Thermal Ablation of Lung Tumors: Focus on Microwave Ablation

Thermoablation von Lungentumoren: Mikrowellenablation im Fokus

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ZUSAMMENFASSUNG


Methode Die englischsprachige Literatur betreffend Thermalablation der Lunge wurde durchgesehen. Die Radiofrequenz-Ablation (RFA) ist das am weitesten verbreitete und erforschte Verfahren dieser Ablationstechniken. Die Mikrowellenablation (MWA) stellt eine relativ neue Alternative dar, die unter gleichen Indikationen und in ähnlicher Weise wie die RFA durchgeführt wird. Es wurde experimentell und klinisch gezeigt, dass mittels MWA größere und sphärischere Ablationszonen über kürzere Zeiträume im Vergleich zu RFA erreicht werden können. In Europa und den USA stehen sieben verschiedene MWA-Systeme zur Verfügung, die signifikante Unterschiede in Größe und Form der erzeugten Ablationszonen aufweisen.

Ergebnisse Die mit der MWA assoziierten Komplikationen, sowie deren Häufigkeiten, sind denen der RFA sehr ähnlich. Die lokalen Progressionsraten nach MWA von Lungentumoren variieren zwischen 0 % und 34 % die mit den Daten der RFA-Literatur vergleichbar sind.

Schlussfolgerung Trotz technischer Verbesserungen hat die aktuelle Generation von MWA-Systemen ähnliche klinische Ergebnisse wie die RFA.

Kernaussagen
- Bei der MWA handelt es sich um ein sicheres Therapieverfahren welches daher als Behandlungsalternative bei nicht operablen Lungentumoren in Erwägung gezogen werden sollte.
- Da die Thermoablation von Lungentumoren immer mehr Anwendung findet, sollten Radiologen mit dem Erscheinungsbild der Ablation in der Bildgebung vertraut sein.
- Obwohl die MWA theoretische Vorteile gegenüber der RFA hat, ist der Therapieerfolg vergleichbar.

ABSTRACT

Background Image-guided thermal ablation can be used for the treatment of medically inoperable primary and metastatic lung cancer. These techniques are based on the heating up or freezing (cryoablation) of a volume of tissue around a percutaneous applicator that induces necrosis of the tumor.

Method The English-language literature concerning thermal ablation of the lung was reviewed. Radiofrequency ablation (RFA) is the most widely performed and investigated of these techniques. Microwave ablation (MWA) represents a relatively new alternative that shares the same indications and is conducted in a very similar fashion as RFA. It has been experimentally and clinically shown that MWA produces larger, more spherical ablation zones over shorter periods of time compar-
ed to RFA. Seven different MWA systems are available in Europe and the USA with significant differences in the size and shape of the produced ablation zones.

**Results** The types of complications caused by MWA and their rates of occurrence are very similar to those caused by RFA. The local progression rates after MWA of lung malignancies vary between 0 % and 34 % and are similar to those in the RFA literature.

**Conclusion** Despite technical improvements, the current generation of MWA systems has comparable clinical outcomes to those of RFA.

**Introduction**

The curative treatment of lung tumors, both primary and metastatic, has undergone substantial diversification in the last two decades. New treatment techniques provide a range of options from parenchyma-sparing surgical resection techniques and video-assisted thoracoscopic surgery (VATS) to the highly efficient radiation delivery method represented by stereotactic body radiation therapy (SBRT) and image-guided thermal ablation therapies, such as radiofrequency (RFA), microwave (MWA), and cryoablation. The multitude of techniques and their constant improvement raise the question of which approach is most beneficial for optimal patient outcome. Although SBRT and the thermal ablation therapies have shown lower control rates compared to surgical resection, their main advantage is their reduced invasiveness and impact on respiratory function. Therefore, they offer patients with medically inoperable early-stage NSCLC or oligometastatic disease a potentially curative treatment option. In comparison to RFA which has been in use since the early 2000 s and is currently the most widely performed and evaluated thermal ablation technique, MWA is a relatively new treatment option, with the first large patient series study being published in 2008 by Wolf et al. [1]. Since then, more than 20 articles have been published in the literature concerning the MW treatment of NSCLC and lung metastases with a main focus on outcome and complications [2 – 22]. The purpose of this paper is to review the literature regarding MWA in the broader context of thermal ablation. RFA and MWA are the most widely used techniques that are based on inducing necrosis through high temperatures with both procedures performed in a similar fashion. Other techniques that are used less often, such as cryoablation and irreversible electroporation, will only be briefly discussed. The imaging follow-up, indications and some of the complications are identical between MWA and RFA. Therefore, complication management is based on the more abundant RFA literature, with differences being highlighted accordingly.

