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Original Article

Clinical outcomes of radioactive seed brachytherapy and microwave ablation in inoperable stage I non-small cell lung cancer

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Abstract: This study assessed the efficacy and safety of radioactive iodine-125 seed ablation brachytherapy (RSABT) in comparison to microwave ablation therapy (MWAT) for treating inoperable stage I non-small cell lung cancer (NSCLC). We conducted a retrospective analysis of data from stage I NSCLC patients who underwent CT-guided RSABT or MWAT. The primary outcomes measured were progression-free survival (PFS), overall survival (OS), and the occurrence of adverse events. Of the patients included in the study, 71 underwent RSABT and 105 received MWAT. The median follow-up time for these groups was 47.4 months and 60 months, respectively. The PFS rates at 1-year, 3-year, and 5-year for the RSABT group were 87.3%, 72.6%, and 65.8%, while for the MWAT group, they were 89.5%, 69.3%, and 43.7%, respectively (P = 0.011). The OS rates at 1-year, 3-year, and 5-year for the RSABT group were 97.2%, 78.1%, and 66.1%, and for the MWAT group, they were 99%, 75.8%, and 55%, respectively (P = 0.112). Upon multivariate analysis, the treatment modality was identified as an independent predictor of PFS (P = 0.008). Additionally, both sex and T stage were found to be independent predictors of both PFS and OS (P < 0.05). Adverse events, such as pneumothorax, occurred in 50% of the MWAT group and 39% of the RSABT group (P = 0.313). The incidence of pleural effusion was 44% in the MWAT group compared to 14% in the RSABT group (P < 0.001). Needle bleeding was observed in 32% of the RSABT group and 5% of the MWAT group (P < 0.001). We conclude RSABT demonstrates promising efficacy and safety in the treatment of stage I NSCLC. However, further studies are essential to validate these preliminary findings.

Keywords: Early stage, non-small cell lung cancer, radioactive seed implantation, microwave ablation, clinical efficacy

Introduction

Stereotactic ablative radiotherapy (SABR) is the standard treatment for inoperable early-stage non-small cell lung cancer (NSCLC) [1]. However, in clinical practice, some patients with early-stage NSCLC who are not surgical candidates receive alternative local treatments, such as microwave ablation therapy (MWAT) and radioactive iodine-125 seed ablation brachytherapy (RSABT), for various reasons. The NCCN guidelines suggest that image-guided thermal ablation, such as MWAT, can be used as a treatment option for selected

patients [1]. RSABT, which involves implanting radioactive iodine-125 seeds in the tumor to produce continuous γ radiation that kills tumor cells [2], is increasingly being used in the local treatment of tumors, despite not being included in the guidelines. RSABT has demonstrated effective local control and safety in the treatment of various recurrent and refractory solid tumors [3-6]. This study retrospectively compared the clinical outcomes of RSABT and MWAT in the treatment of stage I NSCLC to further evaluate the efficacy and safety of RSABT in the treatment of early-stage NSCLC, providing a reference for clinical practice and future research.

Methods

Clinical data

Given the relatively few cases of stage I NSCLC treated with RSABT and MWAT, this study combined data from nine medical centers, retrospectively screening case data from December 2010 to November 2020, and re-staging the cases prior to 2017. The inclusion criteria were as follows: (1) pathologically confirmed diagnosis of NSCLC, (2) stage I (T1a-2aN0M0) based on the UICC TNM classification 8th edition [7], and (3) RSABT or MWAT used as the initial treatment without surgery and radiotherapy. Both the RSABT and MWAT were performed with informed consent from the patients and their families.

Instrument and equipment

The required instruments and equipment included: (1) I-125 seeds: type 6711_1985, from HTA Co., Ltd., with a half-life of 59.4 days and a dose rate constant of 0.965 cGy/(h·U). (2) Brachytherapy treatment planning system (BTPS): The KLSIRPS-3D (Beijing University of Aeronautics and Astronautics, and Beijing Astro Technology Co., Ltd.) which can calculate and display the dose distribution in the target area and generate a dose-volume histogram (DVH). Planning system source data originated from official and supplementary reports updated by the American Association of Physicists in Medicine (AAPM) [8-10]. (3) Microwave generators: (3.1) MTC-3C microwave ablation system (Qi Ya Research Institute of Microwave Electric, Nanjing) or (3.2) ECO-2450B microwave ablation system (ECO Microwave Institute, Nanjing). The emission frequency of the microwave antenna was 2,450 ± 50 MHz, and the output energy ranged from 0 W to 100 W. The microwave antenna had an effective length of 100-180 mm, an outside diameter of 14-20 G, and a long tapered pointed end.

