For reprint orders, please contact: reprints@futuremedicine.com

Understanding the nuances of microwave ablation for more accurate post-treatment assessment

Christy Kim^{*,1}

¹AngioDynamics, Inc., 1850 Mt Diablo Blvd, Ste 660, Walnut Creek, CA 94596, USA

*Author for correspondence: ckim@angiodynamics.com

Microwave ablation (MWA) is a relatively new thermal modality for minimally invasive procedures compared with radiofrequency ablation. Although MWA and radiofrequency ablation are thermal modalities, their underlying physics and principles greatly differ. Consequently, it is imperative that clinicians be aware of how these differences impact realized ablation volumes to consistently ensure technical success and better patient outcomes. This paper will review the nuances specific to MWA technology (i.e., tissue properties, perfusion/heat sink effect, ablation assessment, imaging accuracy and tissue contraction) that are often overlooked based on familiarity with conventional thermal modalities to guide more accurate assessment of post-treatment MWA volumes.

First draft submitted: 28 December 2017; Accepted for publication: 29 January 2018; Published online: 14 February 2018

Keywords: ablation assessment • heat sink effect • imaging accuracy • microwave ablation • microwave ablation devices • radiofrequency ablation • thermal ablation • tissue contraction

Microwave ablation (MWA) has recently become a very popular thermal modality for minimally invasive procedures. Although radiofrequency ablation (RFA) has the longest history of accumulated data as the prototypical thermal ablation technique, MWA is quickly gaining momentum because of its technological advancements, including faster ablation times, larger ablation volumes, effectiveness in many tissue types and an improved convection profile [1–4]. Because the mechanism of action of MWA is distinct from RFA, the assessment of MWA volumes may differ from the conventional methods used to assess RFA volumes. Understanding the nuances of MWA technology over other thermal modalities is critical to determine strategies to more accurately assess post-treatment MWA volumes.

MWA is a different thermal ablation than RFA

Even though MWA and RFA both destroy tissues via thermally mediated coagulative necrosis, MWA and RFA are broadly distinct because of their inherently different mechanisms of energy deposition (Figure 1). RFA is limited in tissues of low electrical conductivity because RFA relies on resistive heating through an electrically conductive path (Figure 1B) [5]. The radiofrequency (RF) electrode is not the source of the heat itself but instead, generates frequencies of 450–500 kHz to frictionally heat up the tissue immediately adjacent to the electrode [5]. The RFA volume is further transmitted by thermal conductance (Figure 1D) [6]. RFA's mechanism of heating necessitates a slow and methodical energy deposition for controlled heating 50–100°C to avoid charring and vaporization, which could compromise electrical current flow because desiccated tissue acts as an insulating 'sleeve' around the electrode to limit energy transfer resulting in smaller ablations [5].

In contrast to RFA's primary reliance on thermal conduction, MWA applies electromagnetic fields with higher frequencies of 915 MHz to 2.45 GHz to directly heat tissue to lethal temperatures greater than 150°C through dielectric hysteresis [4]. Dielectric hysteresis is a process in which polar molecules, primarily water are forced to continuously realign with the oscillating electric field (Figure 1A). This results in the generation of kinetic energy and subsequent heat generation [4]. Since MWA relies predominately on direct heating over thermal conductance (Figure 1C), MWA has the potential to produce faster and larger ablation volumes with less susceptibility to the heat sink effect, the perfusion mediated cooling provided by local blood vessels, compared with RFA [3,6–8].

Figure 1. Underlying mechanism of action and heat transfer for microwave ablation and radiofrequency ablation. Microwave ablation (A & C); radiofrequency ablation (B & D).

Table 1. Parameters that affect ablation volumes using microwave ablation and radiofrequency ablation technologies.			
Parameter	MWA	RFA	Ref.
Tissue properties	+	++	[4,9,10]
Perfusion/heat sink	+	++	[1,6–8,11–13]
Ablation assessment	+	+	[8,14–16]
Imaging accuracy	++	+	[17–19]
Tissue contraction	++	+	[20–22]
+ Sensitive; ++ More sensitive. MWA: Microwave ablation; RFA: Radiofrequency ablation.			

Moreover, MWA in comparison to RFA is capable of propagating through many tissue types despite having high impedance such as in the lung or within charred tissue [4,9]. Given that MWA and RFA achieve different temperature thresholds through varying energy deposition and kinetics, post-treatment imaging using MWA may need to be assessed differently than previously assumed with RFA technology. Table 1 summarizes the parameters that have been shown to affect ablation volumes and assessment using MWA and RFA technologies that will be further explored in this review.

