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Multiple applicator approaches for radiofrequency and microwave ablation

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Abstract
Treatment of tumours greater than 2 cm by radiofrequency (RF) or microwave ablation typically use multiple sequential applications, since most currently available ablation devices are limited to use of a single applicator at a time. A major focus of current ablation research is on methodologies that allow increasing the coagulation zone to more rapidly treat large tumours. The ability to use multiple applicators simultaneously would satisfy this need. It would significantly reduce treatment time and may lead to a reduction in local tumour progression, especially in perivascular locations. Several methods have been suggested that potentially allow simultaneous use of multiple applicators, both with radiofrequency (RF) and microwave (MW) ablation. This review compares the different methods of multiple applicator use, investigating advantages and disadvantages of each modality.

Keywords: *Ablation, tumor therapy, cancer, radiofrequency ablation, microwave ablation.*

Introduction

Both radiofrequency (RF) and microwave (MW) ablation are focal heat-based methods that can be used in the treatment of primary and metastatic cancer of the liver, kidney, bone and lung [1–3]. Because RF and MW ablation can be applied percutaneously or in a minimally invasive fashion, patients tolerate the procedure well and recover much more rapidly than with conventional surgery. Of the two techniques, RF ablation is the most widely used method worldwide, while the clinical use of MW ablation has been largely limited to Asia. Currently, there are no FDA approved commercial MW ablation devices available in the USA. RF ablation creates ablation zones 3–7 cm in diameter with procedural times between 12–30 min, depending on the device and electrode type [4]. Clinically-used MW devices use shorter treatment times (typically 1–5 min) and create ablation zones of up to 2.6 cm in diameter [5–12]; a recent study using an undisclosed prototype antenna allowed creation

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of up to 6 cm diameter ablation zones within 3 min *in vivo* in porcine liver [13]. Both RF ablation and MW ablation necessitate multiple applications or multiple applicators to treat tumours greater than 2 cm, including a 1.0 cm ablative margin. For example, adequate treatment of a 3.0 cm tumour would require creation of a 5.0 cm zone of ablation assuming perfect placement. Since current clinically used RF devices can drive only a single applicator (electrode) at a time, large tumours have to be treated by multiple sequential applications [14]. In contrast, current MW devices allow simultaneous use of multiple applicators. Larger tumours can, thus, be treated either by sequential application or simultaneous application as recently advocated. This manuscript reviews recent developments that allow simultaneous use of multiple applicators for MW and RF ablation.

Clinical relevance of multiple applicator ablation

Despite the obvious advantages of minimally invasive thermal ablation techniques for the destruction of cancer, several shortcomings of RF ablation have led to a relatively high local tumour progression rate when treating hepatic metastases (2–39%) [15–19], as well as prolonged treatment times when treating large or multiple tumours. The following can summarize some of the limitations of current RF systems: (1) an inability to adequately treat even moderate sized tumors (>3.0 cm) with a single ablation, (2) inadequate treatment in perivascular areas where flowing blood cools tumours during RF ablation, and (3) an inability to treat more than one tumour at a time. Current RF technology is limited to a single RF electrode (or several electrodes which behave electrically like a single large electrode). Thus, physicians treating multiple or large tumours are forced to create multiple overlapping or consecutive zones of ablation, greatly increasing treatment time, anaesthetic risks and treatment costs [14]. Multiple applicator ablation would be able to overcome these limitations, but such RF systems are not yet clinically available, whereas MW systems are available only in the Asian market.

Multiple electrode radiofrequency (RF) ablation

Three distinct methods have been investigated by different groups that allow the simultaneous employment of multiple electrodes during RF ablation (Table I). While in the hyperthermia literature different frequencies in the kHz–MHz range have been used,

Table I. Current status of investigation of different multi-array methodologies.

	Current status of investigation
Bipolar RF	Pre-clinical studies of bipolar RF between needles and multi-tine electrodes [20–24]
Simultaneous RF	Currently used clinically in multi-tine electrodes and cluster electrodes [4,30]
Rapidly switched RF	Pre-clinical studies with multi-tine and cluster electrodes [31–33]
Coherent MW	Clinically used outside US (mainly Asia) [5,6,8–12], pre-clinical studies in US [40]
Incoherent MW	Not yet investigated for MW ablation (studies are available in hyperthermia literature)
Phase modulated MW	Not yet investigated for MW ablation (studies are available in hyperthermia literature [44–48])

all recent studies on RF ablation (including the ones cited in this paper) use RF in the range of 460–480 kHz.