Therapeutic method

RSABT involved three stages: (1) Preoperative planning: The first step was to preliminarily determine the treatment range, select the appropriate body position, and perform enhanced computed tomography (CT) scanning of the tumor site one week before the operation, with a layer thickness of 2.5-5 mm. The image was then transmitted to the computer treatment planning system, and a preoperative plan was designed. This included outlining the gross tumor volume (GTV) and adjacent organs at risk (OAR), setting the prescription dose and seed activity, determining the puncture needle path (direction, distribution, and depth), calculating the number of seeds, and simulating the spatial position distribution of seeds. The prescribed dose did not exceed 100 Gy empirically. (2) Intraoperative operation: Local infiltration anesthesia of 1% lidocaine was administered. Based on the preoperative plan, the seed needles were inserted into the target lesion under CT monitoring. The insertion edge of the seed needle reached 0.5 cm from the imaging edge of the tumor, and the spacing between each row of needles was 0.5-1.0 cm. According to the preoperative plan, a Mick applicator was used to implant the seeds with a spacing of 0.5-1.0 cm. CT scan was performed after implantation to determine whether seed distribution was accurate. If the spatial distribution of seeds was not uniform, supplemented seeds could be implanted to avoid cold spots during dosimetry. (3) Postoperative treatment and dose verification: Anti-infective and hemostatic treatments were routinely administered after surgery. Chest CT was performed immediately and 24 h after the operation to determine if there were complications such as pneumothorax and bleeding. Corresponding treatment was administered if necessary, and postoperative dose verification was performed simultaneously (**Figure 1**).

MWAT involved three stages: (1) Preoperative planning: This began by preliminarily determining the gross tumor region (GTR), selecting an

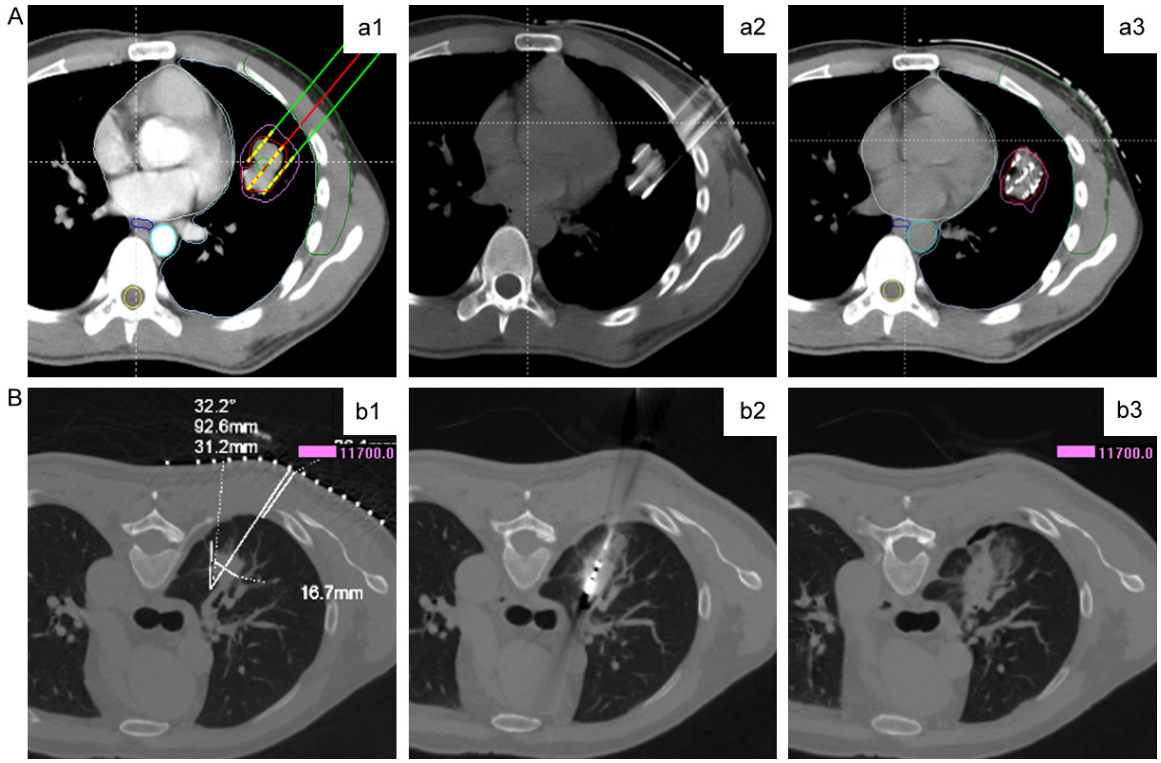

Figure 1. Treatment flow: A. RSABT: a1. Preoperative plan; a2. Intraoperative needle insertion; a3. Postoperative dose verification; B. MWAT: b1. Preoperative planning; b2. Intraoperative needle insertion/ablation; b3. Post ablation manifestations.

appropriate body position, designing the puncture path, and formulating the ablation parameters. (2) Intraoperative operation: Local infiltration anesthesia with 1% lidocaine was administered and ablation needles were inserted under CT monitoring according to the preoperative plan. The thickness of the CT scan layer was 2.5-5 mm. MWAT with an output of 60-80 W has an ablative zone of nearly 3.5 × 3 cm. For tumors of 3.5 cm or more, the ablation procedure was performed with two ablative antennas, with a proposed ablative margin of 0.5-1 cm. During thermal ablation, opaque high-density areas can appear around the tumor due to the damage to the surrounding lung tissue, which is called post ablation GGO (ground glass opacity). When the GGO after ablation was 5 mm-10 mm greater than the GTR boundary before ablation, the ablation was considered sufficient and was terminated. (3) Postoperative treatment: Anti-infection and hemostasis treatments were routinely administered after the operation. Chest CT was performed immediately and 24 h after the operation to determine if there were complications, such as pneumothorax and bleeding, and the corresponding treatment was administered if necessary (**Figure 1**).