Each MWA system is uniquely different

Strengthened by continual advancements in microwave technology, MWA device manufacturers are advancing minimally invasive techniques at a rapid pace with the help of innovative clinicians. However, there are nuances of MWA technology that every clinician must be aware of to effectively plan, perform and evaluate procedural success to ensure that lesions are completely treated with sufficient ablative safety margins (0.5–1 cm).

Every MWA system consists of a generator, a cable and an applicator; however no two MWA systems are alike because these components will vary by manufacturer according to their respective intellectual property. Power is generated from the microwave generator which can have varying frequencies of 915 MHz (low frequency) or

2.45 GHz (high frequency). MWA systems operating at 2.45 GHz generally result in greater power deposition and larger ablation volumes than those operating at 915 MHz, resulting in larger ablations in a shorter period of time [2,11,23–25]. The cable distributes the power from the generator to the applicator tip and the degree of power conservation will also vary by design; therefore, the operating generator wattage should not be confused with the applied power at the applicator tip [24]. Most importantly, every MWA system is unique because of the careful consideration taken into the microwave applicator design with respect to geometry, diameter and cooling mechanism. Consequently, every MWA system will have a characteristic ablation zone shape and size that will be further scalable by power and time settings [24]. Typical MWA systems require 10 min and some systems even require multiple applicators to reach the desired maximum ablation volumes [24,26,27]. To minimize cost, time required for positioning additional applicators, and the higher risk of bleeding from additional penetrations, a one applicator MWA system that can create up to a 5 cm ablation in minimal time would be ideal to ensure adequate safety margins (i.e., Acculis MTA System; Microsulis Medical, Denmead, England) [24]. In summary, generalizations about MWA technology must be refined per MWA device and not misleadingly across all similarly classified technologies because of the range in design specifications across manufacturers.

Ex vivo MWA validations versus in vivo MWA results

Recently, there have been studies evaluating manufacturers' reference values provided with the device's instructions for use and how *ex vivo* ablation volumes are significantly larger than ablation volumes obtained from *in vivo* animal and diseased human tissues [12,27–29]. *Ex vivo* animal models are limited by insufficiently mimicking *in vivo* tissue conditions of perfusion, temperature, cellular morphology, anatomy and tissue contraction. *In vivo* imaging of ablation volumes or technical success is limited by visual interpretation of the imaging modality of choice and the kinetics of dynamic tissue ablation volumes with respect to time in a physiological environment. Nonetheless, ablation volumes derived from *ex vivo* animal models are valuable in that they provide a rough approximation of ablation volumes to be expected in practice.

Winokur *et al.* conducted a clinical study performing percutaneous MWAs using the AMICA (HS Medical, FL, USA) and Certus PR applicators (NeuWave Medical, WI, USA) and found that they produced ablation volumes with significant differences in the short and long axis diameters and resultant volumes compared with the manufacturer's *ex vivo* reference values (note: the short axis diameter tends to be the limiting factor in an ablation because it has to encompass the tumor along with a safety margin) [28]. This study raises concerns about translating manufacturers' *ex vivo* derived ablation volumes into clinical practice. However, some of the shortcomings of this study include heterogeneity of tissue types, relatively small sample size ($n = 25$ and 12), the misuse of the manufacturers' recommended directions for use through the use of serial ablations (eight of 25 and nine of 12) and oversimplification of the kinetics of varying power and time by combining both into a single independent variable. Power and time should not be combined because an equivalent total applied energy of 30 kJ using *in vivo* porcine livers produces significantly different volumes if applied at 25 W (23.7 ± 26.5 cm³) or 100 W (265.7 ± 208.1 cm³) [30]. In addition, simultaneous power delivery has been shown to have differing ablation shapes and sizes in comparison to sequentially applied microwave energy [26].

