Microwave antennas for thermal ablation of benign adrenal adenomas

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Abstract
Microwave thermal ablation is under consideration as a minimally invasive modality to treat 10–20 mm benign adrenal adenomas, while preserving normally functioning adjacent adrenal tissue, and returning the gland to a normally functioning status that is under normal regulation. In contrast to applications for tumor ablation, where devices have been developed with the objective of maximizing the size of the ablation zone for treating large tumors, a challenge for adrenal ablation is to minimize thermal damage to non-targeted adrenal tissue and thereby preserve adrenal function. Here, we investigate methods for creating small spherical ablation zones of volumes in the range 0.5–4 cm³ for the treatment of benign adrenal adenomas using water-loaded microwave monopole antennas operating at 2.45 GHz and 5.8 GHz. Coupled electromagnetic and bioheat transfer simulations and experiments in ex vivo tissue were employed to investigate the effect of frequency, applied power, ablation duration, and coolant temperature on the length and width of the ablation zone. Experimental results showed that small spherical ablation zones with diameters in the range of 7.4–17.6 mm can be obtained by adjusting the applied power and ablation duration. Multi-way ANOVA analysis of the experimentally-measured ablation zone dimensions demonstrated that frequency of operation and ablation duration are the primary parameters for controlling the ablation zone length and width, respectively. Additionally, it was demonstrated that the coolant temperature provides another effective parameter for controlling the ablation zone length without affecting the ablation zone width. Our study demonstrates the feasibility of creating small spherical microwave ablation zones suitable for targeting benign adrenal adenomas.

1. Introduction

Primary aldosteronism involves the excessive secretion of aldosterone from the adrenal gland, and is responsible for up to 11.2% of all cases of hypertension [1]. When this excess of aldosterone is attributable to an adenoma (a benign adrenal gland tumor), the condition is referred to as Conn’s syndrome. The negative effects of chronic hypertension are widely known and include coronary artery disease, congestive heart failure and cardiac arrhythmias [2, 3]. Currently, a patient with Conn’s syndrome must undergo adrenalectomy or receive intensive medical management with significant side-effects [3]. While adrenalectomy is an effective means of definitive therapy, it is only indicated for unilateral disease. Bilateral cases are typically treated with mineralcorticoid receptor antagonists (MRA), which are associated with side effects like gynecomastia and sexual dysfunction in men, while causing menstrual irregularities and conferring risks for teratogenicity in women of reproductive age [4].

Recently, there has been growing interest in the potential of image-guided thermal ablation for minimally-invasive treatment of adrenal adenomas. Thermal ablation is an established treatment modality that uses high temperatures (>~55 °C) to destroy malignant tumors in the liver, kidney, prostate, and the lungs. Systems employing a variety of energy...
modalities have been developed for thermal ablation, including radiofrequency current, laser, microwave, and ultrasound [5, 6]. As a result, ablation research and clinical applications have been primarily focused on achieving large ablation zones that destroy the tumor, as well as a healthy margin around the tumor to reduce the risk of recurrence. There are two key differences between using thermal ablation for treatment of a cancerous lesion and a Conn’s adenoma. Firstly, when treating a Conn’s adenoma, a primary goal is to preserve as much healthy functional tissue as possible rather than continuing ablation until marginal ablation of healthy tissue is established. While complete ablation of the adenoma is necessary for clinical success, large volume marginal ablation is unnecessary because these tumors are benign. Secondly, several studies indicate that the average adrenal adenoma causing Conn’s syndrome is around 5–20 mm wide, which is much smaller than the majority of the malignant tumors in the liver, kidney, and lungs [7]. These two major distinctions made it clear that the technical requirements for an adrenal ablation device were very different from those used routinely for treating tumors in other organs.

We propose the use of microwave ablation (MWA) for minimally-invasive treatment of adrenal adenomas. Thermal ablation systems for treatment of the adrenal gland require antenna designs optimized for the creation of small, spherical ablation zones. Since it is technically challenging to accurately position the ablation device in adenomas with diameter <10 mm, we anticipate candidate patients for this technology will be those with adenomas with diameter ranging between 10–20 mm. Thus, we restricted our MWA antenna design to adenomas with diameter ranging between 10 to 20 mm. Devices affording control of the axial and radial extents of heating will ensure conformal ablation of the targeted adenoma, while maximally preserving the adjacent adrenal tissue to maintain adrenal function. The majority of MWA systems in clinical use have been optimized for creation of large, spherical ablation zones in vascular organs such as the liver, and operate at 915 MHz or 2.45 GHz, both of which are frequencies allocated for industrial, scientific, and medical (ISM) use [8–10]. Compared to MWA systems operating at 915 MHz, systems operating at 2.45 GHz afford more rapid heating to higher tissue temperatures, as well as shorter antenna lengths, which enable creation of short ablation zones [8]. Systems operating at higher frequencies have also been investigated, with studies indicating that ablation zones of comparable volume to ~2 GHz systems are achievable with ablation systems operating at frequencies >10 GHz [11–13].