Outcome measures

The primary outcome of this study was progression-free survival (PFS), and secondary outcomes were overall survival (OS) and adverse events (AE). Changes in tumor size were detected using CT during the follow-up period.

Response evaluation for RSABT: The response evaluation criteria in solid tumors (RECIST) v1.1 was adopted for RSABT [11]; complete response (CR): the target lesion disappears; partial response (PR): the target lesion diameter decreases by at least 30% compared with the baseline level; progressive disease (PD): the target lesion diameter increases by at least 20% or new lesions appear; and stable disease (SD): the degree of reduction in the target lesions does not reach PR, and the degree of increase does not reach the PD level, which was between the two.

Table 1. Comparison of characteristics between the two groups

Characteristic	RSABT	MWAT	*P*-value
Gender			0.558
Male	49 (69%)	68 (65%)	
Female	22 (31%)	37 (35%)	
Age	70 ± 9.0	71 ± 8.7	0.721
KPS	100 (80-100)	100 (90-100)	0.129
Staging			0.642
Ia (T1)	47 (66%)	73 (70%)	
Ib (T2a)	24 (34%)	32 (30%)	
Site of lung			0.375
Left	29 (41%)	50 (48%)	
Right	42 (59%)	55 (52%)	
Site of lobe			0.507
Upper	43 (61%)	63 (60%)	
Middle	3 (4%)	9 (9%)	
Lower	25 (35%)	33 (31%)	
Pathology			0.072
SCC*	26 (37%)	22 (21%)	
ADC*	41 (58%)	76 (72%)	
NSCLC	4 (5%)	7 (7%)	
Year of treatment			< 0.001
2010-2015	24 (34%)	77 (73%)	
2016-2020	47 (66%)	28 (27%)	
Number of needles	7 ± 3.3	1 ± 0.4	< 0.001

*SCC: Squamous cell carcinoma; *ADC: Adenocarcinoma.

Response evaluation for MWAT: For MWAT, bleeding, edema, exudation, inflammatory cell infiltration, and other changes around the ablation area may last for 3-4 months. Therefore, it is better not to rely solely on RECIST for evaluation, but also to dynamically observe the changes in the ablation area. The changes include: 1) complete ablation (any of the following manifestations): the target lesion disappearance, complete formation of a cavity, focal fibrosis (which can be a scar), reduction, no change, or increase in solid nodules (but there is no sign of abnormal enhancement in contrast CT scan), or atelectasis (no sign of abnormal enhancement in contrast CT scan of lesions in atelectasis); 2) incomplete ablation (any of the following manifestations): typical ground glass nodule (GGN) imaging manifestations remaining at the edge of cavity formation and fibrosis of the focus; some solid components in fibrosis of the focus, and the solid part of CT scanning is enhanced and/or PET-CT tumor has metabolic activity; no change or increase in the size of solid nodules, and abnormal enhancement signs of contrast CT (or) PET-CT nodules showing abnormal metabolic activity.

Toxicities evaluation: Referring to the common terminology criteria for adverse events (CTCAE) V5.0 [12], treatment-related side effects were divided into five grades: Grade 1, asymptomatic and without treatment; Grade 2, symptomatic and in need of treatment; Grade 3, cannot be completely controlled with drugs and need to be treated with instruments or invasive operations; Grade 4, life-threatening, requiring emergency treatment and rescue; and Grade 5, death.

Statistical analysis

The t-test and chi-square tests were used to compare the rates of various indicators between groups. Kaplan-Meier survival curves were used to calculate survival rates, which were compared using the log-rank test. Cox and logistic regression analyses were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between variables and outcomes. All statistical analyses were performed using R statistical software version 4.1 and Statistical Product Service Solutions (SPSS) version 23. All tests were conducted at the significance level of $\alpha = 0.05$ (two-tailed).

Results

Patients characteristics

We analyzed a cohort of 176 patients who met our inclusion criteria: 71 underwent RSABT and 105 underwent MWAT. The mean postoperative dose of RSABT group was 132 ± 19.34 Gy (100-240 Gy). The baseline characteristics of the two groups were matched. General patient information is listed in **Table 1**. For all the patients, the pathological diagnosis was obtained through percutaneous lung biopsy. All patients received their pathological diagnosis via percutaneous lung biopsy. In 11 instances, the pathology reports did not specify subtypes, such as squamous cell carcinoma or adenocar-