When ablation measurements are analyzed by manufacturer's power and time settings, more insights pertaining to specific MWA systems may be made on how accurate *ex vivo* data approximate *in vivo* data. Table 2 includes the *in vivo* and *ex vivo* short and long axis diameter comparisons extrapolated from the study conducted by Winokur *et al.* for the AMICA and Certus PR applicators at varying power and time settings. Surprisingly, for the AMICA applicator, the MWA long axis diameter ($p = 0.799$) and short axis diameters ($p = 0.105$) were not statistically different across all time points tested at 40 , 60 and 80 W between *in vivo* and manufacturer's *ex vivo* data (note: time points were selected based on availability of manufacturer's reference data). However, the average relative difference of the short axis diameter of the *in vivo* data to the *ex vivo* data with the AMICA applicator showed a $22.9 \pm 17.4\%$ decrease whereas the long axis diameter decrease was only $2.7 \pm 16.9\%$ (Table 2). Figure 2A & B show the *in vivo* versus *ex vivo* comparison of both the short and long axis ablation diameters obtained with the AMICA applicator at 60 W. Intriguingly, MWAs with the Certus PR at 65 W showed a similar conservation of long axis diameter ($p = 0.223$) and short axis diameter ($p = 0.142$) across *ex vivo* and *in vivo* studies but with average smaller long axis diameters ($17.7 \pm 4.8\%$) in addition to average smaller short axis diameters ($23.2 \pm 1.2\%$) in conservation with the AMICA applicator (Table 2, Figure 2C & D). Although this analysis is limited in sample size and statistical significance, these results suggest that ablation dimensions vary *in vivo* versus *ex vivo* and to what extent will depend on the MWA system's specific applicator design, power and time settings, and tissue property.

Table 2. Summary of average percent differences of *in vivo* short and long axis diameters relative to *ex vivo* references for the AMICA and Certus PR Microwave Ablation Systems at various power and time settings.

Settings		Short axis diameter				Long axis diameter			
Power (W)	Time (min)	<i>In vivo</i> (mm)	<i>Ex vivo</i> (mm)	% Diff. (rel. to <i>ex vivo</i>)	Avg % diff.	<i>In vivo</i> (mm)	<i>Ex vivo</i> (mm)	% Diff. (rel. to <i>ex vivo</i>)	Avg % diff.
AMICA									
40	5	16.3	29	-43.8	-22.9 ± 17.4	36.3	36	0.8	-2.7 ± 16.9
40	15	32.6	42	-22.4		51.9	50	3.8	
60	3	22.8	26	-12.3		33.6	35	-4.0	
60	5	28.95	34	-14.9		45.4	48	-5.4	
60	10	33.1 [†]	40	-17.3		56.35 [†]	54	4.4	
60	15	48.6	48	1.3		75	61	23.0	
80	10	21.7	46	-52.8		41.2	66	-37.6	
80	15	43.5	55	-20.9		68.5	73	-6.2	
Certus PR									
65	5	20.05	26.4	-24.1	-23.2 ± 1.2	32.65	41.4	-21.1	-17.7 ± 4.8
65	10	23.75	30.6	-22.4		39.85	46.5	-14.3	

[†]Taken as an average of 2 data points instead of 3 due to an outlier.
AMICA *in vivo* versus *ex vivo*: short axis diameter *p* = 0.105; long axis diameter *p* = 0.799 (α = 0.05; two-tailed unpaired Student's *t*-test).
Certus PR *in vivo* versus *ex vivo*: short axis diameter *p* = 0.142; long axis diameter *p* = 0.223 (α = 0.05; two-tailed unpaired Student's *t*-test).

Figure 2. Comparison of *in vivo* and *ex vivo* reference ablation diameters for the AMICA and Certus PR applicators at a specified wattage with respect to time.

Figure 3. *Ex vivo* versus *in vivo* parameters that inherently make accurate comparisons a challenge with the use of MWA technology.

Tissue property impact on MWA volumes

With multiple parameters to consider in *ex vivo* versus *in vivo* studies, as summarized in Figure 3, we must understand the nuances of MWA technology studies to be able to accurately assess the underlying differences and to effectively use this modality clinically. Interestingly but often overlooked, the problem with ‘direct comparisons’ of *ex vivo* versus *in vivo* may be more tissue property related rather than an oversimplified *ex vivo* versus *in vivo* difference (e.g., bovine vs porcine vs human, healthy vs diseased tissue, room vs physiological temperature, desiccated vs hydrated tissue, absence or presence of perfusion and central vs peripheral ablations, etc.) [1,10,28].

