Comparison of expected imaging findings following percutaneous microwave and cryoablation of pulmonary tumors: ablation zones and thoracic lymph nodes

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Full Title: Comparison of expected imaging findings following percutaneous microwave and cryoablation of pulmonary tumors: Ablation zones and thoracic lymph nodes.

Abstract

Objective: To compare temporal changes of ablation zones and lymph nodes following lung microwave ablation (MWA) and cryoablation.

Methods: This retrospective cohort study compared lung ablation zones and thoracic lymph nodes following MWA and cryoablation performed 2006-2020. In the ablation zone cohort, ablation zone volumes were measured on serial CT for 12 months. In the lymph node cohort, the sum of bidimensional products of lymph node diameters was measured before (baseline) and up to 6 months following ablation. Cumulative incidence curves estimated the time to 75% ablation zone reduction and linear mixed-effects regression models compared the temporal distribution of ablation zones and lymph node sizes between modalities.

Results: Ablation zones of 59 tumors treated in 45 sessions (16 MWA, 29 cryoablation) in 36 patients were evaluated. Differences in the time to 75% volume reduction between modalities were not detected. Following MWA, half of ablation zones required an estimated time of 340 days to achieve 75% volume reduction compared to 214 days following cryoablation (p=.30). Thoracic lymph node sizes after 33 sessions (13 MWA, 20 cryoablation) differed between modalities (baseline-32 days, p=.01; 32-123 days, p=.001). Following MWA, lymph nodes increased on average by 38mm^2 (95%CI, 5.0–70.7; p=.02) from baseline to 32 days, followed by an estimated decrease of 50mm^2 (32-123 days; p=.001). Following cryoablation, changes in lymph nodes were not detected (baseline-32 days, p=.33).

Conclusion: The rate of ablation zone volume reduction did not differ between MWA and cryoablation. Thoracic lymph nodes enlarged transiently after MWA but not after cryoablation.

Key words:

1. Microwave ablation
2. Cryoablation
3. Computed tomography
4. Lung
5. Imaging follow-up

Key points:

- Contrary to current belief, the rate of lung ablation zone volume reduction did not differ between microwave and cryoablation.
- Transient enlargement of thoracic lymph nodes after microwave ablation was not associated with regional tumor spread and decreased within six months following ablation.
- No significant thoracic lymph node enlargement was observed following cryoablation.

Abbreviations:

- CI – confidence interval
- ECOG - Eastern Cooperative Oncology Group
- HU – Hounsfield Units
- IQR – interquartile range
- mRECIST – modified Response Evaluation Criteria in Solid Tumors
- MWA – microwave ablation
- NE – not estimable
- RFA – radiofrequency ablation

Introduction

Image-guided percutaneous microwave ablation (MWA) and cryoablation are safe and effective treatment options for thoracic tumors [1-7]. A thorough understanding of expected imaging findings following MWA and cryoablation is required to accurately detect local residual or recurrent disease. Viable tumor covered by the ablation zone can be detected on follow-up imaging once post-treatment changes have either stabilized, partially or completely resolved [8, 9].

Reviews have repeatedly suggested that lung cryoablation zones involute faster compared to microwave ablation zones yet data supporting this claim are lacking [4, 8-11]. In clinical practice, more rapid involution could facilitate the early identification of local disease progression and possibly affect the frequency and duration of imaging follow-up. In clinical trials, the rate of ablation zone volume reduction would inform the minimum length of imaging follow-up to achieve thresholds set by the mRECIST (modified Response Evaluation Criteria in Solid Tumors) criteria [12, 13]. The current understanding of lung ablation zone evolution following MWA and cryoablation is predominantly based on two-dimensional assessments [8, 9, 14-16]. To our knowledge, volumetric measurements of lung ablation zone following MWA and cryoablation have not been compared.

In addition to evaluating the ablation zone, response evaluation following lung ablation also includes the assessment of locoregional lymph nodes [17, 18]. Transient enlargement of thoracic lymph nodes has been described following radiofrequency ablation (RFA) of pulmonary tumors and can mimic nodal metastases [17, 19]. Thoracic lymph node enlargement was noted following MWA in one study but a comparison with cryoablation is lacking [20].

We conducted this retrospective study with the *a priori* hypotheses that the rate of lung ablation zone volume reduction differs between MWA and cryoablation, and that MWA of pulmonary tumors, but not cryoablation, is associated with a transient locoregional lymph node enlargement.

Materials and Methods

The Institutional Review Board approved this HIPAA compliant retrospective observational cohort study, and a waiver of written informed consent was obtained. Twenty-eight patients were part of prior reports [21, 22].

Patient selection

A patient cohort was defined to address each hypothesis using prospectively maintained institutional databases containing 128 consecutive patients aged 19-90 years who underwent 211 percutaneous image-guided microwave or cryoablation sessions targeting 317 lung tumors at Massachusetts General Hospital and Brigham and Women's Hospital from 2006 through 2020. Patients could contribute one or multiple sessions to one or both cohorts. Data collection and procedural details are summarized in the **Supplementary Materials and Methods**.

Ablation zone cohort

Inclusion required that patients were treated with the goal of tumor eradication and underwent chest CT within 90 days prior to ablation, and two or more chest CT scans with the same slice thickness (up to ≤ 3.75 mm) within 15-45 days (baseline) and 45-180 days following the ablation. Ablations that were not performed with the 2.45 GHz AMICA system (HS Hospital Service S.P.A.) or the VISUAL ICE system (Boston Scientific) were excluded (n=14 tumors). Lack of primary technical success (n=8 tumors), local tumor progression within 12 months following ablation (n=16 tumors) and the extension of ablation zones into either chest wall or lung parenchyma scarred from prior radiation or prior ablation (n=37 tumors) led to exclusion.

Lymph node cohort

Inclusion required that patients were treated with the goal of tumor eradication and underwent chest CT within 90 days prior to ablation and within 15-45 days and 90-180 days following ablation. All microwave and cryoablation devices were permissible. The exclusion criteria included initiation of systemic therapy, radiation of the ablated tumor and subsequent ipsilateral lung ablation (n=52 tumors). Lack of primary technical success (n=8) and local tumor progression within 12 months following ablation (n=6 tumors) also led to exclusion.

Figure 1 summarizes inclusion and exclusion criteria for both cohorts. 8 patients with 25 tumors treated in 19 sessions (3 MWA, 15 cryoablation) contributed to both cohorts.

Study endpoints

The primary outcome was the rate of ablation zone volume reduction within 12 months (15-365 days) following the ablation and time to 75% volume reduction. The ablation zone was defined as the volume of consolidation and ground glass in treated lung [9, 23] and quantified using 3DSlicer software (www.slicer.org, Version 4.10.2), (**Figure 2**). Ablation zones were segmented on lung window settings (window width, 1,500 HU [Hounsfield Units]; level, -600 HU) on two or more chest CT scans obtained between 15-365 days post ablation. Segmentation relied on a lower threshold of -400 HU; no upper threshold was used. Cavitary areas inside the ablation zone were included in the ablation zone volume. A primary analyst (M.M.W., 3rd year medical student) performed all measurements. Each measurement was reviewed by a thoracic radiologist (F.J.F., 6 years of experience) and corrected if necessary. A random selection of 30 (15%) measurements was reassessed by the primary analyst and independently assessed by a second analyst (K.S.L., 4th year medical student) to determine inter- and intrareader agreement. Using the same approach, volumes of targeted tumors were measured on CT scans obtained within 90 days prior to the ablation.