Bipolar power application

Several groups have investigated bipolar RF ablation [20–25], where RF current is passed between two electrodes instead of between a single electrode and a grounding pad. Thereby, two electrodes heat the tissue instead of one, resulting in larger ablation zones. McGahan et al. [20] placed two 18-gauge needle electrode *ex vivo* at distances between 0.5–5 cm. They produced elliptical ablation zones up to 4 cm long and 1.4 cm wide, compared to cylindrical ablation zones of ~1.5 cm diameter created with a single electrode. Burdio et al. [22] placed two 15-gauge needle electrodes 10 cm apart *ex vivo*. During the treatment, they infused hypertonic saline (14.6% NaCl) through each electrode and compared bipolar ablation to the conventional monopolar method. Ablation volumes were $144.8 \pm 59.8\,cm^3$ for the bipolar method and $62.1 \pm 36.4\,cm^3$ for the monopolar method. Later, Burdio et al. performed *in vivo* experiments where they inserted two 15-gauge needle electrodes from opposing sides, ~10 cm separated. They infused physiological saline through both needles and performed bipolar ablation with and without vascular inflow occlusion (Pringle Maneouvre). Ablation volumes were $123.2 \pm 49.6\,cm^3$ with inflow occlusion and $52.4 \pm 23.6\,cm^3$ without occlusion. Haemmerich et al. [23] performed bipolar RF ablation *in vivo* with two 4-prong electrodes, lined up in parallel and separated by 2.5 cm. Ablation volumes were $12.2 \pm 3\,cm^3$ for bipolar ablation, compared to $3.9 \pm 1.8\,cm^3$ using conventional monopolar ablation.

Bipolar ablation can create ablation zones ~2–3 times larger than conventional monopolar ablation, and bipolar ablation does not require a grounding pad, eliminating the risk of ground pad burns [26]. Recently, the use of multi-prong electrodes for bipolar ablation has been suggested, since with these electrodes electrical current is concentrated between the two electrodes, resulting in preferential heating in that area [25]. It has been shown in computer models that bipolar ablation between separated multi-prong electrodes may be able to create ablation zones immediately adjacent to large vessels [25]. Thereby, bipolar ablation may help overcome the heat sink effect mediated by large vessels [27], potentially leading to reduced local tumour progression when tumours are located close to vessels. In a study examining recurrence after RF ablation, the majority of local tumour progressions were located next to large vessels [28].

In two studies on bipolar ablation, uneven heating around the two electrodes was observed. McGahan et al. [20] noted that, when they used temperature control above 95°C, the temperature of one electrode was typically 20°C lower than the other electrode. Haemmerich et al. [23] also observed non-uniform heating, resulting in a reduced size of the ablation zone around one electrode. One possible explanation that has been suggested is that, during bipolar RF ablation, energy deposition cannot be controlled independently for the two electrodes because all applied current to one electrode must flow to the other electrode [23]. This is a major limitation of bipolar ablation if one electrode is preferentially cooled by a major vessel and would require more power. An increase in applied RF power is not possible since it would result in charring around the second electrode that already is at optimal temperature. The electrical current pathways, and resulting energy deposition patterns for bipolar ablation are dependent on electrode geometry and the spatial relationship between the electrodes. When multi-prong electrodes are used for bipolar ablation, heating patterns will be less than ideal if the electrodes are not arranged symmetrically [25]. These limitations may also help explain the high variability in ablation zone dimensions often seen with bipolar RF ablation.