Ex vivo MWA studies tend to be based on the bovine liver model and *in vivo* MWA studies tend to be based on the porcine liver model for logistical reasons [1,27]. Although the porcine liver model is the gold standard for preclinical studies because it resembles the human liver in size (depending on age/weight), vascularity and metabolic function, the disparate anatomical dimensions of the porcine liver in comparison to the bovine liver (and human liver) may introduce an artificial factor of varying target tissue sizes. Tissue dimensions relative to the expected ablation volume has been shown to alter the size and shape of MWA volumes *ex vivo* [31]. Thin tissue samples, whose dimensions in the plane perpendicular to the applicator were smaller than the short axis, caused an average increase in ablation lesion length by 7.5% in comparison to unrestricted samples [31]. Because porcine liver has lobes with a thinner profile than those in human, this study raises concerns about the validity of the *in vivo* porcine liver model as a gold standard for translational medicine. To corroborate this concern, a study using the AMICA (HS Medical, Rome, Italy) MWA device, showed that *ex vivo* data on bovine liver were more predictive of the actual clinical performance on centrally located liver malignancies than *in vivo* data derived from the porcine model [27].

In addition to tissue dimensions affecting MWA volumes, physical features of diseased tissue relative to healthy tissue may contribute to underlying differences *in vivo* versus *ex vivo*. For example, malignant tissue *ex vivo* has been shown to have different electrical tissue properties from normal tissue [10]; this would impact the absorption of microwave energy and heat generation in the varying tissue types. Further, depending on the tumor properties (i.e., hepatocellular carcinoma which tends to occur in cirrhotic livers vs liver metastases), it has been shown that ablation volumes at the same MWA settings were larger in metastases in comparison to hepatocellular carcinoma, most likely attributed to the reduction in water content and subsequent lower absorption of the microwave energy in cirrhotic tissue [27]. How microwave energy is propagated through a tissue will not only be dependent on the specific MWA device but also on the specific tissue that is to be treated.

Perfusion/heat sink effect on MWA volumes

One of the key differences of *ex vivo* and *in vivo* studies for MWA technologies is the absence or presence of vascular perfusion and the heat sink effect. The heat sink effect is a phenomenon that limits the effectiveness of the ablation when the target lesion is in close proximity (within 1 cm) to a large blood vessel (≥ 3 mm in diameter); the flowing blood causes a cooling effect, thereby reducing the ablation volume [13]. *In vivo* MWA volumes are generally smaller than *ex vivo* MWA volumes and this disparity is mainly attributed to the heat sink effect [1,12]. With the 915 MHz VivaWave MWA System (Vivant Medical, CA, USA) at 45 W for 5–10 min, MWA has been shown to have less susceptibility to the heat sink effect in an *in vivo* porcine model compared with previous data reported with RFA [8,13]. Given that computational modeling shows that perfusion has greater effects on ablation diameter with respect to antennas operating at 915 MHz versus 2.45 GHz, greater effective conductivity and power

deposition associated with MWA systems operating at 2.45 GHz may overcome the effects of perfusion even more so than previously proposed [1,8]. In agreement with this, with the 2.45 GHz Microsulis MTA System (Microsulis Medical) at higher power settings of 100 and 150 W, *in vivo* short axis diameters for treatment durations of 8 min or less were unconventionally larger than for *ex vivo* short axis diameters [1]. MWA technology is generally less susceptible to perfusion and the heat sink effect than RFA, but depending on the power delivery (i.e., operating frequency, MWA applicator design, power and time settings), the severity of the heat sink effect experienced *in vivo* may contribute to differences in MWA volumes obtained from *ex vivo* animal studies.

Although there are clinical studies supporting the efficient and safe use of MWA technology in treating liver tumors adjacent to large vessels [32–34], Vogl *et al.*'s comparison of a 915 MHz (Evident, CO, USA) and a 2.45 GHz (Emprint, Covidien, CO, USA) MWA systems for the treatment of lung metastases, showed that the perivascular location of a tumor was positively associated with local tumor progression [35]. Further, ablations performed with the 915 MHz Evident System led to more local tumor progression than with the use of the 2.45 GHz Emprint System due to the larger ablations and hence sufficiently larger safety margins associated with the high frequency MWA system [35]. Given the many options of commercially available MWA systems, the ability of a specific MWA system to be able to overcome the effects of perfusion will be dependent on the frequency, applicator design and power output that will be unique to each manufacturer.