The secondary outcome was change in lymph node size defined as the sum of bidimensional products of diameters before and over 6 months following the ablation based on an independent assessment by four fellowship-trained radiologists (experience, 1-29 years) blinded to clinical outcomes. Supraclavicular, mediastinal, hilar, intraparenchymal, and extrapleural nodes located ipsilaterally to the ablated tumor were assessed within 90 days prior to ablation (T_0), and at 15-45 days (T_1) and 90-180 days (T_2) post ablation [19]. The sum of bidimensional products of lymph node diameters (mm^2) was calculated for each time point by averaging all ipsilateral lymph node measurements. Lymph nodes not present at T_0 were measured and added to the sum of bidimensional products of lymph node diameters. A contralateral lymph node not related to the drainage pathway of the ablated tumor served as internal control (**Figure 3**). Enlargement of the control lymph node was recorded if any of the four readers determined a short-axis diameter increase of more than 2 mm.

Statistical analysis

Descriptive summaries were computed for each cohort and presented by ablation modality. Categorical variables were summarized as frequencies and percentages, while continuous variables were summarized using the median with IQR. Inferential comparisons of patient, session and tumor characteristics were assessed by constructing separate regression models (linear, logistic) and estimating the effect of ablation modality using generalized estimating equations assuming an independent correlation structure [24, 25]. Inter- and intrareader agreement of volumetric measurements were assessed using intra- and interclass correlation coefficients.

The association between time to 75% reduction in ablation zone volume and ablation modality was assessed with interval-censored survival analysis. Turnbull cumulative incidence curves were compared using the generalized log-rank test [26]. A linear mixed-effects model was developed to quantify the temporal relationship between log-transformed tumor-specific ablation zone volume and ablation modality while accounting for follow-up time in days (continuous) and tumor size (≤1cm vs. >1cm in maximum axial diameter) [27]. Restricted cubic splines were used to model the non-linear relationship between follow-up time and ablation zone volume and linear combinations of model estimates summarized ablation zone volumes by modality at specific follow-up times, absolute rates of change by modality and differences in the absolute rates of change by modality. Similar modeling was used to quantify the association between log-transformed lymph node size and ablation modality while accounting for T0, T1 and T2 (categorical) .

Bootstrapping (1,000 replications) was performed to compute all estimates, their 95%CI, and associated p-values. A p-value <.05 was considered to indicate statistical significance. All analyses were performed using R Software Version 4.0.2 (Foundation for Statistical Computing).

Results

A total of 56 patients with 76 tumors treated in 59 sessions were included. Image acquisition parameters for both cohorts are detailed in **Supplementary Table 1**.

Ablation zone cohort

Thirty-six patients with 59 lung tumors treated in 45 sessions (MWA, 16 sessions; cryoablation, 29 sessions) were used to evaluate ablation zone volumes. MWA was used in 11/36 (31%) patients; cryoablation was used in 20/36 (56%) patients. Both modalities were used in 5/36 (3%) patients with a median time of 301 days (IQR, 77-449 days) between ablation sessions. While 29/36 (81%) patients were treated in one ablation session, 6 (17%) patients and one (3%) patient were treated in two and three ablation sessions, respectively.

Of the 36 patients, 19 (53%) were female; the median age was 65 years (range, 20-84 years; IQR, 56-69 years). Intergroup differences regarding sex, age, ECOG performance status, smoking history, and diagnosis were not detected (**Table 1**). General endotracheal anesthesia was predominantly used in the cryoablation group (38% vs 76%; p=.01). Treatment of multiple tumors within one session was more common with cryoablation (41%) than with MWA (19%), (p=.14). Two cryoablation sessions included a percutaneous needle biopsy.

Tumors treated with MWA were more often located in the upper lobes (70% vs 36%; p<.001) and were all treated with a single applicator (100% vs 56%; p<.001), **Table 2**.

Ablation zone volume

The median number of volumetric measurements per ablation zone was 3 (range 2-6; IQR, 3-4). The initial measurement was collected, on average, 30 days (IQR, 28-35 days) post-ablation with subsequent measurements at approximately 119 days (IQR, 96-145 days) and 279 days (IQR, 187-320 days) post-ablation. Inter- and intraclass correlation coefficients of volumetric measurements were 0.89 (95%CI, 0.72-0.96) and 0.98 (95%CI, 0.97-0.99), respectively. Values between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 are indicative of moderate, good, and excellent reliability, implying excellent reliability of volumetric measurements [28].

Compared to the first assessment post ablation, half of ablation zones achieved at least a 75% volume reduction after an estimated median of 340 days (95%CI, 225, not estimable; NE) following MWA and after an estimated median of 214 days (95%CI, 126, NE) following cryoablation. No statistically significant difference in the cumulative incidence of 75% volume reduction was detected between ablation modalities (generalized log-rank test, p=.30) (**Figure 4**).

Of 52 ablation zones, 11 (21%) followed by CT for 120-365 days involuted to a volume less than the targeted tumor volume (3 following MWA; 8 following cryoablation, p=.66). None of the ablation zones showed complete resolution (volume of zero) within 12 months post ablation.

For tumors >1 cm in maximum diameter treated with MWA the estimated ablation zones at 30-, 60-, and 90-days post ablation were 8.2 cm^3 (95%CI, 7.1-9.3); 5.43 cm^3 (95%CI, 4.7-6.0) and 3.9 cm^3 (95%CI, 3.3-4.4), respectively. These ablation zone volumes decreased by 2.8 cm^3 (95%CI, 2.1-3.6) from 30- to 60-days post ablation, by 1.5 cm^3 (95%CI, 1.3-1.8) from 60- to 90-days post ablation, and by 0.5 cm^3 (95%CI, 0.3-0.7) from 180 to 270 days post ablation. For tumors >1 cm in maximum diameter treated with cryoablation the estimated ablation zones at 30-, 60-, and 90-days post ablation were 6.8 cm^3 (95%CI, 6.2-7.5); 4.2 cm^3 (95%CI, 3.9-4.5) and 2.8 cm^3 (95%CI, 2.5-3.0), respectively (**Supplementary Table 2**, **Figure 5**). These ablation zone volumes decreased by 2.7 cm^3 (95%CI, 2.2- 3.2) from 30- to 60-

days post ablation, by 1.4 cm^3 (95%CI, 1.2-1.5) from 60- to 90-days post ablation and by 0.3 cm^3 (95%CI, 0.2-0.4) from 180 to 270 days post ablation. The estimated difference in rates of change between MWA and cryoablation for tumors >1cm was 0.1 cm^3 (95%CI, -0.7-1.1; p=.72) from 30- to 60-days, 0.2 cm^3 (95%CI, -0.2-0.5; p=.31) from 60- to 90-days and 0.2 cm^3 (95%CI, -0.02-0.5; p=.08) from 180 to 270 days. Estimates for tumors ≤1cm in maximum diameter are summarized in **Supplementary Table 3**.

Lymph node cohort

Twenty-eight patients with 42 lung tumors treated in 33 ablation sessions (MWA, 13 sessions; cryoablation, 18 sessions) were used to evaluate thoracic lymph node sizes. MWA was used in 11/28 (39%) patients, cryoablation was used in 16/28 (57%) patients and 1/28 (4%) patient was treated with both modalities in separate ablation sessions (449 days between sessions). While 23/28 (82%) patients contributed only one session, 5/28 (18%) patients contributed two sessions.