Simultaneous power application

The earliest study examining multiple electrode RF ablation with more than two electrodes was performed by Goldberg et al. [29] In this study, the authors used 18-gauge needle electrodes without cooling and a 150 W RF generator. In different *ex vivo* experiments performed in fresh calf liver, two-to-four electrodes were placed in linear, triangular and square arrays with equidistant inter-electrode spacing of 1, 1.5 and 2 cm. RF power was supplied to all electrodes simultaneously (i.e. same voltage is applied to the electrodes), so that the electrode temperature, as measured by thermocouples inside the electrodes, was maintained between 70–90°C for all electrodes. Each ablation lasted for 6 min from the time that all electrode temperatures exceeded 70°C. With four-electrode arrays, they were able to create ablation zones of 40 cm^3 volume, whereas a single electrode only produced ablation zones of 3.2 cm^3 volume. One adverse effect of simultaneous power application that was observed in this study is electrical interactions between multiple RF electrodes. In a linear array of four electrodes, the inner two electrodes only reached mean temperatures of 57°C, while the outer electrodes reached mean temperatures of 85°C. The inner electrodes were electrically shielded by the outer electrodes. Unfortunately, with simultaneous power application, applied power to the electrodes cannot be controlled independently to bring all electrodes to target temperature, similar to the bipolar method. The electric shielding effects are dependent on electrode distance and spatial layout of the electrode array. Later, Goldberg et al. [30] studied a triangular cluster of three cooled needle electrodes, spaced 5 mm apart. This cluster produced ablation zones *in vivo* in porcine liver of 3.1 ± 0.3 cm diameter, whereas a single cooled electrode produced ablation zones of 1.8 ± 0.1 cm diameter. Later, the cooled cluster electrode (= cluster of three needle electrodes, spaced 5 mm apart) was commercialized (Radionics, Burlington, MA) and is currently the only commercially available multiple-electrode device for clinical RF ablation. Several studies have shown that, if electrodes are closely spaced in an attempt to treat large tumours, reduced heating in-between the electrodes results from electrical interactions; this has been shown for cooled needle electrodes [31], as well as multi-tine electrodes [32]. Further results will be presented below for cooled cluster electrodes.

Two clinically available ablation electrodes are so-called multi-tine electrodes. A shaft contains up to 12 times made of memory alloy, which expand into umbrella- (LeVeen electrode, Boston Scientific, Natick, MA) or star-like shapes (Rita Starburst, Rita Medical, Mountain View, CA) after insertion of the catheter. These electrodes could also be viewed as multi-electrode arrays, even though they expand from a single shaft. RF current is applied to all tines simultaneously, which create a larger ablation zone than a single antenna. For some multi-tine electrodes (Rita Starburst Xli, Rita Medical, Mountain View, CA), stepwise expansion is suggested (i.e. partial expansion, ablation, partial expansion, ablation, . . .) to shut down blood flow and avoid untreated areas in-between tines when creating large ablation zones.

Rapidly switched power application

As the initial study on multi-electrode arrays showed [29], simultaneous RF power application to multiple electrodes is not able to bring all electrodes to target temperature when temperature control is used. Any increase or decrease of RF power affects all electrodes. The amount of power that can be applied to a certain electrode is limited by charring, which occurs when temperatures in excess of 100°C are obtained. For *in vivo* application, this means that electrodes exposed to vascular mediated cooling will perform

