Y, Zheng A, Fan W, Li Y, Li F, Fan H, Zou Z, Li Q and Tian H. Microwave ablation plus chemotherapy versus chemotherapy in advanced non-small cell lung cancer: a multicenter, randomized, controlled,

phase III clinical trial. Eur Radiol 2020; 30: 2692-2702.
[12] Li W, Guan J, Yang L, Zheng X, Yu Y and Jiang J. Iodine-125 brachytherapy improved overall survival of patients with inoperable stage III/IV non-small cell lung cancer versus the conventional radiotherapy. Med Oncol 2015; 32: 395.
[13] Chen C, Wang W, Yu Z, Tian S, Li Y and Wang Y. Combination of computed tomography-guided iodine-125 brachytherapy and bronchial arterial chemoembolization for locally advanced stage III non-small cell lung cancer after failure of concurrent chemoradiotherapy. Lung Cancer 2020; 146: 290-296.
[14] Yue TH and Xing W. 125I seed brachytherapy combined with single-agent chemotherapy in the treatment of non-small-cell lung cancer in the elderly: a valuable solution. Onco Targets Ther 2020; 13: 10581-10591.
[15] Wei Z, Ye X, Yang X, Huang G, Li W, Wang J and Han X. Microwave ablation plus chemotherapy improved progression-free survival of advanced non-small cell lung cancer compared to chemotherapy alone. Med Oncol 2015; 32: 464.
[16] Ji Z, Ni Y, He C, Huo B, Liu S, Ma Y, Song Y, Hu M, Zhang K, Wang Z, Zhao X, Han H, Wang Y, Wang R, Chai S, Hu X, Huang X, Ye X and Wang J. Clinical outcomes of radioactive seed brachytherapy and microwave ablation in inoperable stage I non-small cell lung cancer. Am J Cancer Res 2023; 13: 3753-3762.
[17] Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, Lichtman SM, Gajra A, Bhatia S, Katheria V, Klapper S, Hansen K, Ramani R, Lachs M, Wong FL and Tew WP. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol 2011; 29: 3457-3465.
[18] Chan MV, Huo YR, Cao C and Ridley L. Survival outcomes for surgical resection versus CT-guided percutaneous ablation for stage I non-small cell lung cancer (NSCLC): a systematic review and meta-analysis. Eur Radiol 2021; 31: 5421-5433.
[19] Iguchi T, Hiraki T, Matsui Y, Mitsuhashi T, Katayama N, Katsui K, Soh J, Sakurai J, Gobara H, Toyooka S and Kanazawa S. Survival outcomes of treatment with radiofrequency ablation, stereotactic body radiotherapy, or sublobar resection for patients with clinical stage I non-small-cell lung cancer: a single-center evaluation. J Vasc Interv Radiol 2020; 31: 1044-1051.
[20] Peng JZ, Wang CE, Bie ZX, Li YM and Li XG. Microwave ablation for inoperable stage I non-small cell lung cancer in patients aged ≥70 years: a prospective, single-center study. J Vasc Interv Radiol 2023; 34: 1771-1776.
[21] Zhang YQ, Wu YL, Feng Y and Zhou YX. A clinical study on microwave ablation in combination with chemotherapy in treating peripheral IIIB-IV non-small cell lung cancer. Cancer Biother Radiopharm 2022; 37: 141-146.
[22] Páez-Carpio A, Gómez FM, Isus Olivé G, Paredes P, Baetens T, Carrero E, Sánchez M and Vollmer I. Image-guided percutaneous ablation for the treatment of lung malignancies: current state of the art. Insights Imaging 2021; 12: 57.
[23] Venturini M, Cariati M, Marra P, Masala S, Pereira PL and Carrafiello G. CIRSE standards of practice on thermal ablation of primary and secondary lung tumours. Cardiovasc Intervent Radiol 2020; 43: 667-683.
[24] Li Z, Hu Z, Xiong X and Song X. A review of the efficacy and safety of iodine-125 seed implantation for lung cancer treatment. Cancer Treat Res Commun 2024; 41: 100844.
[25] Zhong L, Sun S, Shi J, Cao F, Han X, Bao X and You Q. Clinical analysis on 113 patients with lung cancer treated by percutaneous CT-guided microwave ablation. J Thorac Dis 2017; 9: 590-597.
[26] Pusceddu C, Melis L, Sotgia B, Guerzoni D, Porcu A and Fancellu A. Usefulness of percutaneous microwave ablation for large non-small cell lung cancer: a preliminary report. Oncol Lett 2019; 18: 659-666.
[27] Zhang F, Wang J, Guo J, Huang X, Guan Z, Lei G, Wang J, Ye X, Zhao X, Wang J, Wang R, Liu B, Zhou Q, Zhao M, Wang C and Li Y. Chinese expert consensus workshop report: guideline for permanent iodine-125 seeds implantation of primary and metastatic lung tumors (2020 edition). J Cancer Res Ther 2020; 16: 1549-1554.
[28] Pîslaru AI, Albisteanu SM, Ilie AC, Stefaniu R, Mârza A, Moscaliuc S, Nicoară M, Turcu AM, Grigoras G and Alexa ID. Lung cancer: new directions in senior patients assessment. Geriatrics (Basel) 2024; 9: 101.