**Technical considerations**

MWA systems generate an ellipsoidal microwave field around a needle-like applicator that is introduced into the tissue. Microwaves are part of the electromagnetic spectrum with frequencies between 300 MHz and 300 GHz. Since water molecules have a positively and a negatively charged pole, they tend to align with the electromagnetic waves. The oscillation of the electromagnetic wave therefore causes a rapid flip motion of the water molecules which results in heating of the adjacent tissue through the mechanism of dielectric hysteresis. If the MW frequency perfectly matched the molecule-specific resonance frequency of the water molecules, all energy would be transformed into heat, but the penetrability into the tissue would be low. The frequencies used by the current MW manufacturers (915 MHz and 2450 MHz) only partially match the resonance frequency of the water molecules and therefore assure efficient energy conversion into heat with satisfactory tissue penetrability [23 – 25].

RFA is based on electromagnetic radio waves with frequencies of less than 1 MHz. An electric field is generated within the body between the active applicator and a grounding pad (monopolar systems) or between two electrodes located within the applicator. The alternating electric field, which is stronger in the vicinity of the applicator, induces the oscillation of ions, which, in turn, induces frictional tissue heating. In contrast to MW, RF energy deposition is dependent on the electrical permittivity of the tissue. Therefore, tissues with increased resistivity such as the aerated lung have an insulating effect by limiting the transformation of RF energy into heat energy to the close proximity of the applicator [26 – 28]. Although the vast majority of RFA ablations are performed percutaneously, bronchoscopy-guided RFA has also been reported. This technique might lead to fewer complications such as pneumothorax, but is limited by the need of having a bronchus in the close proximity of the tumor [29].

Cryoablation is a technique based on generating temperatures as low as −160 °C around an applicator that spread by convection in the surrounding tissue. The ablation process lasts 25 – 30 minutes and consists of successive freezing-thawing cycles which induce cell death by protein denaturation, membrane disruption and microvascular thrombosis. The main advantage of cryoabla-
Advantages of microwave ablation

Despite the differences between MWA and RFA, both techniques induce coagulation necrosis of the tissue caused by temperatures over 60°C, even if the shape and size of the ablation zone, as well as the speed at which the desired ablation volume is reached differ between the two techniques. MWA generally produces larger, more spherical and predictable ablation zones because the microwave field uniformly penetrates the tissue and is less dependent on its properties. In contrast, RFA is hampered by the high electrical resistivity of lung tissue which limits energy deposition. Tissue changes caused by ablation, such as carbonization and desiccation, also increase tissue resistivity, thus further hindering the expansion of the ablation zone [33, 34]. The high electrical resistivity of a ventilated lung and the ablation-induced tissue inhomogeneity make the expansion of the ablation zone particularly reliant on thermal conduction, especially at its periphery. This fact renders the heat produced by RFA vulnerable to being washed out by vessels as small as 3 mm, a phenomenon known as the heat sink effect [35, 36]. In contrast, MWA, whose heating deposition ability is favored by the presence of water, has been proven to be less susceptible to the heat sink effect by inducing complete thrombosis of most vessels with a diameter < 6 mm [37, 38].

While discussing the performance of MWA, it should be taken into account that seven different MWA systems are presently on the European and American markets without considering those that are available only on Asian markets. The individual characteristics of these devices have been thoroughly described elsewhere [23, 24, 39]. These are either low-frequency (915 MHz) or high-frequency (2450 MHz) devices, with the maximum output power varying between 32 W and 140 W and some of them allowing the concomitant use of up to three antennas. The size and shape of the ablation zone created by MWA is most likely the complex result of multiple factors such as the MW frequency, the design and cooling system of the antenna, the power setting and the total ablation time. The combination of these factors leads to significant differences between devices regarding the characteristics of the ablation zones (Fig. 1). This has been demonstrated by Hoffmann et al. who directly compared four different MWA systems under the same conditions using an ex-vivo liver model [40]. Therefore, upon deciding in favor of a specific MWA system, one should be well informed about its performance and how it compares to the other devices on the market.