Most patients (19, 58%) were male with a median age of 65 years (range, 20-87 years; IQR, 58-70 years) (**Table 3**). Intergroup differences regarding sex, age, ECOG performance status, smoking history, and anesthesia were not detected. One cryoablation session included a percutaneous needle biopsy. While all MWA sessions targeted a single tumor, 35% of cryoablation sessions targeted multiple tumors, (p=<.001).

All MWA sessions used a single applicator and predominantly targeted a single tumor (p=.02), **Table 4**.

Thoracic lymph node size

Thoracic lymph node size was evaluated on scans obtained at a median time of 35 days (IQR, 60-22 days) prior to the ablation (T_0), and after a median time of 32 days (T_1; IQR, 27-36 days) and 123 days (T_2; IQR, 114-137 days) post ablation.

Significant differences in lymph node sizes from T_0 to T_1 between modalities were observed (**Figure 6**, **Supplementary Table 4, Supplementary Figure 1**). Following MWA, lymph node sizes increased, on average, by 37.8 mm^2 (95%CI, 5.0–70.7; p=.02), while lymph nodes remained stable following cryoablation (5.8 mm^2 [95%CI, -16.5=.024–5.5; p=.33]). The estimated difference in the rates of change between MWA and cryoablation was 43.6 mm^2 (95%CI, 8.7.4–78.0; p=.01).

Between T_1 and T_2, lymph nodes sizes decreased, on average, 50.4 mm^2 (95%CI, 21.4–70.3; p=.001) following MWA and remained stable following cryoablation (1.4 mm^2 [95%CI, -8.7–10.9; p=.83]). The estimated difference in the rates of change between MWA and cryoablation was 51.8 mm^2 (95%CI, 21.1–80.6; p=.001).

Differences between lymph node size and the session-specific targeted tumor volume were not detected (p=.12). A chest tube was required after a MWA session but was not associated with lymph node enlargement. None of the readers detected a size increase of the control lymph node from T_0 to T_1, regardless of modality.

Discussion

Studies comparing imaging findings following MWA and cryoablation of pulmonary tumors are lacking. First, the rate of lung ablation zone volume reduction did not differ between MWA and cryoablation in our study, contrary to current belief [4, 9, 10, 29, 30]. Second, MWA was associated with transient locoregional lymph node enlargement, which decreased within 6 months post ablation and did not indicate neoplastic involvement. No significant thoracic lymph node enlargement was observed following cryoablation.

Rapid involution of lung ablation zones has been repeatedly touted as an advantage of cryoablation compared to MWA in that cryoablation may allow for earlier identification of residual disease and local tumor progression [4, 8, 9, 29, 30]. However, differences in the rate of volume reduction of ablation zones between MWA and cryoablation of pulmonary tumors were not detected despite detailed volumetric analysis. We measured ablation zones with semi-automated threshold-based volumetric segmentation as suggested by current reporting guidelines [23]. Additionally, we did not observe a difference between modalities regarding the time to 75% volume reduction of the ablation zone, a threshold defining complete responses according to the mRECIST criteria [13]. Therefore, our data do not support the hypothesis that cryoablation allows for earlier evaluation of treatment response.

Our findings extend the understanding of expected imaging findings following percutaneous MWA and cryoablation of pulmonary tumors. Our data show a non-linear trend in ablation zone volumes throughout the observation period following both modalities. We intentionally did not assess imaging findings within two weeks post ablation since prior reports describe that ground-glass opacities surrounding the treatment zone at that time correspond to transient inflammation, alveolar hemorrhage, or edema [8, 9, 15]. Based on the observation by Ito et al. that the rate of volume reduction of ablation zones slows or stops at 6 months following cryoablation, we decided to measure ablation zone volumes over 12 months to capture the point of volume stabilization [8]. At 6 months following cryoablation, the maximum axial diameter of ablation zones has been reported to be less than the target tumor diameter in up to 45% of cases, including instances of complete resolution [9, 31]. However, prior analyses relied predominantly on two-dimensional measurements, whereas our study was based on three-dimensional volumetric analyses. In the current study, only 21% of ablation zones assessed in 3D had involuted to a volume smaller than the target tumor by 6 months, and none resolved completely.

Transient locoregional lymph node enlargement has been reported in up to 63% of RFA of pulmonary tumors, independent of tumor size or location [19]. Wolf et al. described “thoracic lymphadenopathy” in 20% of patients who underwent MWA for pulmonary tumors but did not provide a definition in terms of location and size [19, 20]. To our knowledge, this phenomenon has not yet been studied for cryoablation, and no comparison between MWA and cryoablation has been reported. Our data show that thoracic lymph node sizes significantly increase within the first month following MWA while lymph nodes following cryoablation remain stable. A size increase after MWA resolved within 6 months after ablation did not indicate local tumor progression and was not associated with session-specific targeted tumor volume.

This study has several limitations. First, our data were limited to two institutions and the retrospective nature of the study precluded adjustments for the choice of ablation modality, which may have resulted in selection bias. Second, the strict inclusion and exclusion criteria resulted in a modest sample size and contributed to an unusual study design with two nonidentical but overlapping cohorts. Third, we included only patients without evidence of local tumor progression, and patients who were followed with comparable CT image acquisition parameters to allow for valid inter-subject comparisons. Lastly, our analysis of thoracic lymph node sizes did not stratify by lymph node stations and did not account for lymphatic drainage to the contralateral mediastinum. However, this phenomenon is considered rare [32]. Future studies should address comparisons of procedural complications, progression-free survival, and overall survival between MWA and cryoablation [5, 22].

In conclusion, we did not detect differences in the rate of lung ablation zone volume reduction between microwave ablation and cryoablation of pulmonary tumors. A transient increase in locoregional lymph node sizes within the first month following microwave ablation is likely reactive and can be expected to resolve within 6 months following ablation. Contrary to radiofrequency ablation and microwave ablation, cryoablation of pulmonary tumors is not associated with post-procedural thoracic lymph node enlargement.

1. Funding

The authors state that this work has not received any funding.

Compliance with Ethical Standards

2. Guarantor:

The scientific guarantor of this publication is Florian J. Fintelmann.

3. Conflict of Interest:

Florian J. Fintelmann received salary support from the American Roentgen Ray Society and the William M. Wood Foundation during the study period, as well as research support from Boston Scientific. Amita Sharma reports research support from Hummingbird Diagnostics Inc. for unrelated work. The other authors have no relevant conflicts of interest to report.

4. Statistics and Biometry:

Nathaniel D. Mercaldo, PhD is a biostatistician in the Department of Radiology at Massachusetts General Hospital and performed the statistical analysis for this manuscript.

5. Informed Consent:

Written informed consent was waived by the Institutional Review Board.

6. Ethical Approval:

Institutional Review Board approval was obtained.