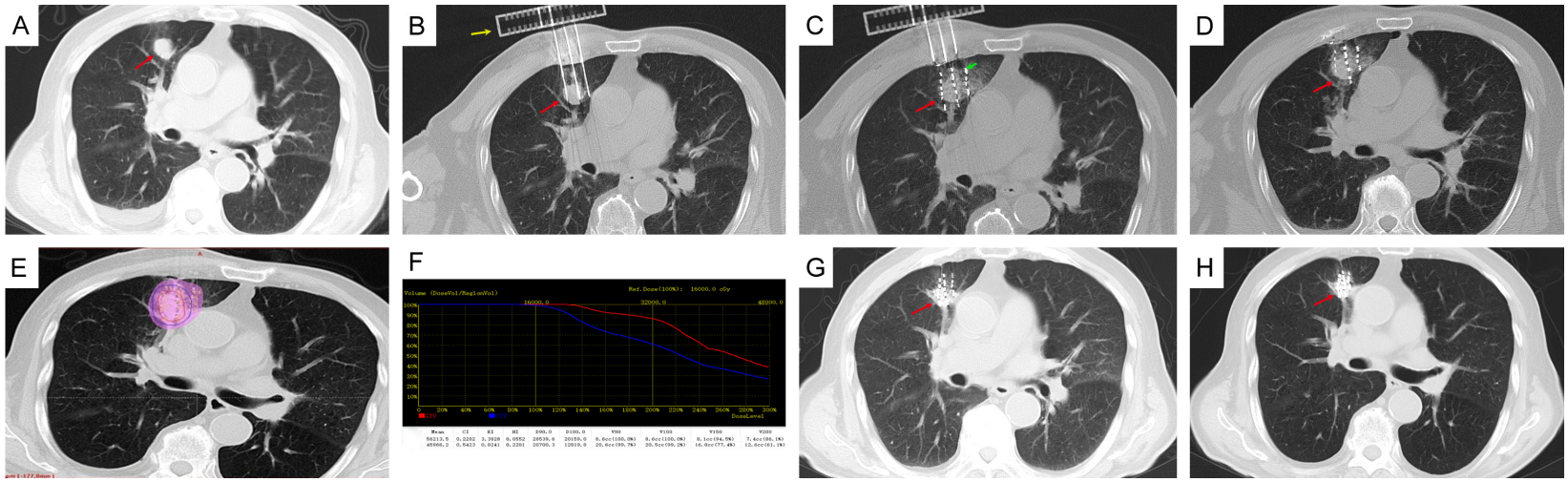

Figure S1. Radioactive iodine-125 seed ablation brachytherapy (RSABT) achieving complete response (CR) in the targeted pulmonary lesion of an 84-year-old patient with advanced lung squamous cell carcinoma. A. Preoperative CT image; B. Insertion of iodine-125 seed needles guided by a 3D-printed coplanar template; C. Implantation of iodine-125 seeds according to preoperative planning; D. Postoperative CT evaluating seed distribution; E. Postoperative isodose distribution map; F. Postoperative dose-volume histogram; G. Follow-up CT at 1 month showing partial response (PR); H. Follow-up CT at 3 months demonstrating CR of the targeted lesion. Arrows: red, target lesion; yellow, 3D-printed coplanar template; green, iodine-125 seed.