Ablation technique

Thermal ablation of a lung malignancy must be proposed to the patient after prior consultation in an interdisciplinary tumor board. The patient will be informed about alternative treatment options while highlighting their advantages and disadvantages. Besides uncorrectable or severe coagulopathies, there is no absolute contraindication regarding thermal ablation of lung tumors. Therefore, the coagulation status has to be verified before the intervention. Anticoagulation and antiplatelet drugs have to be ceased at least 5 days prior to the intervention. The following values are recommended by the consensus guidelines for the periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions: INR< 1.5; aPTT> 1.5x control if heparin is administered; and platelet count> 50 000 [41].

The intervention may be performed under conscious sedation or general anesthesia. Hoffmann et al. concluded that neither approach was associated with different tumor control or complication rates [42]. General anesthesia might prove useful for anxious patients or when multiple tumors are to be ablated during the same session. General anesthesia might also help when the tumor is located in the mobile lower segments of the lung, since a longer breath-hold can be triggered by the anesthetist thus allowing more accurate targeting [42, 43]. At our institution, analgesedation using a combination of Piritramide and Diazepam administered shortly before the intervention is preferred, with additional administration of Piritramide if the need arises.
The antenna insertion technique is almost identical to that of CT-guided biopsies. Immediately prior to the intervention, an unenhanced CT scan of the chest is performed in order to plan the best puncture approach. Intravenous contrast agent might sometimes be necessary in order to visualize intratumoral blood vessels or to differentiate tumor from atelectasis. The patient position will be chosen depending on the location of the lesion, but the prone position is recommended whenever possible, since it is associated with less chest wall motion. Lateral decubitus should be avoided because of the unstable position and the more pronounced chest wall motion [44]. The antenna insertion path should be chosen above the cranial margin of the rib and away from higher caliber intrapulmonary blood vessels in order to prevent intra-pleural and intra-parenchymatous bleeding. Crossing of lung fissures or emphysematous areas should also be avoided to prevent a pneumothorax. After choosing the best path, the skin entry point can be marked with the help of a metallic marker placed on the skin using single-slice scans. The puncture site will then be disinfected and isolated with sterile drapes and local anesthesia will be applied to the skin and pleura. Following a small skin incision using a scalpel, the antenna will be inserted under breath-hold as close as possible to the center of the tumor. Single-slice scans or CT fluoroscopy will be used to verify the position of the antenna and to correct it if necessary [45–47].

The success of the ablation depends mainly on the size of the ablation margin which depends on the size of the tumor, the size of the ablation zone and the position of the antenna relative to the tumor. A tumor is likely to be successfully ablated if it is completely engulfed by the ablation zone with a sufficiently wide safety margin. The importance of the ablation margin has been proven after thermal ablation of both the liver and the lung and most authors agree that an ablation margin of at least 5 mm and, whenever possible, up to 10 mm is required for complete ablation [48–52]. Therefore, as long as a sufficient ablation margin is achieved, it is not necessary for the antenna to be placed in the center of the tumor. However, larger tumors which often have an irregular shape, require a higher level of precision and might necessitate the concomitant placement of multiple antennas or subsequent reablation [43]. Based mainly on the tumor size, but also on other factors such as the distance to the chest wall, mediastinum or large vessels, ablation time and power should be carefully adjusted in order to produce a large enough ablation zone without doing unnecessary damage to the adjacent structures. As previously discussed, the shape and size of the ablation zone is different between the various MWA devices and depends on the power setting and duration of the ablation [40]. For each device, the relationship between ablation time/power and the size of the ablation zone is documented and made available by the manufacturer. These parameters should be well known by the user because the true extent of the ablation zone often cannot be assessed on the scans performed during ablation. Despite the lower susceptibility of MWA to the heat sink effect, it should not be ignored and higher power settings or longer ablation times might be considered if larger blood vessels are close to the tumor. Although it is a rare occurrence, needle-tract seeding can be prevented by ablating the puncture tract while slowly removing the antenna after the treatment is considered to be complete [17, 53, 54].

Imaging follow-up

As local ablative techniques become more widely used, radiologists, even those not working in specialized centers, are more likely to encounter patients who have undergone such therapies and should be familiar with the evolution of ablated lesions. The post-procedural evolution of the ablation zone is usually divided into three continuous phases with corresponding histologic and imaging findings [55–57]. The features of the thermally ablated lung tissue have first been described after RFA, but are similar to those after MWA [37, 38].