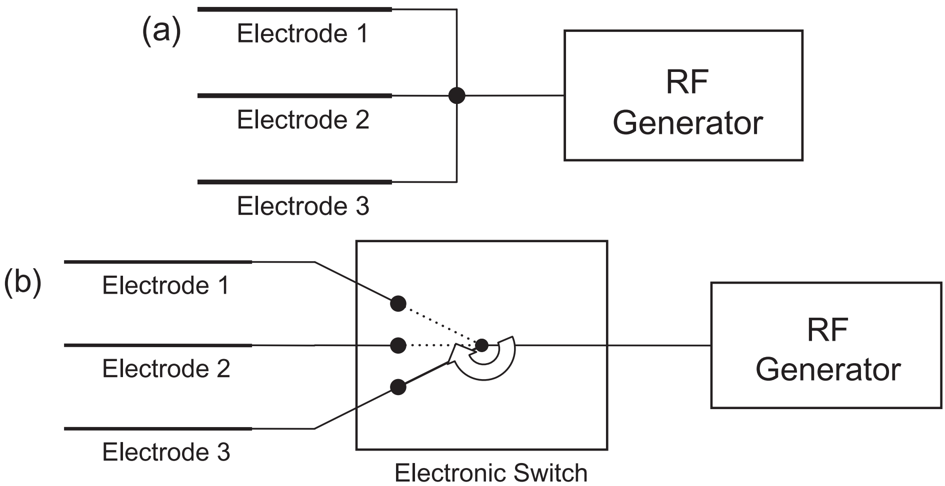

Figure 1. (*a*) Set-up for *simultaneous* power application method. The RF power routed to all three electrodes by a splitter cable. Any changes in applied power are effective for all electrodes. (*b*) Set-up for *rapidly switched* power application method. An electronic switch routes the power to each electrode for a brief time period. The switch is controlled by an algorithm that adjusts the time period for each electrode depending either on electrode temperature or electrode impedance. Thereby, average applied power can be controlled for each electrode individually.

sub-optimally, since an increase in power would lead to charring of other electrodes which are already at target temperature.

One way to overcome the limitation of simultaneously powering all electrodes is the rapidly switched application of RF power. In this method, power is applied to only a single electrode at a time. Power is switched between multiple electrodes at short intervals (see Figure 1(*a*)). The rapidly switched method takes advantage of the fact that tissue heating is a relatively slow process (i.e. tissue temperature does not change significantly within 1 s due to low thermal conductivity of tissue). If RF power is switched between the electrodes faster than the time required for tissue heating and cooling, all electrodes effectively heat tissue simultaneously. The total RF energy is divided between multiple electrodes depending on the time interval for which each electrode is activated (see Figure 1(*b*)). By adjusting the time interval, the RF energy applied to each electrode can be individually adjusted. This allows for controlling each electrode individually by using temperature control or impedance control.

Based on the rapidly switched method, a prototype device that allows RF ablation with two electrically independent electrodes was developed [33]. A commercial 150 W RF generator was used with nine-prong electrodes (Model-90, RITA Medical Systems, Mountain View, CA). Each electrode has five thermocouples placed at the prong tips, which report the tip temperatures to the RF generator. The RF power was switched between the two electrodes at 0.5 s intervals by an electromechanical switch, which was in turn controlled by software running on a PC. The software controlled the time interval for which each electrode was activated. If the electrode temperature at the two electrodes was different, the time interval of the cooler electrode was increased so that both electrodes were kept at equal temperature. *In vivo* experiments were performed in a porcine model, where two nine-prong electrodes were placed >10 cm apart in the liver. Ablation was performed for 10 min with temperature-controlled power application and 100°C target temperature at the electrode tips. It was shown that, in the heterogeneous environment of *in vivo* liver, both electrodes could be kept at target temperature, resulting in two ablation zones (volume $13.6 \pm 9.3\,cm^3$) in the same time as a single ablation zone ($13.7 \pm 7.0\,cm^3$, $p > 0.05$) could be created using conventional ablation with a single electrode using the same RF generator.

Another major advantage of the rapidly switched method is the avoidance of electrical interactions between multiple electrodes. To examine this potential advantage of rapid switching between electrodes, computer models were used to evaluate the rapidly switched method and compare it to the method of applying power simultaneously to the electrodes [32]. Two closely spaced four-prong RF electrodes were examined and it was shown that electrical shielding results in reduced tissue temperatures in-between the electrodes. Higher tissue temperatures could be obtained with the rapidly switched method, which avoids electrical interactions by activating only a single electrode at a time. Since the magnitude of the effect caused by electrical shielding depends on electrode number, distance and arrangement [29], shapes of ablation zones become unpredictable when multiple electrodes are placed arbitrarily. The effect of electrode interactions is demonstrated in Figure 2, where the current density is shown for a triangular array of three cool-tip cluster electrodes, powered by a 200 W generator (Radionics, Burlington, MA). Electrical current travels from regions of high electrical voltage to regions of low voltage. When power is applied simultaneously to all electrodes, all electrodes are at the same electrical voltage and little electrical current is deposited in-between the electrodes. This results in minimal heating between electrodes. Thus, the distance at which electrodes can be separated and still cause enough heating between them to produce coagulation is limited.