The radial depth, and thus the width, of the ablation zone may be controlled by adjusting applied power levels and duration of ablation. However, controlling length of the ablation zone created by microwave devices is more challenging, as detailed below. A number of studies have investigated methods to restrict the axial length of large volume ablation zones, which is typically not collimated to the length of the radiating element due to the use of unbalanced antennas, resulting in currents flowing along the outer surface of the feedline cable [14]. Antenna sleeves or chokes are often used to restrict currents on the outer surface of the feedline cable [15–17]. Luyen et al. presented a balun-free helical antenna design that operates at the second resonant frequency of the antenna and employs impedance matching elements [18]. Due to the attenuation within thin, coaxial cables, active cooling strategies are often employed to limit passive heating of tissue adjacent to the feedline cable [19]. While the above approaches restrict undesirable heating beyond the active length of the antenna, the minimal length of the ablation zone is limited by the active length of the radiating antenna, which in turn is determined by the wavelength at the system operating frequency. Approaches for reducing minimum length of the ablation zone include: dielectric loading of the antenna element to reduce the effective wavelength [20]; use of helical or other coiled antenna elements rather than linear monopoles/dipoles [18]; and designing MWA systems to operate at higher frequencies [21]. Existing microwave ablation devices have been clinically applied for treating malignant tumors in the adrenal gland; however, the targeted tumors have typically been large (2.1–6.1 cm) [22–25]. Technological requirements and feasibility of microwave ablation of adrenal masses were investigated in [26, 27]. For actively cooled applicators, adjustment of coolant flow parameters as well as coolant temperature may provide an additional means for adjusting ablation zone length. There is a lack of studies investigating practical techniques for reducing the length of MWA zones to the range of ~10–20 mm.

Some prior studies have parametrically studied the efficacy of radiofrequency ablation (RFA) for clinical practice [28, 29]. Furthermore, it has been shown that RFA leads to lower post-procedural pain and shorter operative times than laparoscopic adrenalectomy [7, 30]. While these studies demonstrated the technical feasibility of using thermal ablation for targeting adrenal tissue, they employed RFA devices suitable for large-volume tumor ablation. Consequently, these approaches were not well suited for restricting thermal damage to the targeted adenomas, resulted in ablation of the entire adrenal gland, and thus would not be suited for treating patients with bilateral disease.

The objective of this study was to investigate methods for creating short, spherical ablation zones, 0.5–4 cm$^3$ (diameter: 10–20 mm) using linear MWA antennas to treat benign adrenal adenomas. We hypothesized that water-cooled monopole antenna designs operating at 2.45 GHz and 5.8 GHz would afford the creation of short, spherical ablation zones ranging in diameter from 10–20 mm. Here, we investigated the ability to control ablation zone dimensions through...
adjustments of antenna operating frequency, applied power, ablation duration, and coolant temperature. Multiphysics computational models and experiments in ex vivo liver and adrenal gland tissues were employed to assess the impact of these parameters on ablation outcome. The key contribution of this work is demonstration of feasibility of using microwave ablation for creating localized ablation zones of diameter 10–20 mm with application to treatment of unilateral and bilateral adrenal adenomas.

2. Methods

Two approaches for creating ablation zones of length in the range 10–20 mm were investigated. The first approach employs water-cooled antenna designs operating at 2.45 GHz. Since water is a good microwave absorber (effective conductivity, \( \sigma = 1.36 \text{ S m}^{-1} \) and attenuation coefficient, \( \alpha = 28.95 \text{ Np m}^{-1} \) at 2.45 GHz), many MWA antennas employ water-cooling that terminates water flow proximal to the antenna radiating element [20, 31]. Thus, the water serves to remove heat dissipated within the lossy cables, without being exposed to microwaves radiating from the antenna element, thereby limiting microwave absorption within the applicator. Here, we exploit the high dielectric constant of water at 2.45 GHz (\( \epsilon_r \approx 78 \)) that serves to reduce the electromagnetic wavelength and thus the physical length of the antenna, compared to low permittivity materials such as plastics and ceramics commonly used in ablation devices. The second approach employs a water-cooled antenna designed to operate at 5.8 GHz. The higher frequency yields a shorter electromagnetic wavelength, and thus reduces the physical length of the antenna; for example, the wavelength in adrenal tissue at 5.8 GHz is 6.8 mm compared to 16 mm at 2.45 GHz. 5.8 GHz is selected because it is the center of the next frequency band above 2.45 GHz approved for ISM use [32]. To illustrate these concepts for controlling ablation zone size and shape, we designed water-loaded coaxial monopole antennas at 2.45 GHz and 5.8 GHz; these antennas can be readily fabricated and provide a practical means for tissue ablation.