Imaging challenges in assessing MWA volumes

While *ex vivo* ablation volumes are easier to quantitate, ablation assessment is not standardized in freshly ablated *in vivo* tissue because of the hyperemic zone, unclear margins of cell death and the kinetics of the dynamic ablation zone with time. For instance, some studies include the hyperemic zone which may contain viable cells, and this may make comparing ablation volumes fairly across MWA technologies even more challenging, leading to inconsistencies discerning the differences between *ex vivo* versus *in vivo* data [14,36]. In a prospective ablate and resect study, the zone of cell death, which was assessed by triphenyl tetrazolium chloride (TTC) staining, was always greater than the macroscopic gross measurement by approximately 25% [15]. Of note, the same study that was able to detect larger *in vivo* ablation volumes compared with *ex vivo* ablation volumes at high wattages also utilized TTC staining, which may be a more sensitive assay for necrosis than gross margin assessments using calipers [1]. In another study, nicotinamide adenine dinucleotide (NADH) diaphorase staining over hematoxylin and eosin staining provided definitive delineation of the coagulation margins for fresh *in vivo* ablations [8]. A possible reason for the difficulty to discern the margins in freshly ablated tissue *in vivo* may be due to the gradual expansion of the ablation zone that has been reported to occur up to 12-h post ablation [16].

Also, the assumption that imaging findings are equivalent to pathological findings must be carefully assessed [14,17–19]. As noted by Correa-Gallego *et al.*, ultrasound may provide gross estimations of ablation volumes but is unable to predict the degree of cellular injury by significantly underestimating the real ablation volume in the *in vivo* porcine model [17]. Furthermore, in the human model, the same study showed that ultrasound grossly underestimated the ablation volume compared with delayed computed tomography (CT) scans, emphasizing the limitations of imaging modalities and the temporal contributions of ongoing cellular injury and repair to realized ablation volumes. CT may provide a rough ablation zone estimate but on average, differed by 4 mm from gross lesion measurement in Awad *et al.*'s study [19]. Imaging modality and delayed imaging seem to consistently play a critical role in assessing realized ablation volumes because a 24 h delayed magnetic resonance imaging (MRI) study showed a 24.3% increase in mean MWA volume in comparison to CT [16–18]; whether this increase was mainly due to the limitation of imaging modality, enlargement of the zone of coagulated necrosis with time and/or rehydration of contracted tissue and to what extent each factor contributes to the overall assessment will have to be further investigated.

Tissue contraction influence on short axis diameter assessment

Finally, one of the most important parameters that is often overlooked in assessing post-treatment visualized ablation volumes is tissue contraction. Tissue contraction can be caused by dehydration and collapse of tissue architecture during the course of MWA. Because MWA results in very high temperatures of greater than 150°C, MWA associated tissue contraction in *ex vivo* bovine liver along the short axis diameter has been shown to be significantly more pronounced than with RFA, 30 and 15%, respectively, primarily due to tissue dehydration [20]. In addition, the greater degree of contraction experienced with *ex vivo* bovine lung of 49–55% along the short axis diameter highlights the importance of taking into consideration the tissue architecture and composition that may be compromised with thermal ablation [20]. Tissue contraction correlated with the degree of local dehydration

caused by MWA has also been confirmed in *ex vivo* porcine kidneys to cause 26.1–42.1% underestimation of the effective coagulation volume depending on deployed energy (90 W at 5, 7.5 and 10 min) [21]. These *ex vivo* findings were more recently confirmed in *in vivo* human tumors with relative contractions around $9.95 \pm 10.4\%$ using both the Certus 140 LK15 (2.45 GHz) and Evident (915 MHz) Systems (NeuWave Medical; and Medtronic, MN, USA) [22]. However, to better understand how diseased tissue clinically is affected by applied energies from differing MWA systems, the degree of contraction should have been noted per MWA device especially because of the different operating frequencies. More studies will be needed to carefully elucidate the impact of generator operating frequency and specific microwave applicator design and settings (power and time) on the degree of tissue contraction experienced in clinical applications.

Taking tissue contraction into consideration is very important because microwave tissue ablation is a dynamic process and by not taking this phenomenon into account, the clinician may mistakenly assume that the treated volume was insufficient and risk overcompensating with additional applied MWA energy. This would result in unnecessarily destroying healthy tissue in an otherwise potentially compromised patient. The clinician should be aware of tissue contraction as it relates to the specific MWA device and settings in addition to the treating tissue properties. Qualitative differences in tissue desiccation has been reported *in vivo* with higher power settings of 100 W causing more complete desiccation and charring over 50 and 25 W at the same total applied energy of 30 kJ [30]. Additionally, ablation volumes in cirrhotic livers have been shown to be slightly larger than in noncirrhotic livers, suggesting that fibrosis and reduced water content may render certain tissues less susceptible to tissue contraction [29]. To what degree tissue contraction in combination with distinct tissue properties and perfusion all play a role in determining actual MWA volumes *in vivo* will be vital in understanding and effectively using this newer and exciting ablation technology.