The early phase (<1 week)

The post-ablation histological and CT findings remain largely unchanged over the first week [58]. The ablation zone is described by most authors as a succession of three concentric layers of tissue with different histological characteristics. The cells in the innermost layer show signs of thermal damage but the tissue maintains a seemingly intact alveolar structure. The middle layer has a similar appearance as the inner one but the alveolar spaces are filled with effusion and some degree of congestion can be noticed. The outer layer shows strong congestion and hemorrhage and consists of both damaged and viable cells [37, 58, 59].

On CT images acquired at this phase, the ablated lesion appears surrounded by an inner zone of ground glass opacity (GGO) which corresponds to the inner and middle histopathological layers and by a thin, dense outer rim which corresponds to the outer layer (Fig. 1–4) [33, 55, 58, 59]. If contrast agent is administered, the outer rim usually shows circular benign periblational enhancement [60]. The ablated tumor is often still visible within the ablation zone but does not show any contrast enhancement. The ablation should be considered successful if the tumor is completely surrounded by the GGO and a sufficient ablation margin was achieved. The outer hyperdense rim should not be counted as part of the completely ablated area as it might contain viable cells. Incomplete ablation should be considered if the tumor exceeds the GGO and/or continues to show contrast enhancement [55, 58].

Non-contrast or contrast-enhanced CT should be performed within one day after ablation in order to evaluate the completeness of the ablation and to evaluate the potential necessity for an additional procedure. The CT examination also allows for the detection of early complications such as a broncho-pleural fistula that might require a prolonged hospital stay.

The intermediate phase (1 week to 3 months)

During the first 2–3 months after the procedure, the necrotic tissue within the ablation zone undergoes a process of granulation and fibrosis [57, 58]. As this process takes place, the GGO pattern gradually changes into a nodular or fibrotic pattern while the ablation zone steadily decreases in size. At this stage, the vast majority of ablation zones will still exceed the size of the initial tumor. In some cases, it might stagnate in size and in other cases increase in size over time, due to accompanying obstructive pneumonitis (Fig. 2) [58, 61]. Furthermore, the necrotic tissue may be directly evacuated through a bronchoscopy leading to the forma-
tion of a cavity which has been shown to be related to an increased risk of superinfection [1, 58, 62]. Most cavities disappear on follow-up, but some remain unchanged or even increase in size (Fig. 2, 3) [57, 62, 63]. Completely ablated tumors will normally not show contrast enhancement besides the persisting benign periablational enhancement pattern [55]. Except for procedures in which a large part of the tumor remains unablated, local tumor progression will rarely be detected within the intermediate phase.

**The late phase (> 3 months)**

Three months after the procedure, the fibrous transformation is nearly complete, resulting in a stagnation or further decrease of
the ablation zone (▶ Fig. 2–4). At this point, the size can be smaller, larger or similar to that of the tumor prior to ablative treatment [64]. The pattern of the ablation zone can be fibrous, nodular or cavitary [57]. The CT examination performed 3 months after the ablation should be taken as a baseline for subsequent examinations and any further growth of the ablation zone should be considered as local progression [55, 64].

After 3 months, the ablation zone might show slight contrast enhancement which corresponds to a revascularization phenomenon but it should remain weaker than the initial tumor enhancement [65]. The benign periablational enhancement might also persist for up to 6 months after the treatment [60].

▶ Fig. 3 High-frequency ablation of a pulmonary metastasis deriving from a colorectal carcinoma (8 minutes; 62 W). Aspect of the tumor shortly before a and during ablation b. c Image obtained 24 hours after ablation showing a delayed pneumothorax that was successfully managed using pleural drainage. After 3 months the ablation zone has a nodular aspect d, and there were changes into a cavity at 6 months e. f 9 months after ablation, the cavity is replaced by a fibrous pattern, but a new periablational nodularity can be noticed representing local progression of the tumor.