2.1. Water-cooled antenna designs

We consider water-cooled coaxial monopole antennas tuned to 2.45 GHz and 5.8 GHz. The antennas consist of UT-34 coaxial cable with a length \( l_{\text{ao}} \) at the distal end of the outer conductor and dielectric stripped off. The cable and radiating tip are inserted within a concentric set of tubes through which water is circulated in a closed flow circuit. Water, which has a high dielectric constant (\( \epsilon_r \approx 78 \) at 2.45 GHz; \( \epsilon_r \approx 72 \) at 5.8 GHz), shrinks the effective wavelength, thereby reducing the physical length of the resonant antenna, as well as providing a means to maintain low temperatures within the applicator shaft.

2.2. Computational models—SAR and thermal ablation zone analysis (impact of water cooling)

We employed finite element method (FEM) simulations, implemented using COMSOL Multiphysics v5.3, to model electromagnetic power absorption and heat transfer during microwave ablation with the candidate antenna designs. Due to the cylindrically symmetric geometry of the applicator, the 3D geometry can be modeled with a 2D axially symmetric model. The model geometry illustrated in figure 1 consists of the applicator inserted within the adrenal gland, consisting of four layers of tissue (medulla, cortex, fat, and muscle), as described in [33]. We approximated the surrounding tissues as a layer of muscle. The solver computes the electric fields in the model by solving the Helmholtz wave equation:

\[
\nabla^2 \mathbf{E} - k_0^2 \left( \epsilon_r - \frac{j \sigma}{\omega \epsilon_0} \right) \mathbf{E} = 0
\]

where \( \mathbf{E} \) [V m\(^{-1}\)] is the electric field, \( k_0 \) is the free space wave-number, \( \epsilon_r \) is the relative permittivity, \( \sigma [\text{S m}^{-1}] \) is the effective electrical conductivity, \( \omega [\text{rads s}^{-1}] \) is the angular frequency, and \( \epsilon_0 \) is the permittivity of free space. Microwave power was applied to the port defined on the proximal end of the applicator as illustrated in figure 1. A first order scattering boundary condition was used on the external surfaces of the model as:

\[
\mathbf{n} \times (\nabla \times \mathbf{E}) - jk \mathbf{n} \times (\mathbf{E} \times \mathbf{n}) = 0
\]

where \( \mathbf{n} \) is normal vector to the boundary. Time-averaged electromagnetic power losses are calculated from the computed electric field using

\[
Q_{\text{em}} = \frac{1}{2} \sigma |\mathbf{E}|^2
\]

Electromagnetic power loss is coupled to the heat equation in order to compute the temperature profile inside the tissue:

\[
\rho c_T \frac{\partial T}{\partial t} = \nabla \cdot (k \cdot \nabla T) + Q_{\text{em}}
\]

where \( T [\text{K}] \) is temperature, \( \rho [\text{kg m}^{-3}] \) is the density of the tissue, \( c_T \) [J kg\(^{-1} \text{K}^{-1}] \) is the heat capacity at constant pressure, and \( k [\text{W m}^{-1} \text{K}^{-1}] \) is the thermal conductivity. The initial temperature of the tissues was set to 37°C and heat flux boundary conditions were defined on the applicator and tissue boundaries as:

\[
Q_0 = h(T_{\text{ext}} - T)
\]

where \( Q_0 \) is the transferred heat, \( T_{\text{ext}} \) is the external temperature, and \( h \) is the convective heat transfer coefficient. A value of \( h = 10 \text{ W m}^{-2} \text{ K}^{-1} \) is employed on the external tissue surfaces. A value of \( h = 1000 \text{ W m}^{-2} \text{ K}^{-1} \) is employed on the outer surface of the applicator to model convective heat transfer due to circulating water in the applicator similar to [34]. Tables 1 and 2 summarize the nominal thermal properties of adrenal gland, fat, muscle and liver tissue from [35], and measured cortex and
medulla electrical permittivity and conductivity values [36] incorporated in the simulations. In this study, we modeled tissue dielectric properties as being constant across all temperatures. Although it is recognized that dielectric properties of liver tissue are temperature dependent [37–39], in this study, we used static dielectric properties in our simulations since the temperature dependency of liver tissue dielectric properties at ablative temperatures (i.e. $T > 80\, ^\circ C$) has only been reported at 2.45 GHz; liver temperature-dependent dielectric property data are not available at 5.8 GHz. Further, there are no published studies reporting the temperature dependency of dielectric properties of adrenal tissue. Despite these limitations, simulations still provide a qualitative understanding of the effects of changing system operating frequency, applied power, ablation duration, and coolant temperature on ablation zone size and shape, to guide device design and experimental evaluation [11, 21, 40].