Conclusion & future perspective

In summary, the ability to effectively translate *ex vivo* based MWA results *in vivo* clinically with high fidelity has not yet been fully potentiated because every MWA device is unique and clinical results will depend on the specific MWA device being utilized and the underlying tissue characteristics. *Ex vivo* data provided by manufacturers may serve as gross approximations of ablation volumes in their respective *in vivo* human organ counterparts, but the interplay of how tissue properties, perfusion and the heat sink effect, ablation volume assessment, imaging accuracy and tissue contraction all contribute to realized ablation volumes clinically is still under early investigation especially at particular wattage and time settings per MWA device. This review highlights parameters that investigators have started to elucidate with the adoption of MWA technology. By being cognizant of these factors, clinicians should be inspired to formulate additional testable hypotheses to accelerate the standardization of MWA technologies in the clinic to ultimately maximize patient outcomes in a more predictive manner.

Acknowledgements

The author would like to acknowledge S Dietz, Global Director of Oncology/Surgery at AngioDynamics, for identifying the need for a publication to address *ex vivo* and *in vivo* differences and for providing helpful feedback. The author would also like to acknowledge DM Liu, Clinical Associate Professor, Faculty of Medicine, at University of British Columbia for reviewing the paper and encouraging submission to Future Oncology for publication.

Financial & competing interests disclosure

C Kim is an employee of AngioDynamics. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Open access

This work is licensed under the Attribution-NonCommercial-NoDerivatives 4.0 Unported License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>

Executive summary

Microwave ablation is a different thermal ablation than radiofrequency ablation

- Microwave ablation (MWA) and radiofrequency ablation (RFA) achieve different energy deposition and kinetics; therefore, MWA may need to be assessed differently than previously assumed with RFA technology.

Each MWA system is uniquely different

- Because MWA technologies differ in design and energy deposition, generalizations about MWA technologies must be empirically defined per device and not misleadingly across all similarly classified technologies.

Ex vivo MWA validations versus in vivo MWA results

- Ablation dimensions vary *in vivo* versus *ex vivo* and to what extent will depend on the MWA system's specific applicator design, power and time settings, and tissue properties.

Tissue property impact on MWA volumes

- Differences in tissue properties may contribute to differences in realized ablation volumes in clinical practice from manufacturer's reference MWA volumes.

Perfusion/heat sink effect on MWA volumes

- MWA technology is generally less susceptible to the heat sink effect than RFA but the ability to overcome perfusion mediated cooling will be dependent on the MWA system's design and power output.

Imaging challenges in assessing MWA volumes

- Imaging modality and delayed imaging seem to consistently play a critical role in assessing realized ablation volumes.

Tissue contraction influence on short axis diameter assessment

- Tissue contraction can be caused by dehydration and collapse of tissue architecture during the course of MWA and the degree of contraction will be dependent on both the tissue and the MWA device protocol.

Conclusion

- Factors to consider for more accurate MWA assessments are tissue properties, perfusion/heat sink, ablation assessment, imaging accuracy and tissue contraction when assessing post-treatment MWA volumes in comparison to manufacturer's *ex vivo* ablation volumes to ensure that the anticipated ablation volumes closely approximates the actual treatment volumes for better patient outcomes.
- *Ex vivo* data may serve as gross approximations of ablation volumes in their respective *in vivo* human organ counterparts but the interplay of how tissue properties, perfusion/heat sink effect, ablation assessment, imaging accuracy and tissue contraction contribute to realized ablation volumes clinically is still under early investigation especially at particular wattage and time settings per MWA device.