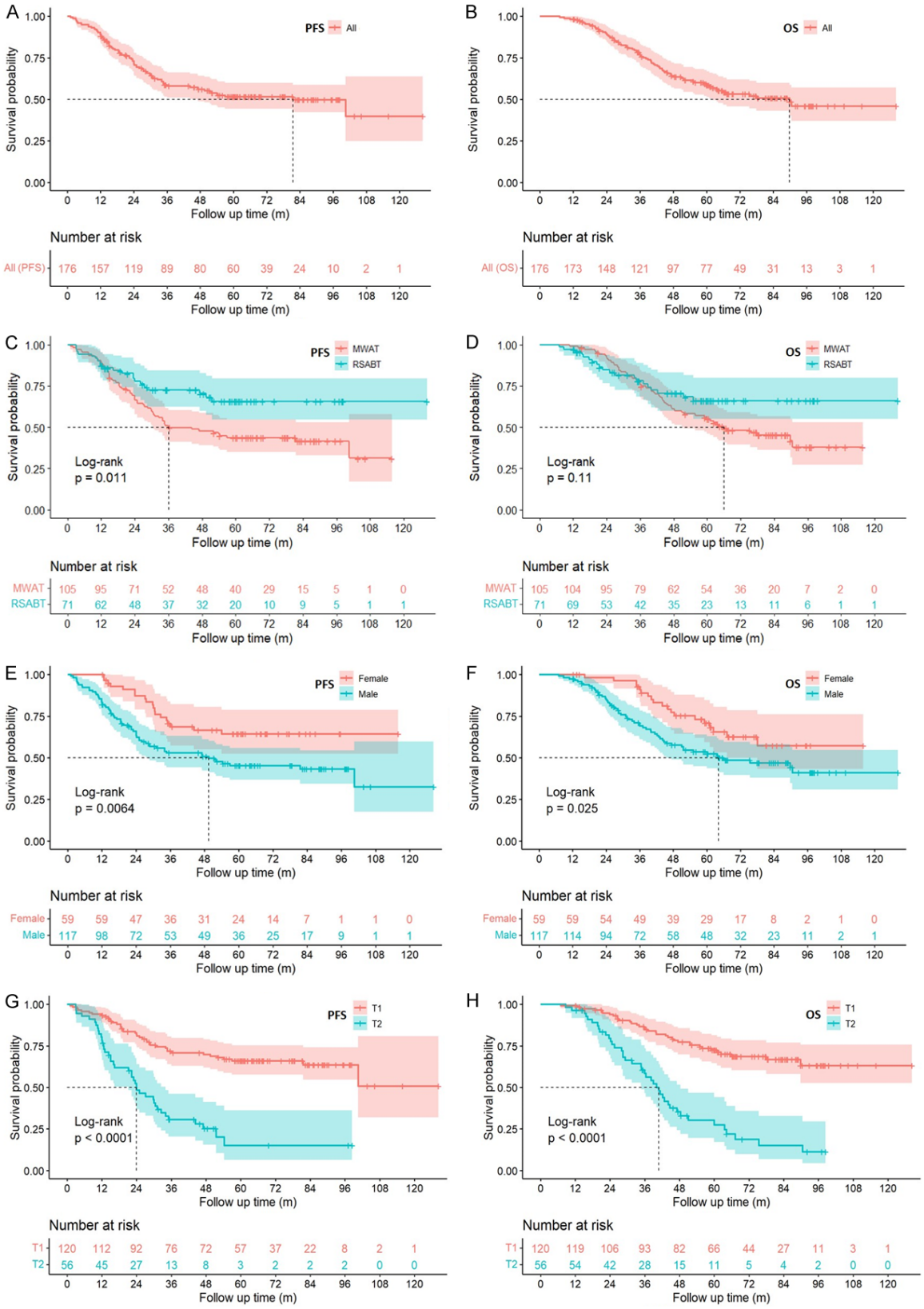

Figure 2. Survival of patients: A. The PFS of the entire group; B. The OS of the entire group; C. The PFS in the RSABT group was better than that in the MWAT group, (P = 0.011); D. The OS in the RSABT group was slightly better than that in the MWAT group There was no significant difference between the two groups (P = 0.112); E, F. The PFS and OS of females was better than that of males, (P = 0.006 and 0.025, respectively); G, H. The PFS and OS of patients with T1 stage was better than that with T2 stage, (P < 0.001).

Table 2. Comparison of failure patterns between groups

Failure patterns	RSABT	MWAT	*P*-value
Progression-free	50 (71%)	45 (43%)	0.032
LR*	5 (7%)	8 (7%)	
RR*	4 (6%)	9 (8%)	
DM*	9 (13%)	27 (26%)	
LR+RR	0	2 (2%)	
LR+DM	1 (1%)	6 (6%)	
RR+DM	1 (1%)	6 (6%)	
LC+RR+DM	1 (1%)	2 (2%)	

*LR: Local recurrence; *RR: Regional recurrence; *DM: Distant metastasis.

cinoma; therefore, these cases were simply classified as NSCLC. Given that only a small portion of NSCLC pathologies were unclassified (11/99) and were unsuitable for independent analysis, we combined unclassified NSCLC and SCC cases during the analysis. This approach aimed to balance the patient distribution across both groups and enhance statistical comparability.