7. Study subjects or cohorts overlap:

The current study overlaps with two previously published reports (references #21, # 22) in that the clinical outcomes of 28 patients in the current study were previously described. The current study differs significantly because it focuses only on imaging features following percutaneous lung ablation, regardless of clinical outcomes. **We withheld the two references referring to overlapping cohorts to enable unbiased peer review.**

Ref #21 assessed the effect of a final active thaw on the incidence and grade of hemoptysis following cryoablation of pulmonary tumors

[Wrobel MM, Bourgouin PP, Abrishami Kashani M et al (2021) Active Versus Passive Thaw Following Percutaneous Cryoablation of Pulmonary Tumors: Effect on Incidence, Grade, and Onset of Hemoptysis. AJR Am J Roentgenol. 10.2214/AJR.21.25872]

Ref #22 evaluated overall survival and local tumor progression in patients treated with microwave and cryoablation for pulmonary sarcoma metastases

[Bourgouin PP, Wrobel MM, Mercaldo ND et al (2021) Comparison of Percutaneous Image-Guided Microwave Ablation and Cryoablation for Sarcoma Lung Metastases: A 10-Year Experience. AJR Am J Roentgenol. 10.2214/AJR.21.26551:1-11]

8. Methodology

- retrospective
- observational
- multicenter study

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Figure legends

Figure 1: Flow chart with inclusion and exclusion criteria for evaluation of ablation zone evolution (ablation zone cohort) and thoracic lymph nodes sizes (lymph node cohort) following MWA, microwave ablation and cryoablation.

Figure 2: 76-year-old male status post percutaneous cryoablation of a right upper lobe 2 cm spindle-cell sarcoma metastasis. Ablation zones with a volume of 10.4cm^3 at 36 days (A) and with a volume of 3.0cm^3 at 318 days post procedure (B); top row shows semi-automated threshold-based segmentation of the ablation zone volume and bottom row shows a selected axial contrast-enhanced CT image of the volume rendering.

Figure 3. 60-year-old female treated with percutaneous microwave ablation for a right upper lobe sarcoma metastasis. Figure shows thoracic lymph nodes on axial computed tomography 18 days before (A, right upper paratracheal lymph node related to drainage pathway; C, control lymph node) and 17 days following ablation (B, right upper paratracheal lymph node related to drainage pathway; D, control lymph node). Note size increase of mediastinal lymph node following the ablation while the control lymph node is unchanged.

Figure 4: Turnbull cumulative incidence curves of a 75% percent ablation zone volume reduction (solid line) with 95% confidence intervals (dashed line) by ablation modality and time (days relative to first post ablation CT [computed tomography] scan). Differences in cumulative incidence curves were not detected between ablation modalities (generalized log-rank test; p=0.30).

Figure 5: Relationship between log-transformed ablation zone volume and time following ablation procedure by ablation modality and maximum axial tumor diameter (A= ≤1cm; B= >1cm). Lines represent both tumor-specific raw data of each ablation zone (light) and estimated curves (bold).

Figure 6: Fitted curves illustrating relationship between means of sums of bidimensional products of lymph node diameters (in logarithmic scale) and time (categorical) following microwave (red) and cryoablation (blue) of pulmonary tumors. Box plots and points represent raw data for microwave (red) and cryoablation (blue).

Table legends

Table 1. Patient characteristics and procedural details of ablation zone cohort at time of each ablation by modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

IQR, Interquartile range; ECOG, Eastern Cooperative Oncology Group; INR, International Normalized Ratio

Table 2. Tumor characteristics of ablation zone cohort by ablation modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

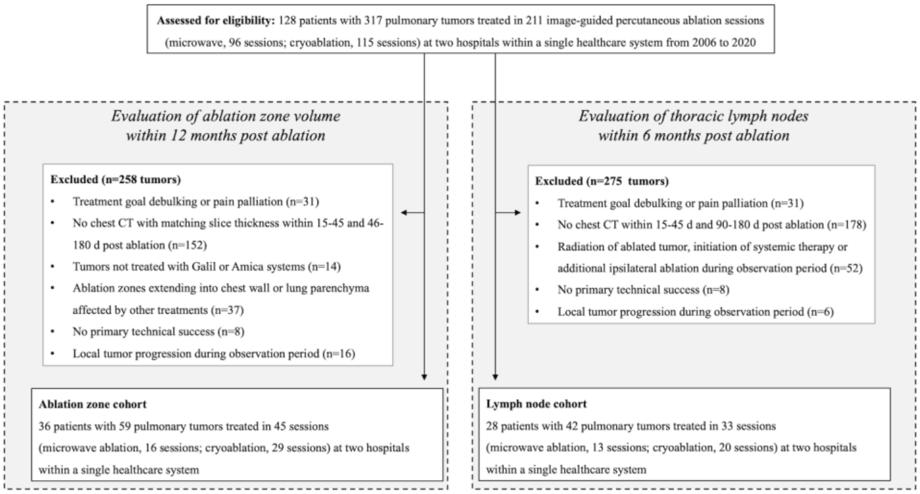
IQR, Interquartile range; SCC, squamous cell carcinoma

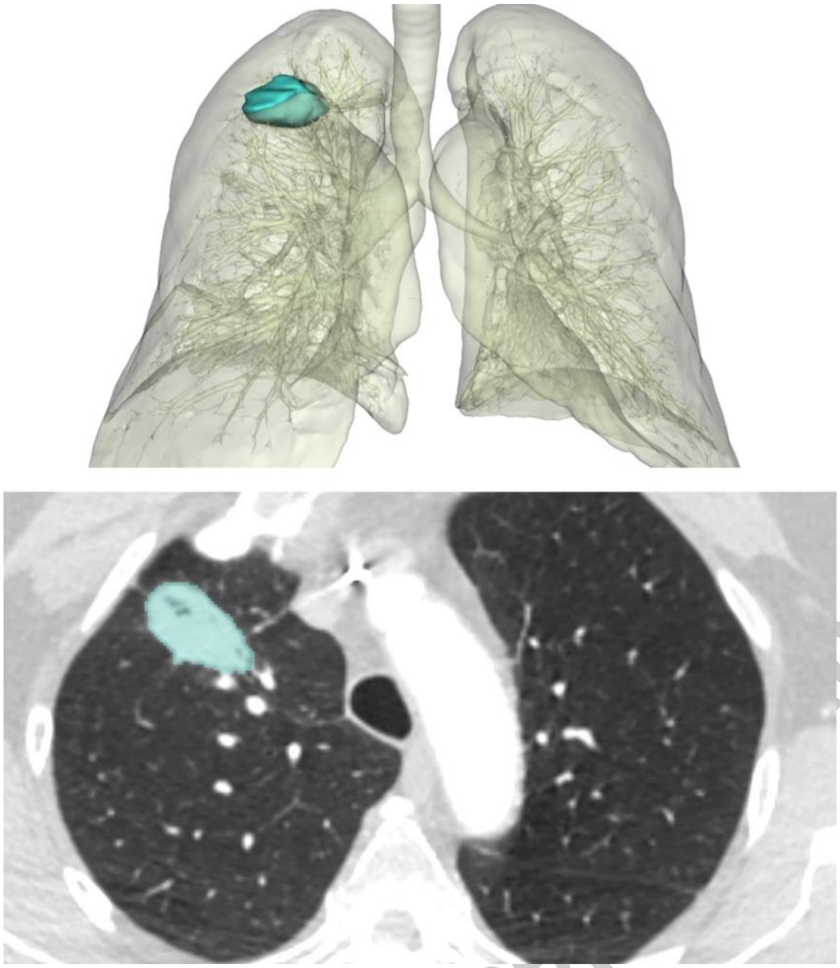
Table 3. Patient characteristics and procedural details of lymph node cohort at time of each ablation by modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