▶ Abb. 3 Hochfrequenzablation einer kolorektalen Lungenmetastase (8 Minuten, 62 W). Gezeigt ist der Aspekt des Tumors kurz vor a und während der Ablation b. c Das Bild, das 24 Stunden nach der Ablation akquiriert wurde, zeigte einen verzögerten Pneumothorax, der erfolgreich mit einer Pleuradrainage behandelt wurde. Nach 3 Monaten hat die Ablationszone einen knotigen Aspekt d und wandelt sich nach 6 Monaten e in einen Hohlraum um. f Neun Monate nach der Ablation wird der Hohlraum durch fibröses Gewebe ersetzt. Zusätzlich jedoch zeigte sich eine neue periablatorische Nodularität, die die locale Progression des Tumors darstellt.
PET/CT

PET/CT is a technique with the potential for improving the early detection of local tumor progression in certain situations. The $^{18}$F-FDG-pattern immediately after successful ablation consists in most cases of a high-uptake ring with central photopenia, but diffuse or heterogeneous uptake might also be encountered (Fig. 5) [66]. Three months after treatment, 57 – 68 % of the ablation zones will show no or mild $^{18}$F-FDG uptake which has a high negative predictive value [67, 68]. In the remaining cases, a
except for the lack of radiation, and because of its susceptibility to artifacts and higher costs, MRI follow-up has not become part of the clinical routine in most centers.

Follow-up protocol

To date, there is no consensus regarding the ideal follow-up protocol. Most authors employ a succession of enhanced or non-enhanced CT examinations with occasional or regular PET/CT examinations [1, 2, 55, 56, 76]. At our institution, follow-up consists mostly of unenhanced CT scans. The first CT examination is performed the day after ablation, not only to detect complications, but also to evaluate whether the ablation was complete, or an additional ablation of the same tumor may be necessary. The second CT examination is performed three months later with the main purpose of providing a baseline for the subsequent examinations which are performed in 3-month intervals within the first year and at 6-month intervals thereafter. PET/CTs are only employed to confirm unclear cases of local progression.

Safety

Pain and chest wall damage

During the ablation of subpleural tumors, the heat expands into the surrounding tissue which is the cause of chest wall burns. Pain can be encountered after 2 – 27.6 % of MWA ablations (Table 1) [1, 3, 8, 12]. Generally, the severity is mild to moderate, and it persists for a few days to a few weeks. Pain related to ablative treatment usually responds well to analgesics, but cases of severe pain lasting up to a few months have also been reported. In addition to nerve damage, small number of rib fractures and skin burns following MWA have also been reported [1, 2, 7, 17]. Alexander et al. have shown that RFA has a significantly higher risk of inducing rib fractures compared to MWA (15.9 % vs. 2.7 %) [7]. The induction of an artificial pneumothorax has been proposed as a safe method of preventing pain and chest wall damage [79].