Clinical efficacy

As of August 2021, the median follow-up time (MST) for all patients was 53.7 months (ranging from 7-128.3 months). The MST for the RSABT and MWAT groups was 47.4 months (7-128.3 months) and 60 months (10.8-115.9 months), respectively. The 1-year, 3-year, and 5-year progression-free survival (PFS) and overall survival (OS) rates of the entire cohort were 88.6%, 58.1%, and 51.6% (**Figure 2A**), 98.3%, 76.4%, and 58.6%, for the RSABT and MWAT groups, respectively (**Figure 2B**). Notably, the RSABT group exhibited superior PFS compared to the MWAT group. The 1-year, 3-year, and 5-year PFS of two groups were 87.3%, 72.6%, and 65.8%, 89.5%, 69.3%, and 43.7%, respectively, with a statistically significant difference between the two groups of P = 0.011 (**Figure 2C**). The OS rate for the RSABT group was marginally better than the MWAT group, but the difference was not statistically significant (P = 0.112, **Figure 2D**). The 1-year, 3-year and 5-year OS rates of the two groups were 97.2%, 78.1%, and 66.1%, 99%, 75.8%, and 55%, respectively with no significant difference between the two groups (P = 0.112) (**Figure 2D**). Distant metastasis was the primary cause of treatment failure in both groups, observed in 16% of RSABT patients and 40% of MWAT patients. Local recurrence rates were 9% and 17% for the RSABT and MWAT groups, respectively, with a significant difference between the groups (P = 0.032, **Table 2**).

Influencing factors

Patients were divided into subgroups and included in the univariate logistic analysis according to several factors potentially influencing treatment, such as disease progression and patient survival. These factors encompassed sex, age, KPS score, T stage, lesion location, pathology, and treatment year. Analysis revealed that RSABT conferred protective effects across all subgroups, with statistical significance observed in the majority of these subgroups (P < 0.001, **Figure 3**). In the multivariate Cox analysis, all factors, including treatment modality, were considered. The analysis indicated that RSABT-treated patients exhibited a reduced risk of disease progression (HR 0.48, 95% CI: 0.28-0.83). Conversely, male gender (HR 2.20, 95% CI: 1.28-3.76) and T2a stage (HR 4.08, 95% CI: 2.51-6.64) were associated with an elevated risk of progression. Additionally, female gender (HR 1.78, 95% CI: 1.02-3.11) and T1 stage (HR 4.23, 95% CI: 2.56-6.98) were linked to an increased risk of mortality (**Figure 4**). The progression-free survival (PFS) rates at 1-year, 3-year, and 5-year intervals for males and females were 82.9%, 52.9%, and 45.4%, 100%, 68.6%, and 64.3%, respectively (**Figure 2E**) (P = 0.006). The overall survival (OS) rates at these intervals for males and females were 97.4%, 69.2%, and 52.5%, 100%, 90.8%, and 70.8%, respectively (**Figure 2F**) (P = 0.025). For patients with T1 and T2 stages, the 1-year, 3-year, and 5-year PFS rates were 93.3%, 70.9%, and 65.9%, 78.6%, 30.7%, and 15.2%, respectively (**Figure 2G**) (P < 0.001). The corresponding OS rates for these stages were 99.2%, 84.9%, and 72.4%, 96.4%, 58.4%, and 27.5%, respectively (**Figure 2H**) (P < 0.001).

Toxicities

Surgical interventions led to several complications, including pneumothorax, pleural effusion, fever, infection, and needle bleeding. Among these, pneumothorax emerged as the predominant complication. The MWAT group

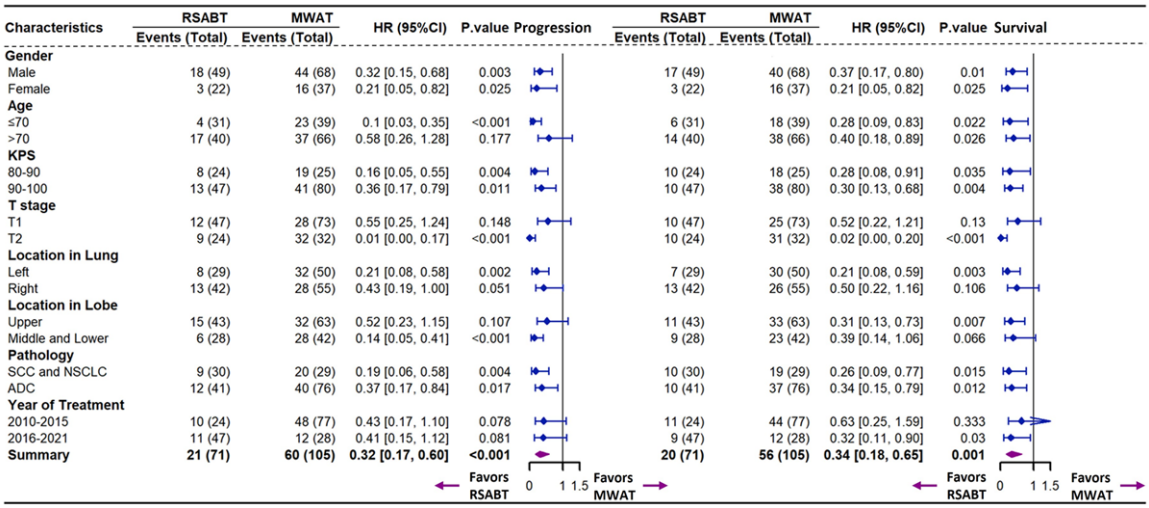

Figure 3. Association of treatment technology with disease progression and patients' survival by subgroup.