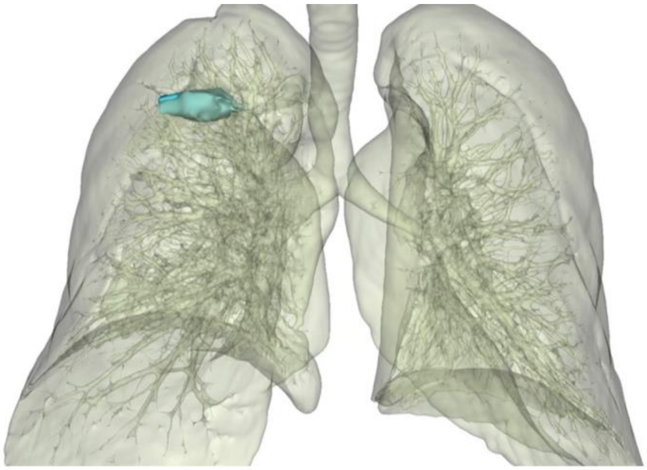
IQR, Interquartile range; ECOG, Eastern Cooperative Oncology Group; INR, International Normalized Ratio

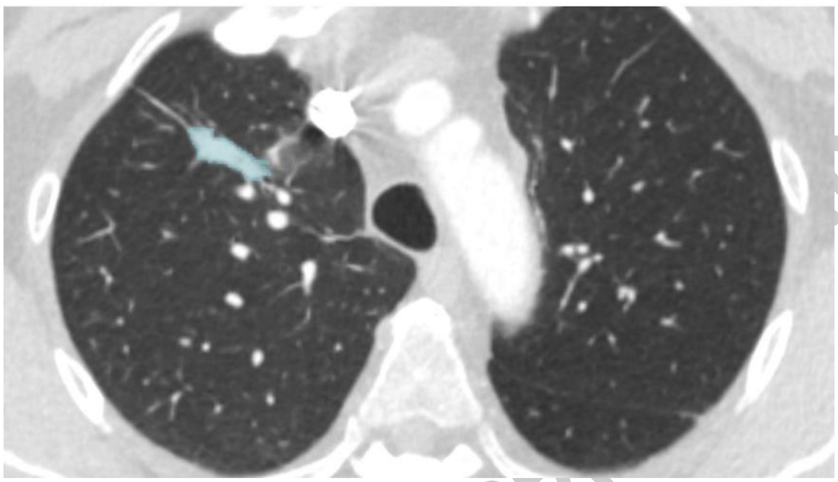
Table 4. Tumor characteristics of lymph node cohort by ablation modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

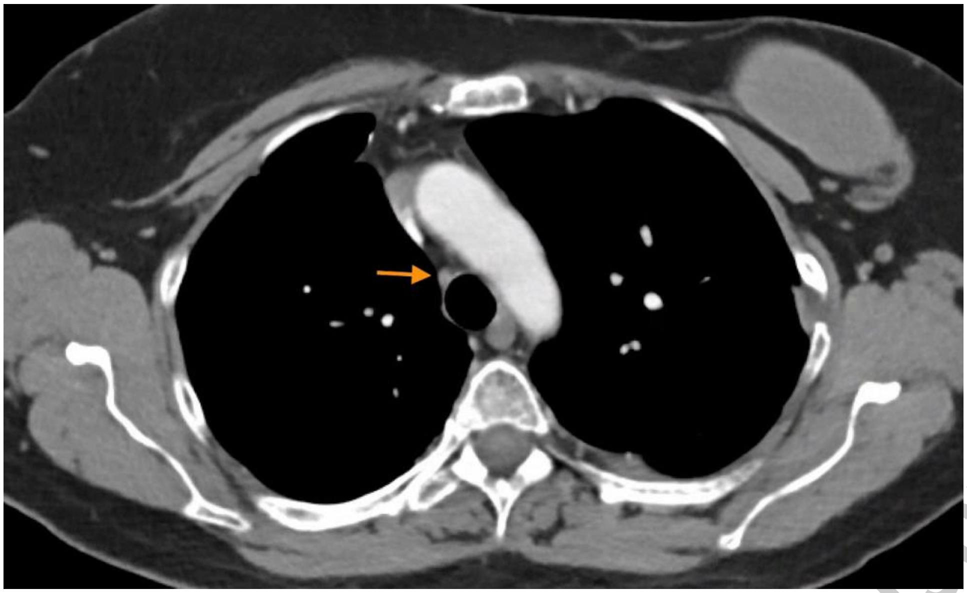
IQR, Interquartile range

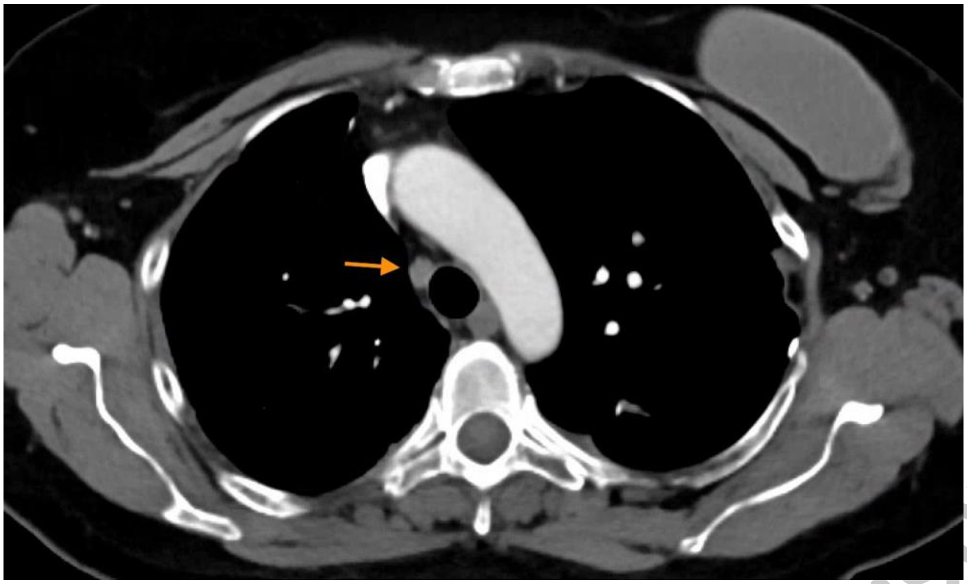

Assessed for eligibility: 128 patients with 317 pulmonary tumors treated in 211 image-guided percutaneous ablation sessions (microwave, 96 sessions; cryoablation, 115 sessions) at two hospitals within a single healthcare system from 2006 to 2020
Evaluation of ablation zone volume within 12 months post ablation
Excluded (n=258 tumors)
• Treatment goal debulking or pain palliation (n=31)
• No chest CT with matching slice thickness within 15-45 and 46-180 d post ablation (n=152)
• Tumors not treated with Galil or Amica systems (n=14)
• Ablation zones extending into chest wall or lung parenchyma affected by other treatments (n=37)
• No primary technical success (n=8)
• Local tumor progression during observation period (n=16)
Ablation zone cohort
36 patients with 59 pulmonary tumors treated in 45 sessions (microwave ablation, 16 sessions; cryoablation, 29 sessions) at two hospitals within a single healthcare system
Evaluation of thoracic lymph nodes within 6 months post ablation
Excluded (n=275 tumors)
• Treatment goal debulking or pain palliation (n=31)
• No chest CT within 15-45 d and 90-180 d post ablation (n=178)
• Radiation of ablated tumor, initiation of systemic therapy or additional ipsilateral ablation during observation period (n=52)
• No primary technical success (n=8)
• Local tumor progression during observation period (n=6)
Lymph node cohort
28 patients with 42 pulmonary tumors treated in 33 sessions (microwave ablation, 13 sessions; cryoablation, 20 sessions) at two hospitals within a single healthcare system