Temperature-dependent changes in heat capacity and thermal conductivity, as described in [41], were used in the simulations. In each simulation, thermal damage induced by microwave radiation in tissue was computed as a function of time and temperature by using an Arrhenius model [42] to obtain the ablation profile

$$\Omega(\tau) = \int_0^{\tau} A \exp\left( -\frac{E_a}{RT(t)} \right) dt \quad (6)$$

where $\Omega(\tau)$ is a dimensionless damage parameter, $A$ is frequency factor ($5.51 \times 10^{41}$ s$^{-1}$), $E_a$ is energy barrier ($2.769 \times 10^5$ J⋅mol$^{-1}$), $R$ is gas constant ($8.3143$ J⋅mol$^{-1}$⋅$^\circ C^{-1}$), $T(t)$ stands for the time development of the spatial temperature profile, and $\tau$ is the total time for which the thermal damage in the tissue was accumulated. These values of $E_a$ and $A$ were selected to model tissue discoloration following heating, allowing for comparison with experimental ablation zones [43]. A damage contour with a value of $\Omega = 1$ (corresponding to 63% of the thermal damage process being complete) was also overlaid on the temperature profile as a threshold for assessing the extent of the ablation zone. A non-uniform mesh was employed, with finest meshing at the antenna feed (maximum element size = 0.015 mm) and coarsest mesh in regions further away from the radiating element (maximum element size = 4.45 mm). The number of degrees of freedom in each model was 212,000 on average.

The computational models were used to determine the monopole length, $l_m$ that yielded the lowest antenna reflection coefficient at the desired operating frequency. Nominally, the length is expected to be $l_m = \sim \lambda/4$ at the operating frequency for a monopole antenna. At each frequency of interest, we iteratively adjusted $l_m$ in simulations to identify the frequency at which reflected power is minimized, indicating the best impedance match to the feeding transmission line.

### 2.3. Experimental platform for evaluating ablation zones

Antennas were fabricated from UT-34 semi-rigid coaxial cable inserted within a stainless-steel tube (1.82 mm O.D. and 1.37 mm I.D.), and the entire assembly subsequently inserted within a thin-walled PEEK tube (2.46 mm O.D.). The broadband reflection
coefficients of the fabricated antennas were measured with a vector network analyzer (HP 8753D) to confirm adequate impedance matching at the desired operating frequency.

Following confirmation of impedance match (|S11| < −10 dB), ablation experiments were then performed in freshly excised ex vivo bovine liver and adrenal gland tissues. We selected fresh ex vivo bovine liver tissue for the majority of experimental evaluations since it is a well-established tissue model for benchtop evaluation of novel thermal ablation technologies [44]; unlike the adrenal gland, it would not require embedding within a larger lossy medium to simulate the body [26]; and the contrast in color of ablated tissue versus unablated tissue is readily observed in liver, but not clear in adrenal gland tissue.

Freshly excised bovine liver and adrenal gland tissues were obtained from a local meat locker and transported to the lab within sealed plastic bags placed on ice. At the lab, the liver was sectioned into ∼8 cm × 8 cm × 6 cm blocks, placed within thin-walled plastic bags that were sealed and immersed within a ∼35 °C−37 °C water bath. Once samples were warmed to ∼37 °C, they were removed from the bath. The applicator was introduced into the liver and positioned such that the applicator tip was 60 mm below the liver surface. For adrenal gland ablations, the glands were similarly warmed up and they were sandwiched between porcine muscle with temperature of ∼35 °C−37 °C during ablation. Insertion depth of the microwave applicator in the adrenal glands ranged between 20 to 25 mm. An HP 83752B signal generator provided a continuous wave sinusoidal signal at the frequency of interest. Solid-state microwave amplifiers were then used to amplify the signal to 30 and 50 W. During ablations, a microwave power meter (Bird 7022, statistical power sensor) was connected in line with the applicator to monitor forward and reflected power for all applications. Chilled water (∼10 °C) was circulated through the applicator via a peristaltic pump (Cole Parmer 7554−90, Vernon Hills, IL, USA) at a rate of 80 ml·min⁻¹.