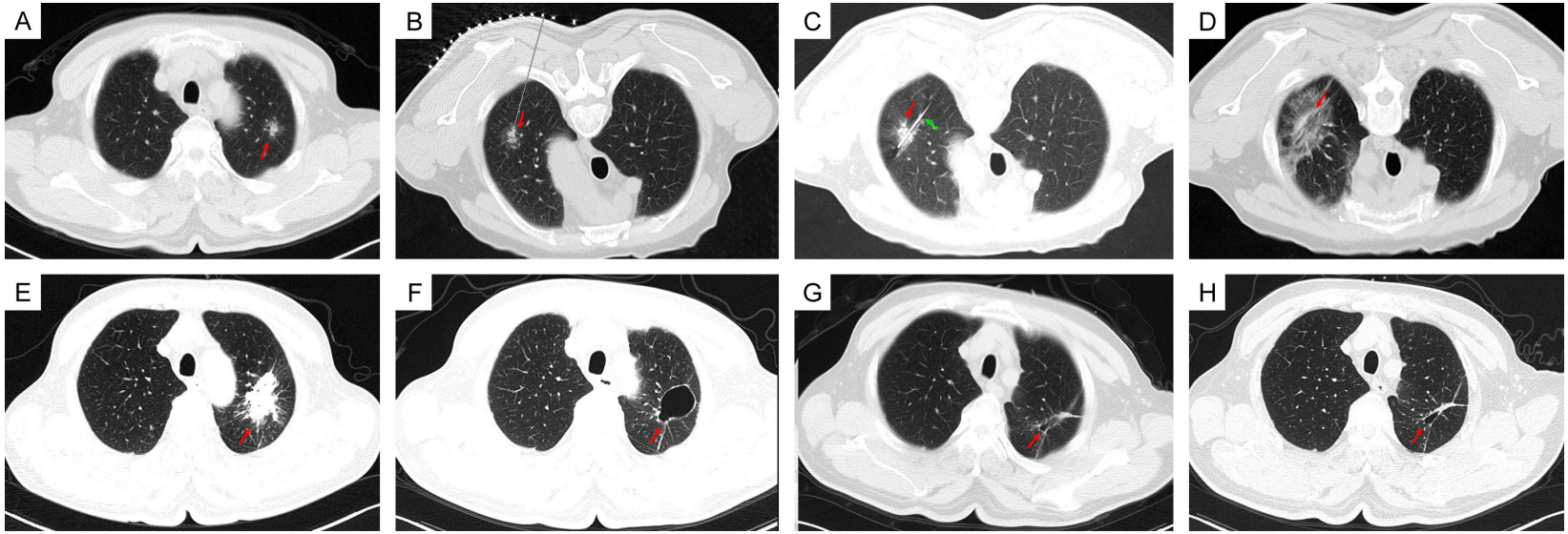

Figure S2. Microwave ablation (MWA) achieving complete ablation in the targeted pulmonary lesion of a 76-year-old patient with advanced lung adenocarcinoma. A. Preoperative CT; B. Preoperative planning; C. Insertion of the microwave antenna extending 0.5 cm beyond the tumor margin; D. Immediate post-ablation CT demonstrating ground-glass opacity (GGO) fully covering the gross tumor region; E. 1-month follow-up CT showing fibrosis within the ablation zone; F. 3-month follow-up CT showing complete cavitation of the lesion; G. 6-month follow-up CT showing cavity resolution and fibrotic scar formation; H. 12-month follow-up CT demonstrating a stable fibrotic scar. Arrows: red, target lesion; green, microwave antenna.