Electrical shielding was demonstrated in *ex vivo* experiments with a multiple-electrode prototype that allowed simultaneous use of three impedance-controlled cooled cluster electrodes. The cluster electrodes (each electrode represents a cluster of three electrodes) were arranged in a triangular array with 4 cm spacing and tissue temperature was measured at the centre of the array. RF power was switched between the electrodes at 0.5 s intervals and each electrode was impedance-controlled individually. If the impedance of a single electrode exceeded 120% of baseline level, power was shut down for this electrode for 15 s. RF power was applied either simultaneously to all electrodes ($n = 8$) or using the rapidly

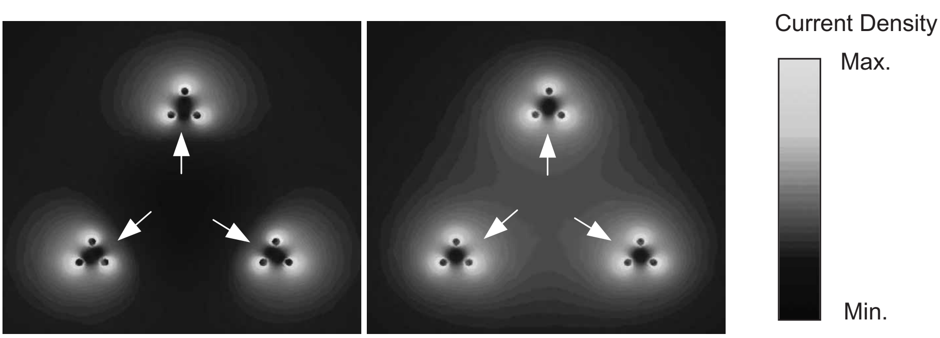

Figure 2. Three cooled cluster electrodes (Radionics, Burlington, MA) are arranged in a triangular array. The electrical current density profile is shown for simultaneous (left) and rapidly switched (right) power application. For rapidly switched power application, the average current density is shown (each electrode is energized for a brief time period). Electrical shielding results in little current deposition towards the centre for simultaneous power application (left, arrows). Rapidly switched power application (right, arrows) provides uniform heating around each cluster electrode. Since applied power and resulting current density changes during the ablation, no absolute values are shown for current densities.

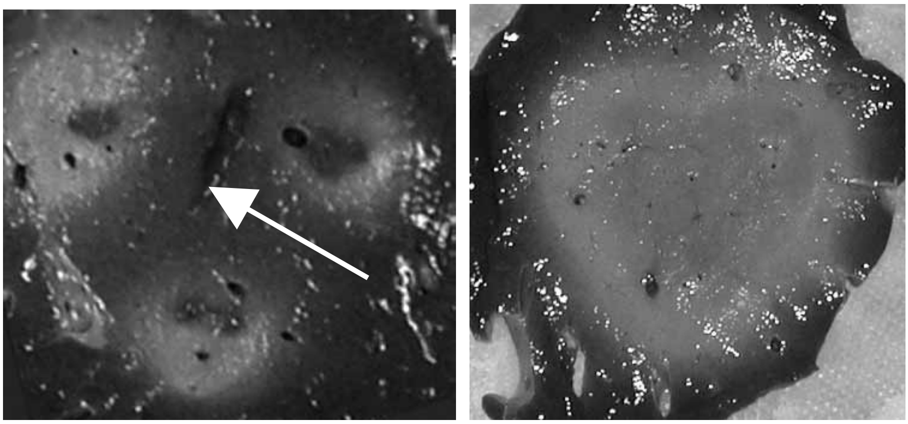

Figure 3. Three cooled cluster electrodes (Radionics) are arranged in a triangular array. This image shows cross-sections of representative ablation zones for simultaneous (left) and rapidly switched (right) power application. The light gray areas represent coagulated tissue, dark areas show untreated tissue. No coagulation is seen for simultaneous power application at the centre of the electrode array (left, arrow) due to electrical shielding between the electrodes.