### 2.4. Experimental protocol

We employed experiments to assess ablation zone size/shape when delivering ablation with the following parameters:

- Input power: 30 and 40 W
- Frequency: 2.45 GHz and 5.8 GHz
- Ablation duration: 30, 60 and 90 s
- Coolant water temperature: 10 °C

Experiments using each combination (power, frequency, duration) were repeated five times (n = 5). In a second set of experiments, the effect of coolant water temperatures was investigated (Tcoolant = 20 and 30 °C) with frequency = 5.8 GHz, Pin = 30 W, and ablation duration of 90 s (n = 3). Following each experimental ablation, the tissue sample was sliced along the applicator axis, and the ablation zone length and width were measured using a ruler. The sphericity of the ablation zone shape was assessed using the axial ratio, defined as the ratio of the ablation zone width to the ablation zone length. Finally, we analyzed the measured length and width of ablations by using multi-way ANOVA. In a 3-way ANOVA, the main effects (frequency, power, time) and interaction terms (frequency X power, power X time, time X frequency) were studied.

After ensuring that it was feasible to use microwave ablation for creation of small ablation zones, two sets of ablation experiments (f = 2.45 GHz, Pin = 50 W, t = 180 s, Tcoolant = 10 °C) and (f = 5.8 GHz, Pin = 40 W, t = 90 s, Tcoolant = 30 °C) were performed three times (n = 3) for each combination in bovine adrenal gland.

### 3. Results

The optimal antenna tip length, ltip, was determined to be 6 and 2.5 mm for monopole antennas operating at 2.45 GHz and 5.8 GHz, respectively. Simulated normalized electromagnetic power absorption profiles in liver tissue for both frequencies are shown in figure 2.
These simulations illustrate the reduced electromagnetic power absorption along the applicator length at 5.8 GHz.

Figure 3 illustrates temperatures profiles in the multi-layer adrenal and liver tissue models following 40 W, 60 s microwave ablation with a 2.45 GHz monopole antenna. The black solid lines represent the $\Omega = 1$ thermal damage contour, and serve as an estimate of the ablation zone boundary (i.e. the $\Omega = 1$ contour represents the thermal damage process as being 63% complete). The ablation zone in the multi-layered adrenal model has an axial ratio of 0.99 (width/length) compared to 0.86 of the liver tissue. Although the size and the shape of the ablation zones are not identical, the ablation zone dimensions are similar (within 11.8%) in both tissue models, suggesting that liver serves as a suitable surrogate tissue model for design and experimental evaluation of devices for adrenal ablation. Liver tissue was used for all subsequent modeling experimental studies.

Figure 4 illustrates simulated temperature profiles following 40 W ablations at 2.45 and 5.8 GHz for durations of 30, 60 and 90 s. As suggested by the electromagnetic power absorption profiles shown in figure 2, the ablation zone length is shorter at 5.8 GHz compared to 2.45 GHz, due to the shorter wavelength,
and thus shorter antenna length at the higher frequency. For both frequencies, the overall ablation size becomes larger for longer durations. It is observed that axial ratio, a measure of the sphericity of the ablation zone, increases with frequency, and remains steady for all treatment durations for each power and frequency combination, with the exception of 30 W, 30 s at 2.45 GHz. Table 3 summarizes the ablation zone dimensions predicted by simulations.

Figure 5 shows example experimental ablation zones when using 30 W and 40 W input power, for 60 s at both frequencies. When increasing applied power level from 30 W to 40 W, we observe that the ablation volume increases 125.5% for the 2.45 GHz antenna, compared to 203.4% for 5.8 GHz. As anticipated, the length of the ablation zone (14.4 mm) created by the 2.45 GHz antenna was shorter than the ablation zone (8.8 mm) created by the 5.8 GHz antenna, attributed to the shorter antenna length at 5.8 GHz.

Figure 6 shows example experimental ablation zones following 30, 60, and 90 s for 40 W power applied at 2.45 GHz and 5.8 GHz. Higher frequency gives rise to higher axial ratio and longer ablation time creates larger ablation zones. Table 4 lists the experimentally observed ablation zone dimensions in ex vivo liver tissue.

As shown in table 4, the ablation zone width is larger than the ablation zone length at 5.8 GHz, yielding an axial ratio greater than 1, in contrast to the observations at 2.45 GHz, for which the ratio is close to 1. We performed a second set of experiments at 5.8 GHz with different water temperatures to investigate the utility of adjusting ablation zone length by adjusting coolant temperature. Figure 7 shows ablation zones at 5.8 GHz for input power of 30 W and 90 s duration with coolant temperatures of 10, 20 and 30 °C. Table 5 summarizes the measured ablation dimensions. These results suggest that increasing the temperature of the cooling water from 10–30 °C has the primary effect of increasing the ablation zone length, with minimal change in the ablation zone width (average change of 0.27 mm in ablation zone width across all coolant temperatures).