References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

1. Hines-Peralta AU, Pirani N, Clegg P *et al.* Microwave ablation: results with a 2.45-GHz applicator in *ex vivo* bovine and *in vivo* porcine liver. *Radiology* 239(1), 94–102 (2006).
- **Compares *in vivo* and *ex vivo* microwave ablation (MWA) volume differences based on power and time settings.**
2. Simo KA, Tsirline VB, Sindram D *et al.* Microwave ablation using 915-MHz and 2.45-GHz systems: what are the differences? *HPB (Oxford)* 15(12), 991–996 (2013).
3. Wright AS, Sampson LA, Warner TF, Mahvi DM, Lee FT Jr. Radiofrequency versus microwave ablation in a hepatic porcine model. *Radiology* 236(1), 132–139 (2005).
4. Lubner MG, Brace CL, Hinshaw JL, Lee FT Jr. Microwave tumor ablation: mechanism of action, clinical results, and devices. *J. Vasc. Interv. Radiol.* 21(8 Suppl.), S192–S203 (2010).
- **Provides an excellent review on MWA mechanism of action.**
5. Hong K, Georgiades C. Radiofrequency ablation: mechanism of action and devices. *J. Vasc. Interv. Radiol.* 21(8 Suppl.), S179–S186 (2010).
- **Provides an excellent review on radiofrequency ablation (RFA) mechanism of action.**
6. Schramm W, Yang D, Haemmerich D. Contribution of direct heating, thermal conduction and perfusion during radiofrequency and microwave ablation. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* 1, 5013–5016 (2006).
7. Ringe KI, Lutat C, Rieder C, Schenk A, Wacker F, Raatschen HJ. Experimental evaluation of the heat sink effect in hepatic microwave ablation. *PLoS ONE* 10(7), e0134301 (2015).
8. Yu NC, Raman SS, Kim YJ, Lassman C, Chang X, Lu DS. Microwave liver ablation: influence of hepatic vein size on heat-sink effect in a porcine model. *J. Vasc. Interv. Radiol.* 19(7), 1087–1092 (2008).
- **Shows how hepatic vein size affects MWA in an *in vivo* porcine liver model.**