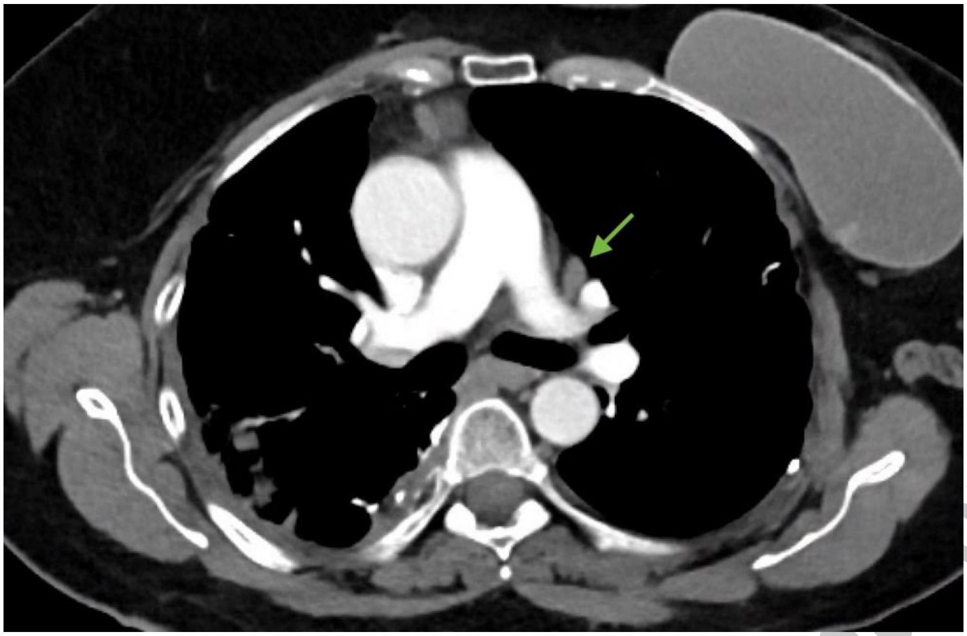


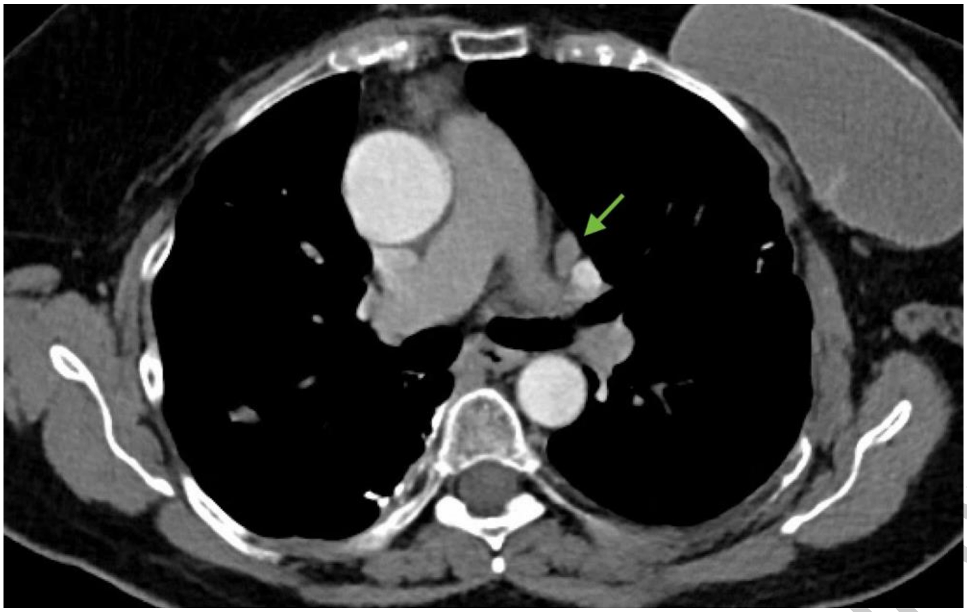


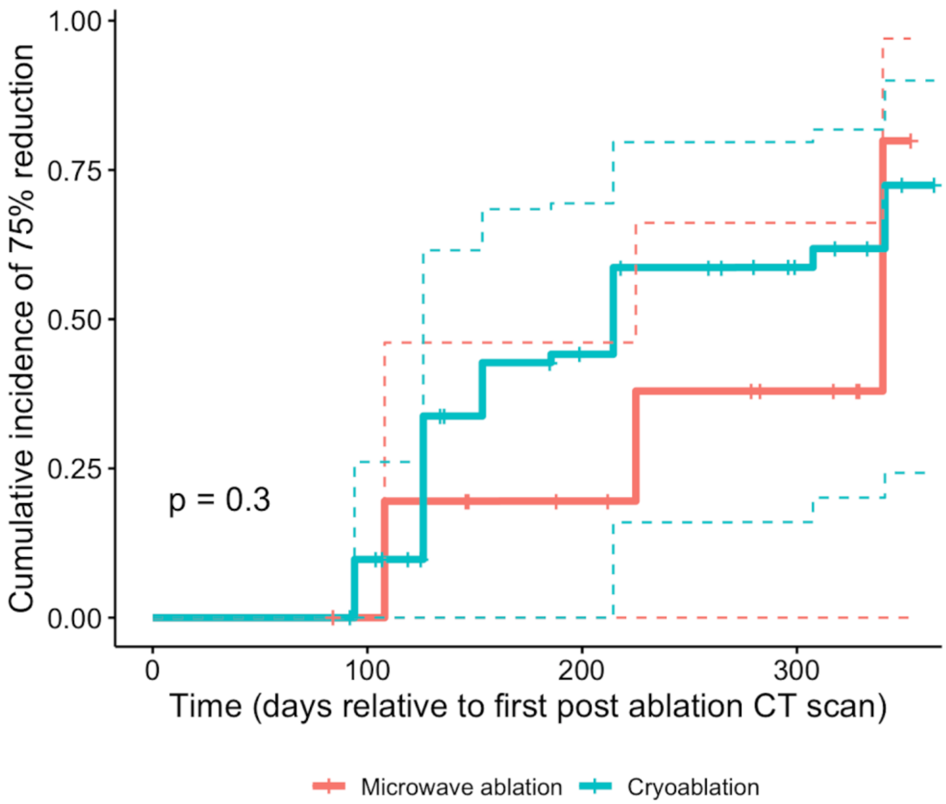


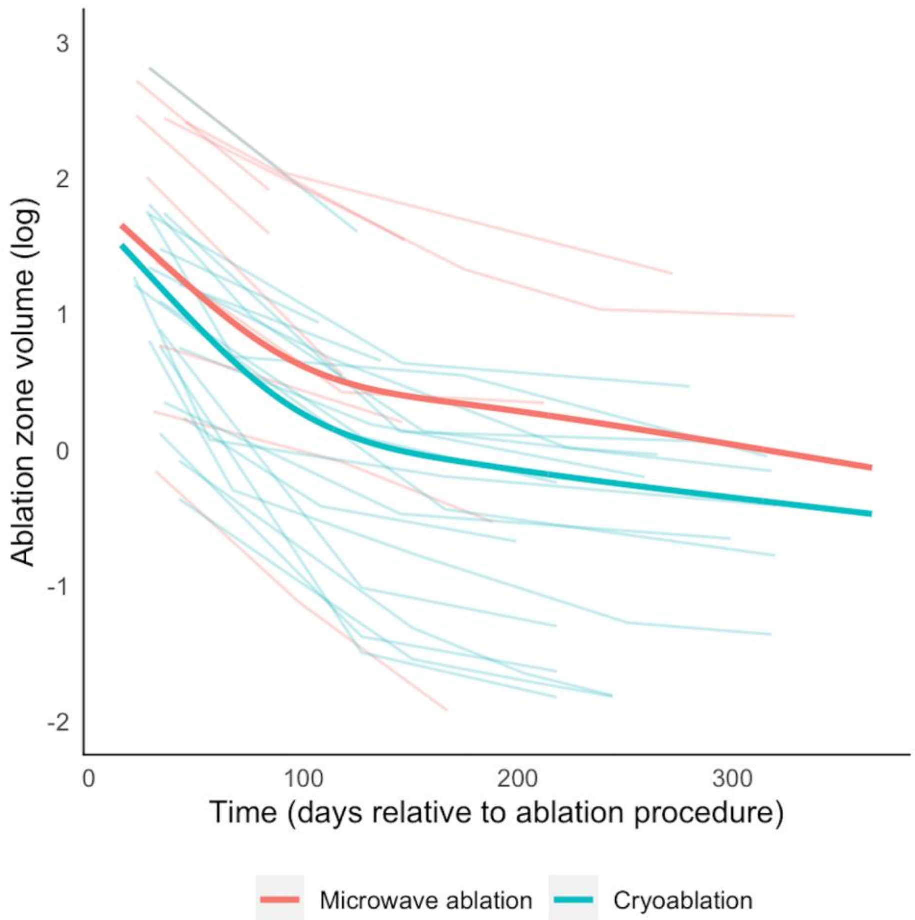


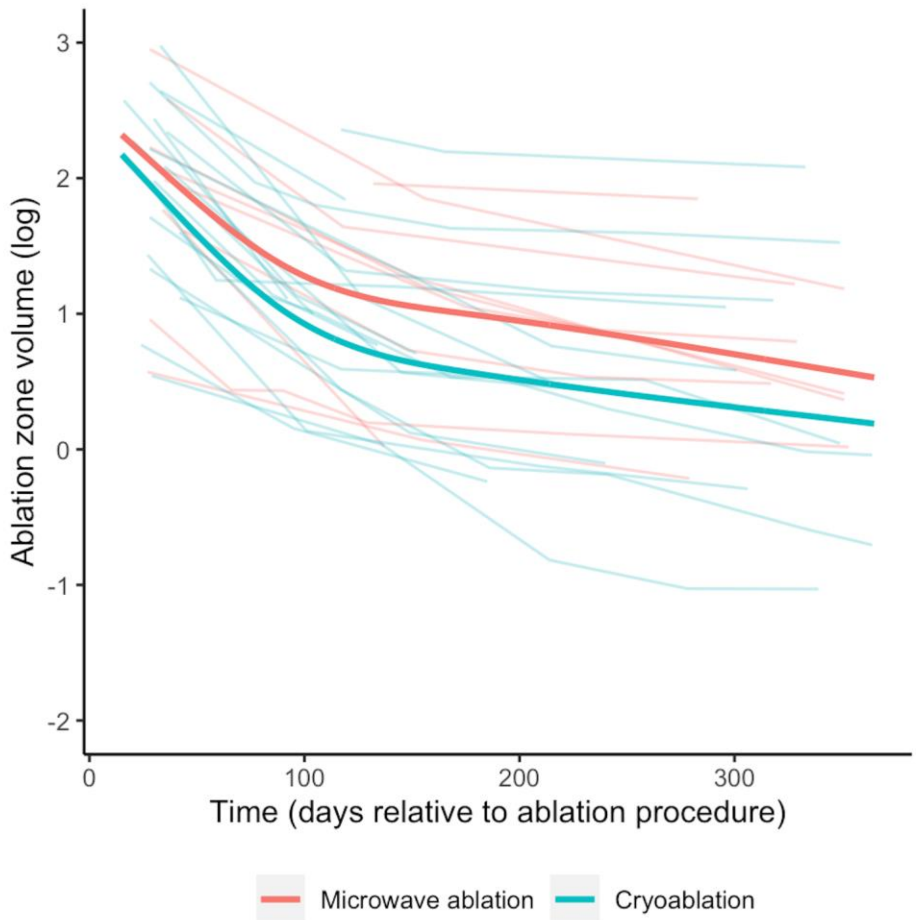







1.00
0.75
0.50
0.25
0.00
Cumulative incidence of 75% reduction
p = 0.3
0
100
200
300
Time (days relative to first post ablation CT scan)
Microwave ablation
Cryoablation


3
2
1
0
-1
-2