Pneumothorax

The pneumothorax rates after MWA vary widely, ranging between 8.5 – 63 % and are similar to those reported after RFA, ranging between 11 % and 67 % [1 – 3, 8, 9, 11, 12, 54, 80]. The high variability of the reports is most likely a consequence of the threshold chosen by the authors. The main cause for pneumothorax seems to be associated with the insertion of the antenna and not with the thermal effect of the ablation [81]. Therefore, the ablation of more than one tumor, very large or small tumors, and tumors located deep within the lung parenchyma that require multiple pleural punctures or antenna repositioning is associated with a
<table>
<thead>
<tr>
<th>author, year of publication</th>
<th>patient number (n)</th>
<th>procedure-related deaths (%)</th>
<th>pneumothorax (%)</th>
<th>severe pneumothorax (%)</th>
<th>hemorrhage(H)</th>
<th>hemoptysis (P)</th>
<th>hemothorax (T) (%)</th>
<th>skin burns (B)</th>
<th>pain (P)</th>
<th>pneumonia (%)</th>
<th>pleural effusion (%)</th>
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<tr>
<td>Wolf, 2008 [1]</td>
<td>50</td>
<td>1.5</td>
<td>39</td>
<td>12</td>
<td>6 (P)</td>
<td>3 (B)</td>
<td>2 (P)</td>
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<td>Vogl, 2011 [2]</td>
<td>80</td>
<td>0</td>
<td>8.5</td>
<td>0.8</td>
<td>6 (H) 4.6</td>
<td>0.8 (B) 9 (P)</td>
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<td>Lu, 2012 [3]</td>
<td>69</td>
<td>0</td>
<td>18.8</td>
<td>7.2</td>
<td>7.2 (P) 2.9</td>
<td>2.9 (P)</td>
<td>–</td>
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<tr>
<td>Belfiore, 2013 [8]</td>
<td>56</td>
<td>0</td>
<td>32</td>
<td>14</td>
<td>–</td>
<td>17.8 (P)</td>
<td>–</td>
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<tr>
<td>Carrafiello 2013 [9]</td>
<td>24</td>
<td>0</td>
<td>37.5</td>
<td>0</td>
<td>3.8 (P)</td>
<td>–</td>
<td>–</td>
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<td>–</td>
<td>3.8</td>
<td>–</td>
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<tr>
<td>Wei, 2015 [11]</td>
<td>39</td>
<td>0</td>
<td>30.8</td>
<td>7.7</td>
<td>15.3 (T)</td>
<td>–</td>
<td>18</td>
<td></td>
<td>18</td>
<td>18</td>
<td></td>
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<tr>
<td>Yang, 2014 [12]</td>
<td>47</td>
<td>0</td>
<td>63.8</td>
<td>13.5</td>
<td>31.9 (P)</td>
<td>27.6 (P)</td>
<td>14.9</td>
<td></td>
<td>34</td>
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<tr>
<td>Zheng, 2014 [13] (major complications)</td>
<td>184</td>
<td>0.5</td>
<td>–</td>
<td>15.7</td>
<td>–</td>
<td>–</td>
<td>0.5 (abscess)</td>
<td>2.9</td>
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<td>Han, 2015 [15]</td>
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<td>50</td>
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<td>7.1</td>
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<td>Ni, 2015 [16]</td>
<td>35</td>
<td>0</td>
<td>20.5</td>
<td>7.7</td>
<td>5.1 (H) 2.6</td>
<td>2.9 (H) 1.4 (B)</td>
<td>2.9</td>
<td></td>
<td>5.7</td>
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<tr>
<td>Splatt, 2015 [17] (major complications)</td>
<td>51</td>
<td>1.4</td>
<td>–</td>
<td>12.9</td>
<td>2.9 (H)</td>
<td>1.4 (B)</td>
<td>2.9</td>
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<td>5.7</td>
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<td>Egashira, 2016 [22]</td>
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<td>0</td>
<td>–</td>
<td>13</td>
<td>6.9 (H)</td>
<td>–</td>
<td>–</td>
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</table>

H = Hemorrhage; P = Hemoptysis; T = Hemothorax; P = Pain; B = Skin Burns.
higher risk of development of a pneumothorax. Tumors located in 
the lower parts of the lungs (higher mobility), the traversal of lung 
 fissures and lung emphysema, are also associated with an 
increased pneumothorax risk [13, 54, 81, 82]. In most cases, the 
pneumothorax is small and does not require additional treatment. 
Between 0.8 – 15% of ablations result in a large or progressive 
pneumothorax that requires placement of a drain [1 – 3, 8, 11 – 
13, 17, 22]. The occurrence of a pneumothorax may be particula-


rly problematic if it appears before the definitive placement of 
the antenna. In this case, a new puncture can be attempted after 
evacuating the air. The possibility of a delayed or recurrent pneu-
mothorax that may require additional treatment also exists. 
Therefore, a chest radiography or CT is recommended within 
24 hours after ablation, since most pneumothoraces appear 
within this interval. Although rare, a significant pneumothorax 
can occur even later. Thus, it is crucial to inform patients and their 
relatives of this potential complication and the related symptomat-
ology [2, 82, 83].

A broncho-pleural fistula is a complication caused by direct 
communication between a bronchus and the pleural space. It 
occurs as a pneumothorax persisting despite the presence of a 
chest drain. A fistula can become manifest during or shortly after 
ablation or it can appear in the weeks or months subsequent to 
the treatment, as the necrotic tissue of a subpleural ablation is 
evacuated and a new communication is formed. This complica-
tion is very rare and the treatment consists of pleurodesis, 
surgery, bronchoscopic management or a combination of these 
[13, 17, 54, 84].