Multi-way ANOVA using a 5% significance level was used to identify the main factors determining the

| P<sub>in</sub>, duration | Length [mm] | Width [mm] | Axial ratio | Length [mm] | Width [mm] | Axial ratio |
|------------------------|------------|------------|-------------|------------|------------|-------------|
| 30 W, 30 s             | 4.01       | 7.00       | 1.75        | 10.49      | 11.43      | 1.09        |
| 30 W, 60 s             | 12.60      | 11.81      | 0.94        | 13.33      | 14.52      | 1.09        |
| 30 W, 90 s             | 15.92      | 14.78      | 0.93        | 15.39      | 16.76      | 1.09        |
| 40 W, 30 s             | 10.99      | 9.52       | 0.87        | 12.04      | 12.12      | 1.00        |
| 40 W, 60 s             | 16.72      | 14.33      | 0.86        | 15.22      | 15.21      | 1.00        |
| 40 W, 90 s             | 20.04      | 17.30      | 0.86        | 17.97      | 17.96      | 1.00        |
Figure 5. Example ablation patterns following 60 s microwave ablation in \textit{ex vivo} liver tissue: (a) 30 W, 2.45 GHz; (b) 30 W, 5.8 GHz; (c) 40 W, 2.45 GHz; and (d) 40 W, 5.8 GHz.

Figure 6. Example ablation patterns following 40 W microwave ablation in \textit{ex vivo} liver tissue for 30, 60 and 90 s at 2.45 and 5.8 GHz.
interaction affected the ablation zone width. According to the length. Ablation time was the primary factor that affected the ablation zone width. Table 6 shows the -values for ablation zone length and width, respectively. These results indicate that operating frequency was the primary factor that affected the ablation zone length. Ablation time was the primary factor that affected the ablation zone width. According to the interaction -values, the interactive effects were not statistically significant.

Ablations were performed on bovine adrenal glands in order to verify the ability to create ~10–20 mm spherical ablation zones with the antennas investigated in this study. Figure 8 compares example ablation zones created by the water-cooled 2.45 and 5.8 GHz antennas. As evident in figure 8(a), which illustrates a section adrenal gland where no ablation was performed, it is challenging to assess the extent of ablation using the zone of visibly discolored tissue due to the distinct coloration of the adrenal medulla and cortex. Ablation length and width at 2.45 GHz were \( L = 16.0 \pm 0.5 \) and \( W = 15.2 \pm 0.3 \) for input power of 50 W and ablation time of 180 s. For the 5.8 GHz ablation, length and width were \( L = 10.2 \pm 0.4 \) and \( W = 11.8 \pm 0.6 \) for input power of 40 W, ablation time of 90 s and water temperature of 30 °C.

### 4. Discussion

This study was conducted to assess methods for creating short, spherical MWA zones in the range of 0.5–4 cm³ using water-cooled coaxial monopole antennas, with application to treatment of benign adrenal adenomas. We hypothesized that using water-loaded antennas operating at 2.45 and 5.8 GHz would enable the creation of ablation zone lengths in the range of 10–20 mm. The simulated electromagnetic power absorption profiles illustrated in figure 2, indicate that the shorter antenna length at 5.8 GHz

### Table 4. Experimentally measured ablation zone dimensions ex vivo in liver tissue with water-cooled 2.45 GHz and 5.8 GHz antennas. Data are presented as mean ± standard deviation (\( n = 5 \) for each combination).

| \( P_{in}, \text{duration} \) | 2.45 GHz | 5.8 GHz |
|-----------------------------|----------|----------|
|                             | Length [mm] | Width [mm] | Axial ratio | Length [mm] | Width [mm] | Axial ratio |
| 30 W, 30 s                  | 9.2 ± 0.4  | 6.6 ± 0.5  | 0.72       | 5.9 ± 0.5  | 7.4 ± 0.4  | 1.25       |
| 30 W, 60 s                  | 11 ± 0.6   | 11.2 ± 0.7 | 1.02       | 6.0 ± 1.0   | 8.9 ± 1.1  | 1.49       |
| 30 W, 90 s                  | 11.6 ± 1.0 | 12.7 ± 1.0 | 1.09       | 9.0 ± 0.0   | 12.9 ± 0.5 | 1.43       |
| 40 W, 30 s                  | 8.2 ± 1.9   | 7.3 ± 1.4   | 0.89       | 6.7 ± 0.8   | 9.2 ± 1.2  | 1.38       |
| 40 W, 60 s                  | 14.4 ± 1.1 | 14.7 ± 1.4 | 1.02       | 8.8 ± 1.0  | 12.8 ± 0.7 | 1.47       |
| 40 W, 90 s                  | 17.1 ± 1.6 | 17.6 ± 1.5 | 1.03       | 10.2 ± 1.2 | 13.6 ± 0.7 | 1.33       |