Ablation zone volume (log)
0
100
200
300
Time (days relative to ablation procedure)
Microwave ablation
Cryoablation



3
2
1
0
-1
-2
Ablation zone volume (log)
0
100
200
300
Time (days relative to ablation procedure)
Microwave ablation
Cryoablation

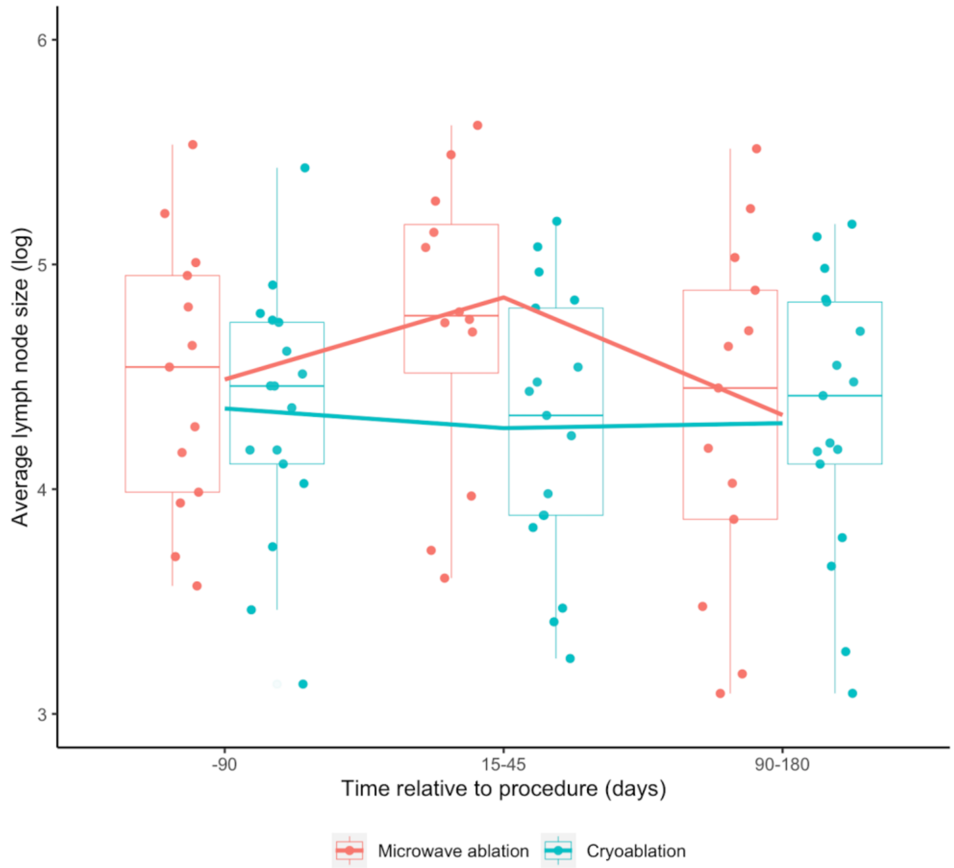

6
5
4
3
Average lymph node size (log)
-90
15-45
90-180
Time relative to procedure (days)
Microwave ablation
Cryoablation