Hemorrhage

A hemorrhage can occur by damaging an intrapulmonary or 
tercostal blood vessel. An intrapulmonary hemorrhage appears 
as a rapidly expanding GGO starting from the antenna and can 
be associated with hemoptysis. Intraparenchymal hemorrhages 
occur in 6 – 10% of MWAs and lead to hemoptysis in 0 – 7% of 
cases [2, 3, 16, 22]. Yang et al. reported a hemoptysis rate as 
high as 36% [12]. These rates have been reported to be higher 
after RFA with 3 – 9% resulting in hemoptysis and an almost 
double in hemorrhage [54]. Although the data are insufficient to 
draw a firm conclusion, the better results might be explained by 
the lower susceptibility of MWA for the heat sink effect and a 
stronger coagulative effect. Usually the hemorrhage is self-limit-
ing and no action is needed except to carry on with the ablation 
which promotes coagulation. If the bleeding continues and is 
associated with uncontrollable cough, one should react quickly 
as heavy pulmonary bleeding might be lethal. The patient should 
be positioned on the side of the ablation and hemostatic agents 
should be injected. A split intubation might be needed in order 
to prevent asphyxia. In severe cases, only an embolization or 
explorative thoracotomy is able to stop the bleeding [54, 76, 85]. 
Damaging an intercostal vessel may result in a rapidly progressive 
hemorrhothorax that usually requires endovascular or surgical treat-
ment [54]. The best way to avoid hemorrhagic complications is 
to choose a puncture pathway that avoids intersecting larger 
blood vessels, especially in patients with high pulmonary blood 
pressure [85].

Pleural effusion

Small asymptomatic pleural effusions are common after MWA 
and usually do not require treatment. They appear more often if 
the ablation is subpleural and are caused by an inflammatory reac-
tion of the pleura [13, 86]. Large, symptomatic pleural effusions 
occur after 0 – 7.7% of treatments and can be managed by inser-
ction of a drain [12, 13, 16, 17, 22].

Infection

Postprocedural pneumonia is relatively common with rates 
following MWA ranging between 2 – 18% [1, 11 – 13, 16, 17]. 
The risk of pneumonia seems to be increased for patients who 
have previously undergone radiotherapy [87]. Some authors 
recommend prophylactic antibiotic before and two days after 
ablation. In our institution, however, therapy is considered only 
in clinically manifest cases [13]. Lung abscess is another infectious 
periprocedural complication that can appear in 0.5 – 1.5% of 
cases [1, 13]. Patients with cavity formation, but also with emphy-
sema have been reported to have an increased risk for abscesses 
[1, 13, 87]. Both pneumonia and abscesses should be regarded as 
serious complications that can result in procedure-related death 
[1, 87].

Other complications, such as pulmonary artery aneurysms and 
 systemic air embolism, have been reported following RFA of lung 
tumors, but they are exceedingly rare [54].

Indications and outcome

NSCLC

Thermal ablation can be used with a curative intent only in stage I 
NSCLC, because it cannot address lymph nodes directly and it 
has a lower chance of success in complete ablation of tumors 
larger than 3 cm [1, 2]. Given the better local control rates, the 
treatment of choice for stage I NSCLC is considered to be either 
open or video-assisted thoracic surgery [88]. However, in the 
case of patients with early-stage NSCLC and severely impaired 
lung function, a local ablative therapy (SBRT or RFA) can be con-
sidered [89].

Randomized controlled studies comparing radiotherapy (espe-
cially SBRT) to thermal ablation therapies are currently not avail-
able and most of the data regarding these techniques consist of 
retrospective case series with low levels of evidence. A recent 
 systematic review and pooled analysis by Bi et al. compared the 
results of RFA (328 patients) and SBRT (2767 patients) in the 
treatment of stage I NSCLC [90]. The authors showed that the 
local control rates were significantly superior for SBRT compared 
to RFA (1 year: 97% vs. 77%, 2 years: 92% vs. 48%, 3 years: 88% 
vs. 55%, 5 years: 86% vs. 42%) even after correcting for tumor 
sizes < 3 cm and age [90]. In 2015, Dupuy et al. published the 
results of the American College of Surgeons Oncology Group

Vogl TJ et al. Thermal Ablation of... Fortschr Röntgenstr 2017; 189: 828–843
The ability of MWA to create larger, more spherical ablation zones, as well as the lower susceptibility to the heat sink effect should theoretically lead to lower local progression rates (LPR). However, the patient series involving MWA treatment of stage I NSCLC show similar outcomes with RFA. Liu et al. reported an LPR of 31% (median follow-up of 12 months) while Yang et al. reported an LPR of 27.7% (median follow-up 30 months), local control rates at 1, 2 and 3 years of 96%, 64% and 48%, respectively, and OS rates at 1, 2 and 3 years of 89%, 63% and 43%, respectively [10, 12]. Similarly, Han et al. reported an LPR of 32% (median follow-up 22 months) with local control rates at 1, 2 and 3 years of 80.5%, 74.8% and 22.1%, respectively, and cancer-specific survival rates at 1, 2 and 3 years of 95%, 74% and 65%, respectively. (Table 2) [15]. The other case series involving MWA of NSCLC were either pooled together with metastases or involved locally advanced or metastatic NSCLC.