9. Brace CL. Radiofrequency and microwave ablation of the liver, lung, kidney, and bone: what are the differences? *Curr. Probl. Diagn. Radiol.* 38(3), 135–143 (2009).
10. O’rourke AP, Lazebnik M, Bertram JM *et al.* Dielectric properties of human normal, malignant and cirrhotic liver tissue: *in vivo* and *ex vivo* measurements from 0.5 to 20 GHz using a precision open-ended coaxial probe. *Phys. Med. Biol.* 52(15), 4707–4719 (2007).
11. Curto S, Taj-Eldin M, Fairchild D, Prakash P. Microwave ablation at 915 MHz vs 2.45 GHz: a theoretical and experimental investigation. *Med. Phys.* 42(11), 6152–6161 (2015).
12. Siriwardana PN, Singh S, Johnston EW *et al.* Effect of hepatic perfusion on microwave ablation zones in an *ex vivo* porcine liver model. *J. Vasc. Interv. Radiol.* 28(5), 732–739 (2016).
13. Goldberg SN, Hahn PF, Tanabe KK *et al.* Percutaneous radiofrequency tissue ablation: does perfusion-mediated tissue cooling limit coagulation necrosis? *J. Vasc. Interv. Radiol.* 9(1 Pt 1), 101–111 (1998).
14. Goldberg SN, Charboneau JW, Dodd GD 3rd *et al.* Image-guided tumor ablation: proposal for standardization of terms and reporting criteria. *Radiology* 228(2), 335–345 (2003).
15. Ratanaprasatporn L, Charpentier KP, Resnick M, Lu S, Dupuy D. Intra-operative microwave ablation of liver malignancies with tumour permittivity feedback control: a prospective ablate and resect study. *HPB (Oxford)* 15(12), 997–1001 (2013).
16. Ohno T, Kawano K, Sasaki A, Aramaki M, Yoshida T, Kitano S. Expansion of an ablated site and induction of apoptosis after microwave coagulation therapy in rat liver. *J. Hepatobiliary Pancreat. Surg.* 8(4), 360–366 (2001).
17. Correa-Gallego C, Karkar AM, Monette S, Ezell PC, Jarnagin WR, Kingham TP. Intraoperative ultrasound and tissue elastography measurements do not predict the size of hepatic microwave ablations. *Acad. Radiol.* 21(1), 72–78 (2014).
18. Ringe KL, Wacker F, Raatschen HJ. Is there a need for MRI within 24 hours after CT-guided percutaneous thermoablation of the liver? *Acta Radiol.* 56(1), 10–17 (2015).
19. Awad MM, Devgan L, Kamel IR, Torbensen M, Choti MA. Microwave ablation in a hepatic porcine model: correlation of CT and histopathologic findings. *HPB (Oxford)* 9(5), 357–362 (2007).
20. Brace CL, Diaz TA, Hinshaw JL, Lee FT Jr. Tissue contraction caused by radiofrequency and microwave ablation: a laboratory study in liver and lung. *J. Vasc. Interv. Radiol.* 21(8), 1280–1286 (2010).
- **Compares tissue contraction using RFA and MWA in *ex vivo* liver and lung.**
21. Sommer CM, Sommer SA, Mokry T *et al.* Quantification of tissue shrinkage and dehydration caused by microwave ablation: experimental study in kidneys for the estimation of effective coagulation volume. *J. Vasc. Interv. Radiol.* 24(8), 1241–1248 (2013).
22. Lee JK, Siripongsakun S, Bahrami S, Raman SS, Sayre J, Lu DS. Microwave ablation of liver tumors: degree of tissue contraction as compared to RF ablation. *Abdom. Radiol. (NY)* 41(4), 659–666 (2016).
- **Compares tissue contraction using RFA and MWA in liver tumors.**
23. Vogl TJ, Hagar A, Nour-Eldin NA *et al.* High-frequency versus low-frequency microwave ablation in malignant liver tumours: evaluation of local tumour control and survival. *Int. J. Hyperthermia* 32(8), 868–875 (2016).
24. Hoffmann R, Rempp H, Erhard L *et al.* Comparison of four microwave ablation devices: an experimental study in *ex vivo* bovine liver. *Radiology* 268(1), 89–97 (2013).
- **Provides an excellent comparison of MWA devices in an *ex vivo* model.**
25. Saccomandi P, Schena E, Massaroni C *et al.* Temperature monitoring during microwave ablation in *ex vivo* porcine livers. *Eur. J. Surg. Oncol.* 41(12), 1699–1705 (2015).
26. Harari CM, Magagna M, Bedoya M *et al.* Microwave ablation: comparison of simultaneous and sequential activation of multiple antennas in liver model systems. *Radiology* 278(1), 95–103 (2016).
27. Amabile C, Ahmed M, Solbiati L *et al.* Microwave ablation of primary and secondary liver tumours: *ex vivo*, *in vivo*, and clinical characterisation. *Int. J. Hyperthermia* 33(1), 34–42 (2017).
28. Winokur RS, Du JY, Pua BB *et al.* Characterization of *in vivo* ablation zones following percutaneous microwave ablation of the liver with two commercially available devices: are manufacturer published reference values useful? *J. Vasc. Interv. Radiol.* 25(12), 1939e1931–1946e1931 (2014).
29. Shyn PB, Bird JR, Koch RM *et al.* Hepatic microwave ablation zone size: correlation with total energy, net energy, and manufacturer-provided chart predictions. *J. Vasc. Interv. Radiol.* 27(9), 1389–1396 (2016).
30. Bedoya M, Del Rio AM, Chiang J, Brace CL. Microwave ablation energy delivery: influence of power pulsing on ablation results in an *ex vivo* and *in vivo* liver model. *Med. Phys.* 41(12), 123301 (2014).
31. Cavagnaro M, Amabile C, Cassarino S, Tosoratti N, Pinto R, Lopresto V. Influence of the target tissue size on the shape of *ex vivo* microwave ablation zones. *Int. J. Hyperthermia* 31(1), 48–57 (2015).
32. Yu J, Liang P, Yu XL *et al.* Local tumour progression after ultrasound-guided microwave ablation of liver malignancies: risk factors analysis of 2529 tumours. *Eur. Radiol.* 25(4), 1119–1126 (2015).
33. Dou JP, Yu J, Yang XH *et al.* Outcomes of microwave ablation for hepatocellular carcinoma adjacent to large vessels: a propensity score analysis. *Oncotarget* 8(17), 28758–28768 (2017).

34. Huang S, Yu J, Liang P *et al.* Percutaneous microwave ablation for hepatocellular carcinoma adjacent to large vessels: a long-term follow-up. *Eur. J. Radiol.* 83(3), 552–558 (2014).
35. Vogl TJ, Roman A, Nour-Eldin NA, Hohenforst-Schmidt W, Bednarova I, Kaltenbach B. A comparison between 915 MHz and 2450 MHz microwave ablation systems for the treatment of small diameter lung metastases. *Diagn. Interv. Radiol.* 24(1), 31–37 (2018).
36. Howk K, Ladtkow C, Peterson D, Cafaro A. Consistent and predictable spherical ablation shape in both liver and lung: performance of the emprint ablation system with thermosphere technology in an *in vivo* porcine model. [Poster 129]. *J. Vasc. Interv. Radiol.* 26(5), e89–e90 (2015).