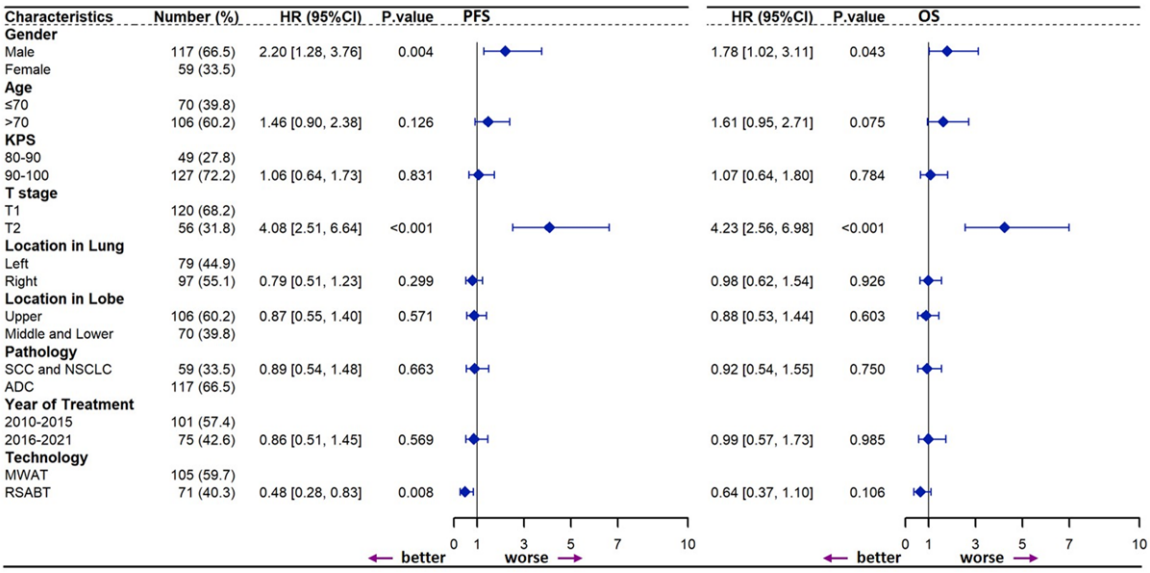

Figure 4. Analysis of prognostic factors in the entire group: male, T2 stage and patients receiving MWAT have worse PFS ($P < 0.01$); male and T2 stage have worse OS ($P < 0.05$).

exhibited a slightly elevated incidence rate compared to the RSABT group (50% vs. 39%). The frequency of closed thoracic drainage procedures was 20% in the MWAT group and 10% in the RSABT group. This difference was not significant ($P = 0.313$). The incidence of pleural effusion in MWAT group was higher than in the RSABT group (44% and 14%, respectively, $P < 0.001$). Furthermore, the RSABT group demonstrated a greater incidence of needle bleeding compared to the MWAT group (32% and 5%, respectively, $P < 0.001$, **Table 3**).

Discussion

Patients with early-stage NSCLC typically undergo surgery or radical external radiotherapy, including SABR [1], while a few patients receive other local treatments. This study aggregated case data from nine centers over a span of 10 years, comparing the outcomes of RSABT and MWAT across a substantial patient cohort.

Our findings suggest that RSABT outcomes are comparable to, if not superior to, those of

Table 3. Comparison of operation related complications between groups

Complications	RSABT	MWAT	*P*-value
Pneumothorax			0.313
G*0	43 (61%)	53 (50%)	
G1	18 (25%)	26 (25%)	
G2	3 (4%)	5 (5%)	
G3	7 (10%)	21 (20%)	
Pleural effusion			< 0.001
G0	61 (86%)	59 (56%)	
G1	10 (14%)	35 (33%)	
G2	0	2 (2%)	
G3	0	9 (9%)	
Fever/infection			0.642
G0-1	68 (96%)	98 (93%)	
G2	3 (4%)	6 (6%)	
G3	0	1	
Needle bleeding			< 0.001
G0	48 (68%)	100 (95%)	
G1	22 (31%)	4 (4%)	
G2	1 (1%)	1 (1%)	

*G: Grade.

MWAT. This may imply that the continuous irradiation and subsequent tumor cell eradication by RSABT are more favorable for tumor control. However, the overall survival (OS) between the two groups did not differ significantly (P = 0.112). This could be attributed to the availability of salvage treatments for patients with disease progression, leading to comparable survival rates across both groups. The survival curves showed that the OS of MWAT group was better than that of RSABT group before 30 months; however, RSABT provided higher survival rates post-30 months, suggesting that RSABT may have better long-term efficacy. Due to incomplete records of gene testing information and patients' systemic therapy (approximately one-third of patients have no record of systematic therapy, and another one-third of patients have missing information), we were unable to further analyze the impact of molecular pattern and medication treatment on patient outcomes. However, the multivariate analysis revealed that the treatment period (2010-2015 vs. 2016-2021) did not affect survival. Therefore, we postulate that, in contrast to RSABT and MWAT, other treatments might exert minimal influence on this patient subset.