### Table 5. Ablation zone dimensions in ex vivo liver tissue at 5.8 GHz for power of 30 W and 90 s duration with coolant temperatures of 10, 20 and 30 °C (\( n = 3 \)).

| Temp. [°C] | Length [mm] | Width [mm] | Axial ratio |
|------------|-------------|------------|-------------|
| 10         | 9.00 ± 0.00 | 12.90 ± 0.49 | 1.43         |
| 20         | 9.17 ± 0.62 | 12.00 ± 0.82 | 1.31         |
| 30         | 12.50 ± 0.71 | 13.17 ± 0.62 | 1.05         |

### Table 6. \( p \)-values of main effects and their interaction for length and width of ablation zone in ex vivo liver tissue following 3-way ANOVA analysis.

| Effect/interaction | Ablation zone length | Ablation zone width |
|--------------------|----------------------|---------------------|
| Frequency           | 0.0426\(^a\)       | 0.4091              |
| Power               | 0.1417              | 0.0917              |
| Time                | 0.1042              | 0.0446\(^a\)       |
| Frequency*Power     | 0.6140              | 0.6497              |
| Frequency*Time      | 0.4943              | 0.3600              |
| Power*Time          | 0.3859              | 0.5709              |

\(^a\) \( p \)-values with statistical significance.
(l_m = 2.5 mm) provides improved control of microwave heating along the length of the applicator, compared to the 2.45 GHz antenna (l_m = 6 mm). We found that 5.8 GHz MWA antennas yielded power deposition more localized to the applicator, compared to 2.45 GHz, similar to other studies [21]. In previous studies with uncooled dipole antennas, it was shown that this more localized power deposition led to higher temperatures in proximity to the antenna. This led to a more prominent role of thermal conduction in growth of the ablation zone over ~5–10 min, yielding ablation zone of similar size to ~2 GHz devices. However, in our study, which considered ~30–90 s ablations with cooled devices, operating at 5.8 GHz yielded ablation zones of smaller diameter. This can be attributed to the shorter ablation duration, where thermal conductivity plays a limited role.

The primary findings from the simulation results presented in figure 4 and table 3 are: (1) water-cooled monopole antennas designed to operate at 5.8 GHz yield smaller ablation zone lengths compared to those designed to operate at 2.45 GHz, (2) the ablation zone width grows with increased ablation duration, and (3) increased applied power yields increases in both ablation zone width and length. The simulations further suggested that for a given applied power level and operating frequency, the ablation zone shape generally remained steady (within 1%) for heating durations ranging from 30–90 s. An exception to this trend was the 30 W, 30 s ablation zone at 2.45 GHz, for which simulations predicted an axial ratio of 1.75, compared to 0.94 and 0.93 for 60 s and 90 s ablations, respectively. This unusually large axial ratio at 30 W, 30 s is primarily due to the short simulated ablation zone length (4 mm), which could be attributed to the convective cooling boundary condition employed for simulating cooling along the applicator shaft, the effects of which may be more pronounced for low power, short duration ablations.

Experimentally observed ablation zones in ex vivo liver tissue for fixed durations indicated that both ablation zone width and length grow with increased applied input power (figure 5 and table 4). Thus, applied power alone does not allow for independent control of ablation zone length or width. Figure 6 shows example ablation zone images following experimental ablations in ex vivo liver tissue using the same applied energy levels as in the simulations shown in figure 4. The ablation profiles and dimensions summarized in table 4 demonstrate trends similar to the simulations in terms of adjustment of ablation length and width by choice of frequency and ablation time, respectively. These observations were also statistically confirmed by 3-way ANOVA tests (summarized in table 6) at 5% significance level. A p-value of 0.0426 indicated frequency as the main factor for controlling the ablation zone length, and a p-value of 0.0446 indicated ablation duration as the main factor for controlling the ablation zone width.

The experimentally observed ablation zones reported in table 4 show that spherical ablation zones (axial ratio ≈ 1) can be created in the diameter range of 10–20 mm with the following combinations: (2.45 GHz, 30 W, 60 s, diameter ≈ 11 mm), (2.45 GHz, 40 W, 60 s, diameter ≈ 14.5 mm), and (2.45 GHz, 40 W, 90 s, diameter ≈ 17.3 mm). However, all the axial ratios were greater than 1 for the 5.8 GHz antenna. In other words, the ablation zone width is larger than the ablation zone length at 5.8 GHz. To assess the feasibility of creating spherical ablation zones (axial ratio = 1) at 5.8 GHz, we experimentally investigated the impact of adjusting temperature of the cooling water on the ablation zone length. The experimental results shown in figure 7 and table 5 illustrate how using cooling water at a temperature of 30 °C, compared to 10 °C in the earlier experiments, allowed for increased heating along the applicator length. The experimentally measured axial ratio decreased from 1.43 to 1.05 by changing cooling water temperature from 10 to 30 °C for ablation combination of (5.8 GHz, 30 W, 90 s, diameter ≈ 12.8 mm). It is noted that if ablative temperatures are