In the case of local progression after radiotherapy, reirradiation has limited effectiveness in extending survival [93]. RFA and MWA have been shown to prolong local tumor control and to alleviate symptomatology in patients with local progression within the radiation field and therefore, if available, should be recommended as a salvage therapy [21, 93, 94]. The currently accepted treatment for inoperable stage III and IV NSCLC consists of radiochemotherapy, but studies have suggested that these patients might benefit from thermal ablation techniques. A randomized prospective study by Xu et al. compared the effectiveness of MWA vs. RT of the primary tumor in patients with inoperable stage III NSCLC combined with chemotherapy and RT of the lymph nodes. They reported lower radiation pneumonitis rates (3.9% vs. 31.9%) and a lower incidence of progressive disease in the MWA group (0% vs. 17%) [20]. Wei et al. compared the effectiveness of MWA and chemotherapy to chemotherapy alone and concluded that the MWA group had a prolonged progression-free survival compared to the chemotherapy-only group (10.9 months vs. 4.8 months) [19]. Both studies showed a tendency towards an improved OS that was, however, not statistically significant.

It has been shown that tissue heating increases the penetration and retention of drugs co-administered at the time of ablation [95, 96]. The heat also has an immunomodulatory effect by releasing intact antigens that can trigger an antitumor immune response [97, 98]. Therefore, the size of the ablation zone can be enhanced by the concomitant local application of cytotoxic drugs [95, 99]. In a recent randomized study, Zhao et al. compared the intratumoral administration of 131I-labeled mouse/human chimeric monoclonal antibodies against intracellular DNA combined with MWA to postoperative adjuvant chemoradiation of stage II and III NSCLC. They found that the 1- and 2-year survival rates of the MWA group were significantly better than those of the chemoradiation group [96]. The synergic effects of cytotoxic drugs seem to be a promising approach to improve the results of lung thermal ablations, but more studies are required to prove their utility in the clinical routine.

In brief, the survival rates of patients suffering from inoperable early stage NSCLC treated with RFA or MWA do not show any significant difference compared to SBRT though the local control rates seem to be inferior. Therefore, whenever available, both techniques should be discussed with the patient while highlighting their advantages and disadvantages. The thermal ablation techniques can also be effectively employed as a salvage therapy after unsuccessful RT and as a means of prolonging local tumor control in stage III and IV NSCLC. Currently there is no evidence that MWA is superior to RFA regarding local tumor control and overall survival.
<table>
<thead>
<tr>
<th>author, year of publication</th>
<th>patient number (n)</th>
<th>pathology (number of ablated lesions)</th>
<th>follow-up (months)</th>
<th>LTP (%)</th>
<th>overall survival (OS) (%)</th>
<th>cancer-specific survival (CSS) (%)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td>1 year</td>
<td>2 years</td>
</tr>
<tr>
<td>Belfiore, 2013 [8]</td>
<td>56</td>
<td>NSCLC: 44 Met: 25</td>
<td>N/A</td>
<td>0</td>
<td>CSS: 69</td>
<td>54</td>
</tr>
</tbody>
</table>

LTP = Local Tumor Progression; OS = Overall Survival; CSS = Cancer-Specific Survival; NSCLC = Non-Small Cell Lung Cancer; Met = Metastases.
Clinical Relevance of the Study

- Thermal ablation and SBRT are currently the main curative treatment options for medically inoperable lung tumors.
- Despite a slightly lower local control rate for thermal ablation, there is no evidence for a difference in survival rates between thermal ablation and SBRT.
- MWA has some theoretical advantages over RFA, but the complications and clinical outcomes are similar.

Conflict of Interest

The authors declare that they have no conflict of interest.

References


[34] Andreano A, Huang Y, Meloni MF et al. Microwaves create larger ablations than radiofrequency when controlled for power in ex vivo tissue. Medical physics 2010; 37: 2967 – 2973