Earlier research has evaluated the therapeutic efficacy of RSABT and MWAT for early-stage NSCLC. Martinez Monge R., et al., reported local or regional recurrence in seven T1N0M0 stage NSCLC patients treated with RSABT after a median follow-up of 13 months [13]. Ji et al. documented 3-year and 5-year local control rates of 77.5% and 75.7%, respectively, for RSABT in treating stage I-II NSCLC, with corresponding OS rates of 70.1% and 54.4% [14]. These findings underscore RSABT's potential in treating early-stage NSCLC. In contrast, Yang et al. reported 3-year and 5-year local control rates of 64% and 48% for MWAT in stage I NSCLC, with OS rates of 63% and 43%, respectively [15]. Chan et al.'s meta-analysis of MWAT in stage I NSCLC revealed 3-year and 5-year PFS and OS rates of 43% and 20%, 93% and 50%, respectively [16]. Our results align with these studies, further reinforcing the findings of previous research. For stage I NSCLC, SABR data indicated 3-year PFS and OS rates ranging from 33%-78%, and 41%-68%, respectively [17-19]. Recent research on operable NSCLC treated with SABR showed 3-year and 5-year OS rates of 91% and 87%, and PFS rates of 80% and 77%, respectively [20]. Thus, while SABR may remain the optimal non-surgical treatment for early-stage NSCLC, MWAT and RSABT could be viable alternatives for those unsuitable for SABR.

RSABT and MWAT offer several advantages: 1) Single-session treatment minimizes positioning errors and organ movement, enhancing tumor targeting. 2) Only one hospitalization is required. 3) The cost of treatment is relatively low, which is particularly beneficial in areas where radiotherapy expenses are not covered by medical insurance or have a low coverage proportion. 4) The equipment is cost-effective, allowing even primary hospitals without accelerators to offer treatment, enabling more primary patients to benefit. However, their shortcomings include: 1) Both treatments can lead to complications like pneumothorax (with incidences up to 40%-50%), bleeding, fever, and pleural effusions. Although patients generally recover well post-treatment, they must maintain good physical health. The RSABT group, despite requiring multi-needle puncture, did not exhibit a higher pneumothorax incidence than the MWAT group. This could be due to RSABT's smaller needle diameter and the peripheral location of most lesions. However, the RSABT group had a significantly higher needle bleeding incidence (P < 0.001), which was

presumed to be associated with the multi-needle puncture. 2) Procedures often rely on the physician's experience, potentially affecting treatment precision and quality. 3) Some treatment parameters, like RSABT dose and MWAT's temperature, power, and ablation time, lack standardization. Clinical practice often leans on empirical data and retrospective studies, which might influence outcomes. Advances in treatment technology, especially the emergence of puncture technology guided by 3D printing templates [21], is expected to further improve puncture accuracy and treatment effect, thereby reducing the risk of complications.

Conclusion

The therapeutic efficacy of RSABT in treating stage I NSCLC is comparable to that of MWAT, with both treatments exhibiting similar rates of surgical complications. For patients who decline radical external radiotherapy, alternative treatment modalities should be explored. The predominant complications observed were pneumothorax and needle bleeding. These findings warrant validation through high-quality, prospective studies. As implantation equipment and technology advance, we anticipate enhanced therapeutic outcomes and a reduction in associated complications.

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Disclosure of conflict of interest

None.

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References

[1] NCCN. National comprehensive cancer network, clinical practice guidelines in oncology: non-small cell lung cancer, version 3 (2023). 2023; Available from: https://www.nccn.org/login?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.

[2] Zhang F, Wang J, Guo J, Li Y, Huang X, Guan Z, Lei G, Wang J, Ye X, Zhao X, Wang J, Wang R and Liu B. Chinese Expert Consensus Workshop Report: guideline for permanent iodine-125 seed implantation of primary and metastatic lung tumors. Thorac Cancer 2019; 10: 388-394.

[3] Ji Z, Jiang Y, Tian S, Guo F, Peng R, Xu F, Sun H, Fan J and Wang J. The effectiveness and prognostic factors of CT-guided radioactive I-125 seed implantation for the treatment of recurrent head and neck cancer after external beam radiation therapy. Int J Radiat Oncol Biol Phys 2019; 103: 638-645.

[4] Jiang P, Liu C, Wang J, Yang R, Jiang Y and Tian S. Computed tomography (CT)-guided interstitial permanent implantation of (125)I seeds for refractory chest wall metastasis or recurrence. Technol Cancer Res Treat 2015; 14: 11-18.

[5] Yao L, Cao Q, Wang J, Yang J, Meng N, Guo F, Jiang Y, Tian S and Sun H. CT-Guided (125)I seed interstitial brachytherapy as a salvage treatment for recurrent spinal metastases after external beam radiotherapy. Biomed Res Int 2016; 2016: 8265907.