Figure 8. Comparison of the observed ablation zones in bovine adrenal gland at different frequencies with a non-ablated gland: (a) control sample f = 2.45 GHz, P_in = 0 W, t = 180 s, T_coolant = 10 °C, (b) ablated sample at f = 2.45 GHz, P_in = 50 W, t = 180 s, T_coolant = 10 °C, and (c) ablated sample at f = 5.8 GHz, P_in = 40 W, t = 90 s, T_coolant = 30 °C. The dashed line illustrates the antenna insertion track into the adrenal tissue sample.
not achieved along the antenna insertion path when coolant temperature is low (10 °C), track ablation techniques can be utilized which is common in clinical practice during RF and MWA. During track ablation, low power levels without coolant flow is applied while slowly retracting the ablation applicator, thereby allowing tissue immediately adjacent to the applicator to be ablated [45, 46].

Ablations performed in bovine adrenal glands showed that the 5.8 GHz antenna could create spherical ablation zones in the lower range of the targets with diameter 10–20 mm whereas the 2.45 GHz antenna could be used in the higher range. Input power and time combination were obtained empirically for both frequencies. We found that we had to use different power and time combinations compared to those in liver tissue. This may be because the discoloration of adrenal tissue at elevated temperatures was less clear than in liver, and the thermal dose required to observe this discoloration may be different in liver and adrenal tissue. Additionally, the color of the adrenal medulla, which is similar to that of ablated cortex, makes it challenging to accurately assess the zone of tissue ablation by observing extent of tissue discoloration.

A prior clinical study employed a monopolar radiofrequency electrode for thermal ablation of the adrenal gland [30]. While successful in destroying the targeted adenoma, the approach also thermally ablated surrounding adrenocortical and medullary tissue. Although RFA was both minimally invasive and clinically efficacious procedure for PA, it is useful only in the context of unilateral disease, given the collateral destruction of normal tissue with current RFA technology optimized for creating large ablation volumes. This therefore leaves a considerable clinical need to develop selective ablation, which can be used for unilateral and bilateral disease. Currently available microwave ablation devices have primarily been designed to create large volume ablation zones [15, 20], and do not provide a means for scaling thermal ablation zone size to the range of 10–20 mm in diameter, while maintaining the ablation zone sphericity. The results presented here demonstrate the feasibility of creating 10–20 mm diameter spherical ablation zones using water-cooled monopole antennas, by appropriate selection of operating frequency, cooling water temperature, applied power level, and ablation duration. While we investigated MWA for selective adrenal ablation, we note that other minimally-invasive thermal therapy modalities such as RFA [47] and lasers [48], as well as non-thermal approaches such as irreversible electroporation [49], may also have potential for treatment of benign adrenal adenomas, if optimized to deliver small treatment zones and maximally spare normal adrenocortical cells.

A limitation of this study is the use of static values for dielectric properties in the simulations, since there are no reported temperature-dependent dielectric property data available for adrenal tissue. Similarly, temperature dependent dielectric properties of liver were unavailable at 5.8 GHz. The discrepancy in dimensions of ablation zones predicted by simulations compared to experiment may be due to the use of static tissue dielectric properties in the simulations. Ongoing efforts in our lab are geared towards assessing the relationship between residual adrenal function following selective thermal ablation of targeted regions within the adrenal medulla and cortex. Similar to other reports on design of devices for microwave ablation employing computational models and experiments in ex vivo tissue [16, 29, 41], perfusion effects were not considered in our simulations and experiments. Compared to longer treatment durations used for creation of large ablation zones (e.g. in the liver), it is likely that perfusion will have a reduced impact for short duration ablations and can be compensated by increasing the applied input power.

5. Conclusion

We evaluated water-cooled monopole antennas, designed to operated 2.45 GHz and 5.8 GHz, for creating short spherical ablation zones with application to thermal ablation of benign adrenal adenomas. Computational models and experiments in ex vivo tissue were used to analyze the effect of frequency, applied power, ablation duration, and coolant temperature on the ablation length and width. Both simulation and measured results demonstrated the ability to create spherical ablation zones with a diameter in the range of 10–20 mm through appropriate selection of applied power, ablation duration, and coolant temperature. Statistical analysis of the experimentally measured ablation zones showed that ablation length is primarily controlled by the operating frequency, while ablation width is primarily controlled by the ablation duration and temperature of the cooling water.

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Declaration of Interest

The authors report no conflicts of interest.

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