switched method ($n = 8$). For all experiments, maximum power was applied using a 200 W RF generator for 12 min. Tissue temperature at the array centre was $41 \pm 3°C$ with simultaneous power application and $97 \pm 8°C$ using the rapidly switched method ($p<0.001$). Short axis ablation diameters were 3.4 ± 0.7 cm with simultaneous power application and 4.8 ± 0.5 cm with the rapidly switched method ($p<0.01$); the short axis is in this case parallel to the RF electrode or orthogonal to the slices shown in Figure 3. Ablation volume was $22.3 \pm 6.4\,cm^3$ with simultaneous power application and $116.4 \pm 15.2\,cm^3$ with rapidly switched power application ($p<0.001$, unpublished results). The vast differences between the two methods are a result of the electrical interactions between electrodes described above, and it should be noted that same power was applied for both methods. Representative ablations are shown in Figure 3. When power is applied simultaneously, tissue heating occurs mainly radially outwards from the electrode array, with little heating towards the centre of the array. The result is three small, discontinuous ablation zones. The general conclusion from these and a previous study [32] is that multiple closely spaced multi-tine and cluster-electrodes provide little heating in-between electrodes and should be driven using rapid switching between electrodes.

Radiofrequency electrodes in hyperthermia

In hyperthermia therapy, which uses elevated temperatures typically in the range of 43–45°C to treat cancer mostly as adjuvant therapy, several different RF electrode arrays have been investigated. RF frequencies in the range of 0.5–1 MHz have typically been used. Manning et al. [34] examined two arrays of needle electrodes arranged in two planes, with RF current applied bipolar between the arrays. A system developed at Stanford University employs needle electrodes arranged in one of a number of possible configurations, with up to 32 electrodes [35,36]. RF current is applied bipolar between two electrodes of the array and rapidly switched between different electrode pairs, so that all electrodes reach a desired temperature. Temperature is monitored by thermocouples located inside the electrodes. Other groups investigated different array configurations [37,38] and segmented needle electrodes have been suggested to allow for better control of tissue heating [39]. Currently commercially available RF systems for interstitial hyperthermia use up to 32 electrodes (Intertherm 100, Labthermics Technologies, Champaign, IL).

Conclusions

In terms of the design of multiple electrode systems, the simultaneous application of power to multiple RF electrodes (the current approach to multi-needle and multi-tine electrodes) is fundamentally limited by electrical interactions that limit heating between electrodes. Thus, increasing the distance between electrodes to increase the zone of thermal ablation is likely to result in insufficient central ablation. The rapid switching method presented above is one method for overcoming some of the limitations of current RF systems. For simultaneous use of multiple RF electrodes with any of the described methods, higher power will likely be required than current RF generators can deliver above a certain number of electrodes. This may increase the risk of ground pad burns and may require new ground pad designs to avoid heating of ground pads. Bipolar application does not require ground pads, but performance is dependent on spatial relationship between the electrodes. If a defined distance and orientation can be ensured, a clinical application in the near future is feasible.

The decision whether a single multi-tined electrode with a large ablation zone or multiple electrodes requiring multiple insertions are preferred is dependent on the specific case. For irregular shaped tumours, tumours close to large vessels or tumours near vulnerable structures multiple electrodes are a better choice, since they allow more accurate control of shape and size of the ablation zone. For roughly spherical tumours, a single electrode creating a large ablation zone is the better choice.

Multiple antenna microwave (MW) ablation

Whereas RF ablation heats the tissue by electrical resistive heating, MW ablation works on a different principle. An antenna emits microwave radiation into the tissue, which results in excitation and oscillation of polar molecules (especially water). Even though the method of heating is different, the resulting coagulation and pathology of the ablation zone is comparable to RF ablation. Table II shows a comparison of RF and MW ablation. Microwave ablation has some potential advantages over RF ablation. The propagation of

Table II. Comparison between RF and MW ablation.