[6] Wang H, Wang L, Jiang Y, Ji Z, Guo F, Jiang P, Li X, Chen Y, Sun H, Fan J, Du G and Wang J. Long-term outcomes and prognostic analysis of computed tomography-guided radioactive

(125)I seed implantation for locally recurrent rectal cancer after external beam radiotherapy or surgery. Front Oncol 2020; 10: 540096.
[7] Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, Nicholson AG, Groome P, Mitchell A and Bolejack V; International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee, Advisory Boards, and Participating Institutions; International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee Advisory Boards and Participating Institutions. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the forthcoming (Eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 2016; 11: 39-51.
[8] Nath R, Anderson LL, Luxton G, Weaver KA, Williamson JF and Meigooni AS. Dosimetry of interstitial brachytherapy sources: recommendations of the AAPM radiation therapy committee task group No. 43. American Association of Physicists in Medicine. Med Phys 1995; 22: 209-234.
[9] Yu Y, Anderson LL, Li Z, Mellenberg DE, Nath R, Schell MC, Waterman FM, Wu A and Blasko JC. Permanent prostate seed implant brachytherapy: report of the American Association of Physicists in Medicine Task Group No. 64. Med Phys 1999; 26: 2054-2076.
[10] Rivard MJ, Coursey BM, DeWerd LA, Hanson WF, Huq MS, Ibbott GS, Mitch MG, Nath R and Williamson JF. Update of AAPM task group No. 43 report: a revised AAPM protocol for brachytherapy dose calculations. Med Phys 2004; 31: 633-674.
[11] Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D and Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009; 45: 228-247.
[12] U.S. Department of Health and Human Services. Common terminology criteria for adverse events (CTCAE) v5.0. 2017; Available from: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50.
[13] Martinez-Monge R, Pagola M, Vivas I and Lopez-Picazo JM. CT-guided permanent brachytherapy for patients with medically inoperable early-stage non-small cell lung cancer (NSCLC). Lung Cancer 2008; 61: 209-213.
[14] Ji Z, Huo B, Liu S, Liang Q, Xing C, Hu M, Ma Y, Wang Z, Zhao X, Song Y, Wang Y, Han H, Zhang K, Wang R, Chai S, Huang X, Hu X and Wang J. Clinical outcome of CT-guided stereotactic ablative brachytherapy for unresectable early non-small cell lung cancer: a retrospective, multicenter study. Front Oncol 2021; 11: 706242.
[15] Yang X, Ye X, Zheng A, Huang G, Ni X, Wang J, Han X, Li W and Wei Z. Percutaneous microwave ablation of stage I medically inoperable non-small cell lung cancer: clinical evaluation of 47 cases. J Surg Oncol 2014; 110: 758-763.
[16] 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.
[17] Timmerman RD, Paulus R, Pass HI, Gore EM, Edelman MJ, Galvin J, Straube WL, Nedzi LA, McGarry RC, Robinson CG, Schiff PB, Chang G, Loo BW Jr, Bradley JD and ChoyH. Stereotactic body radiation therapy for operable early-stage lung cancer: findings from the NRG oncology RTOG 0618 trial. JAMA Oncol 2018; 4: 1263-1266.
[18] Videtic GM, Paulus R, Singh AK, Chang JY, Parker W, Olivier KR, Timmerman RD, Komaki RR, Urbanic JJ, Stephans KL, Yom SS, Robinson CG, Belani CP, Iyengar P, Ajlouni MI, Gopaul DD, Gomez Suescun JB, McGarry RC, Choy H and Bradley JD. Long-term follow-up on NRG oncology RTOG 0915 (NCCTG N0927): a randomized phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer. Int J Radiat Oncol Biol Phys 2019; 103: 1077-1084.
[19] Bezjak A, Paulus R, Gaspar LE, Timmerman RD, Straube WL, Ryan WF, Garces YI, Pu AT, Singh AK, Videtic GM, McGarry RC, Iyengar P, Pantarotto JR, Urbanic JJ, Sun AY, Daly ME, Grills IS, Sperduto P, Normolle DP, Bradley JD and Choy H. Safety and efficacy of a five-fraction stereotactic body radiotherapy schedule for centrally located non-small-cell lung cancer: NRG oncology/RTOG 0813 trial. J Clin Oncol 2019; 37: 1316-1325.
[20] Chang JY, Mehran RJ, Feng L, Verma V, Liao Z, Welsh JW, Lin SH, O'Reilly MS, Jeter MD, Balter PA, McRae SE, Berry D, Heymach JV and Roth JA; STARS Lung Cancer Trials Group. Stereotactic ablative radiotherapy for operable stage I non-small-cell lung cancer (revised STARS): long-term results of a single-arm, prospective trial with prespecified comparison to surgery. Lancet Oncol 2021; 22: 1448-1457.
[21] Ji Z, Sun H, Jiang Y, Guo F, Peng R, Fan J and Wang J. Comparative study for CT-guided (125) I seed implantation assisted by 3D printing coplanar and non-coplanar template in peripheral lung cancer. J Contemp Brachytherapy 2019; 11: 169-173.