Table 1. Patient characteristics and procedural details of ablation zone cohort at time of each ablation by modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

Characteristic	**MWA (N=16)**	**CA (N=29)**	**Overall (N=45)**	**p**
Sex				.10
Male	5 (31%)	16 (55%)	21 (47%)	
Female	11 (69%)	13 (45%)	24 (53%)	
Age in years, Median (IQR)	57 [52, 65]	65 [61, 69]	65 [56, 69]	.09
ECOG performance status				.23
0	12 (75%)	17 (59%)	29 (64%)	
1-2	4 (25%)	12 (41%)	16 (36%)	
Diagnosis				
Primary lung cancer	3 (19%)	4 (14%)	7 (16%)	.34
Metastatic disease	13 (81%)	25 (86%)	38 (84%)	
Smoking history				.39
No	5 (31%)	6 (21%)	11 (24%)	
Yes	11 (69%)	23 (79%)	34 (76%)	
Anesthesia				.01
Moderate sedation	7 (44%)	4 (14%)	11 (24%)	
Monitored anesthesia care	3 (19%)	3 (10%)	6 (13%)	
General endotracheal anesthesia	6 (38%)	22 (76%)	28 (62%)	

Targets per session				.14
Single-target session	13 (81%)	17 (59%)	30 (67%)	
Multiple-target session	3 (19%)	12 (41%)	15 (33%)	

IQR, Interquartile range; ECOG, Eastern Cooperative Oncology Group; INR, International Normalized Ratio

Table 2. Tumor characteristics of ablation zone cohort by ablation modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

Characteristic	**MWA (N=20)**	**Cryoablation (N=39)**	**Overall (N=59)**	**p**
Maximum tumor diameter, cm				
Median (IQR)	1.1 [1.0, 1.3]	1.0 [0.8, 1.4]	1.0 [0.8, 1.4]	.81
Maximum tumor diameter ≤1cm	10 (50%)	20 (51%)	30 (51%)	.93
Maximum tumor diameter >1cm	10 (50%)	19 (49%)	29 (49%)	
Lobe				<.001
Right upper lobe	7 (35%)	8 (21%)	15 (25%)	
Right middle lobe	0 (0%)	1 (3%)	1 (2%)	
Right lower lobe	3 (15%)	13 (33%)	16 (27%)	
Left upper lobe	7 (35%)	6 (15%)	13 (22%)	
Left lower lobe	3 (15%)	11 (28%)	14 (24%)	
Lung zone				.21
Peripheral	9 (45%)	22 (56%)	31 (53%)	
Intermediate	10 (50%)	11 (28%)	21 (36%)	
Central	1 (5%)	6 (15%)	7 (12%)	
Distance to costal pleura, cm Median (IQR)	2 [1.6, 2.9]	1.4 [0.7, 3.0]	1.8 [1.0, 3.0]	.82
Histology				<.001
Non-small cell lung cancer	3 (15%)	3 (8%)	6 (10%)	

Small cell lung cancer	0 (0%)	1 (3%)	1 (2%)	
Metastatic SCC	0 (0%)	2 (5%)	2 (3%)	
Metastatic sarcoma	6 (30%)	13 (33%)	19 (32%)	
Metastatic colorectal carcinoma	10 (50%)	14 (36%)	24 (41%)	
Other metastatic histology	1 (5%)	6 (15%)	7 (12%)	
Number of applicators per tumor				<.001
1	20 (100%)	22 (56%)	42 (71%)	
≥2	0 (0%)	17 (44%)	17 (29%)	

IQR, Interquartile range; SCC, squamous cell carcinoma

Table 3. Patient characteristics and procedural details of lymph node cohort at time of each ablation by modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

Characteristic	**MWA (N=13)**	**Cryoablation (N=20)**	**Overall (N=33)**	**p**
Sex				
Male	6 (46%)	13 (65%)	19 (58%)	.30
Female	7 (54%)	7 (35%)	14 (42%)	
Age in years, Median (IQR)	61 [57,65]	66 [62,76]	65 [58,70]	.87
ECOG performance status				.07
0	11 (85%)	10 (50%)	21 (64%)	
1-2	2 (15%)	10 (50%)	12 (36%)	
Smoking history				.81
Yes	4 (31%)	7 (35%)	11 (33%)	

No	9 (69%)	13 (65%)	22 (67%)	
Diagnosis				.26
Primary lung cancer	5 (38%)	4 (20%)	9 (27%)	
Metastatic disease	8 (62%)	16 (80%)	24 (73%)	
Anesthesia				.08
Moderate sedation	6 (46%)	5 (25%)	11 (33%)	
Monitored anesthesia care	3 (23%)	2 (10%)	5 (15%)	
General endotracheal anesthesia	4 (31%)	13 (65%)	17 (52%)	
Tumors treated in				
Single-target session	13 (100%)	13 (65%)	26 (79%)	<.001
Multiple-target session	0 (0%)	7 (35%)	7 (21%)	

IQR, Interquartile range; ECOG, Eastern Cooperative Oncology Group; INR, International Normalized Ratio

Table 4. Tumor characteristics of lymph node cohort by ablation modality. Categorical variables are summarized as frequencies (percentages) and continuous variables are summarized as median (interquartile range). P-values (*p*) are based on univariable regression models whose parameters are estimated with generalized estimating equations using an independence correlation structure.

Characteristic	**MWA (N=13)**	**Cryoablation (N=29)**	**Overall (N=42)**	**p**
Maximum tumor diameter, cm				
Median (IQR)	1.0 [0.9,1.4]	1.0 [0.8,1.5]	1.0 [0.8,1.4]	.98
≤1cm	7 (54%)	16 (55%)	23 (55%)	.94
>1cm	6 (46%)	13 (45%)	19 (45%)	
Lobe				.09
Right upper lobe	6 (46%)	4 (14%)	10 (24%)	
Right middle lobe	0 (0%)	1 (3%)	1 (2%)	
Right lower lobe	1 (8%)	16 (55%)	17 (40%)	

Left upper lobe	6 (46%)	1 (3%)	7 (17%)	
Left lower lobe	0 (0%)	7 (24%)	7 (17%)	
Lung zone				.49
Peripheral	7 (54%)	19 (66%)	26 (62%)	
Intermediate	5 (38%)	6 (21%)	11 (26%)	
Central	1 (8%)	4 (14%)	5 (12%)	
Distance to costal pleura, cm Median [p25, p75]	1.7 [1.2, 3.0]	1.4 [0.6, 3.0]	1.6 [0.9, 3.0]	.67
Histology				.10
Non-small cell lung cancer	5 (38%)	4 (14%)	9 (21%)	
Metastatic sarcoma	4 (31%)	13 (45%)	17 (40%)	
Metastatic colorectal carcinoma	4 (31%)	7 (24%)	11 (26%)	
Other metastatic histology	0 (0%)	5 (17%)	5 (12%)	
Number of applicators per tumor				
1	13 (100%)	17 (59%)	30 (71%)	<.001
≥2	0 (0%)	12 (41%)	12 (29%)	

IQR, Interquartile range