	RF	Microwave
Frequencies used	460–480 kHz	915 MHz, 2.45 GHz
Heating mechanism	Resistive heating by RF current	Heating by propagating electromagnetic wave
Power control methods	Temperature, impedance feedback	No feedback currently used (constant power)
Cooled applicators	Available	Not available yet, but possible (and used e.g. for prostate devices)
Independent applicator control	Limited (time interleaving)	Amplitude, phase
Advantages	Simple applicator and generator design	SAR drops off less rapidly than RF, higher temperatures possible, no ground pads required
Availability	Worldwide commercially available	Limited (Asia)

microwaves is not limited by charring and tissue boiling around the applicator and, therefore, higher temperatures can be obtained, up to 150°C in one study [40]. MW ablation does not require a grounding pad and ablation times are shorter (typically on the order of 1–5 min) [8,10–12]. Furthermore the SAR (specific absorption rate ($W\,kg^{-1}$)) of microwave possibly extends deeper into the tissue compared to RF energy, which may allow for more uniform tumour kill next to large vessels [41]. Furthermore, contrary to RF ablation, dessicated tissue next to the applicator does not limit microwave propagation. Nevertheless, despite these potential advantages, the development of RF ablation devices has led to the ability to create ablation zones up to 7 cm in diameter. This is likely a result of the greater attention given to RF ablation compared to MW ablation than an inherent limitation. Current clinically used microwave devices create ellipsoid ablation zones of ~2.5 cm in diameter and 3.0 cm in length [12].

Similar to current clinical practice in RF ablation, multiple sequential insertions are typically used to treat large tumours by microwave ablation [6,8,9,11]. Due to the limited size of the ablation zone, this practice can require a large number of applications; in one study a mean of 46 antenna insertions were required for treatment of hepatocellular carcinoma [5]. Three different methods have been described in the literature that allow simultaneous use of multiple MW antennas (Table I).

Coherent driven antenna arrays

In coherent driven antenna arrays, the power of one microwave generator is distributed among all antennae in an array (similar to Figure 1(*a*), where electrodes are replaced with antennae and the RF generator is replaced with a MW generator). The current is applied to all antennae in phase; the SAR at the array centre is N [2] times that of a single antenna. This is a major advantage of MW antenna arrays compared to RF electrode arrays where the SAR at the centre is only improved by a factor of N. Coherently driven systems are the only ones investigated for MW ablation so far.

Several recent studies advocate the simultaneous use of multiple MW antennae [12,40,42,43]. Saito et al. [42] examined an array of two microwave antennae at different distances from 5–30 mm, with 50 W applied for 90 s *ex vivo*. They found they could create a circular ablation zone of 30 mm diameter with two antennae spaced 10 mm apart, whereas a single antenna created ablation zones of 18.5 mm diameter. Liang et al. [43] also investigated an array of two antennae where they applied 60 W for 5 min *in vivo*. They found an increase in ablation size from $26 \times 26 \times 34$ mm with a single antenna to $34 \times 26 \times 46$ mm with two antennaes. Wright et al. [40] performed *in vivo* experiments with a single microwave antenna and a triangular three-antenna array with 5–30 mm antenna separation. They ablated for 10 min at 40 W power using dipole antennae at 915 MHz (Vivant Medical, Moutain View, CA). Ablation volumes were $7.4 \pm 3.9\,cm^3$ for single antenna and $43.1 \pm 4.3\,cm^3$ for multi-antenna ablations. Ablation diameters were 2.1 ± 0.3 cm and 4.8 ± 0.3 cm and short axis diameters were 4.4 ± 0.4 cm and 4.3 ± 0.4 cm for single- and multi-antenna ablations, respectively. Discontinuity in ablation zones appeared at 16 mm antenna separation for sequential multi-antenna ablations and at 30 mm antenna separation for simultaneous multi-antenna ablations. The ablation volume was six times as large with multi-antenna ablations, compared to single antenna ablation. The fraction of reflected power typically increased during the ablation procedure, sometimes resulting in significant heating of the feeding cable. The average of maximum reflected power during each ablation procedure was 16% (6.4 W) of applied power. Another important finding of this study was

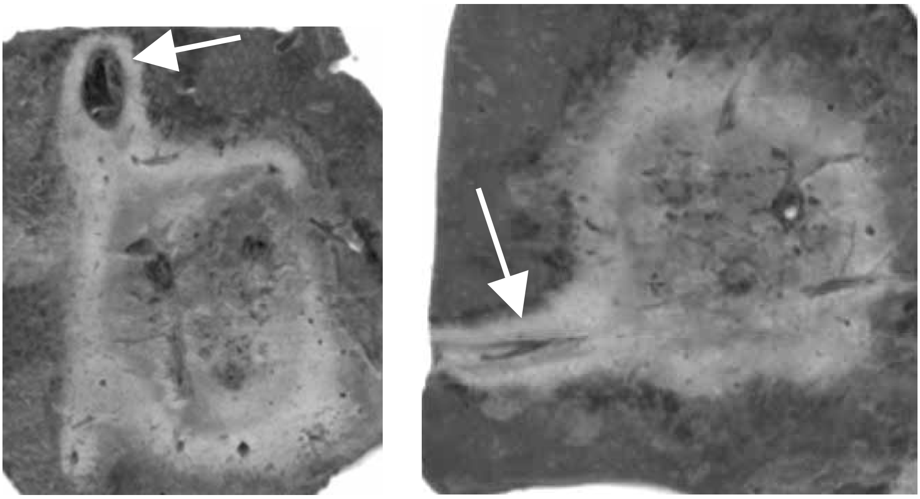

Figure 4. Images of ablation zones created *in vivo* in liver with three MW dipole antennae (915 MHz) simultaneously. An extension of the ablation zone around large vessels is observed (arrows). This perivascular ablation zone formation may lead to reduction in local tumour progression for tumours located close to large vessels.

the presence of selective tracking of ablation zones along blood vessels (see Figure 4). This effect was seen in several of the simultaneous multi-antenna ablations and was seen for vessels up to 5 mm diameter. From pathology performed after ablation, it appeared that blood inside the vessels was also coagulated. The exact mechanisms behind this effect are not yet completely understood. Deardorff et al. [44] observed this effect during single antenna ablations and suggested that the presence of a vessel causes a distortion or extension of the energy radiation pattern. Wright et al. [40] speculated that the high temperatures reached during microwave ablation result in formation of water vapour, which then travels along the blood vessels following the path of least resistance. The tracking of ablation zones along vessels may help reduce local tumour progression caused by the heat sink effect next to large vessels [27]. However, the superior performance next to vessels inherent in multiple antenna MW ablation and potentially with multiple electrode RF may also increase the risk of complications associated with thrombosis of major vessels. This issue will need to be examined in more detail prior to the widespread application of multiple applicator RF or microwave systems.

Incoherent driven antenna arrays

Incoherently driven systems can be constructed in one of two ways: either a single microwave generator output is rapidly switched between multiple antennae (similar to Figure 1(*b*), where electrodes are replaced with antennae and the RF generator is replaced with a MW generator) or each antenna is supplied by a separate microwave generator (each with a slightly different frequency). The SAR at the centre of the antenna array is in this case N times the SAR of a single antenna. This is an obvious disadvantage compared to coherently driven antenna arrays, since the goal is to heat the region in-between the antennae [45] and as a result incoherently driven systems have received little attention so far.

Phase modulated antenna arrays

To the authors' knowledge, phase modulated arrays have not been investigated in the ablation literature. A large amount of research on phase modulated MW antenna arrays, however, can be found in the hyperthermia literature [44–48]. Even though much lower temperatures (and power levels) are applied during MW hyperthermia, general principles and data on SAR patterns of antenna arrays are directly applicable to MW ablation. The higher power levels required in MW ablation compared to hyperthermia make it necessary to closely match tissue impedance and antenna impedance (i.e. length) to avoid excessive heating of the feeding cable [40]. Since hyperthermia relies much less on thermal conduction than ablative therapies, uniform power deposition is much more essential for hyperthermia.

Trembly [46] performed theoretical calculations of SAR patterns of an array of four dipole antennae arranged on a 3 cm square. He investigated different frequencies (300–915 MHz) and antenna lengths (3–6 cm) while applying the current to all antennas in phase. He found that antenna lengths significantly different from the resonance length ($\lambda/2$) deposit little power at the array centre. While low frequencies produced the most uniform power deposition, the long resonance length ($\lambda/2 = 18.8$ cm) make them unfeasible.

Wong et al. [45] investigated an array of four dipole antennae arranged on a 2 cm square, while applying 915 MHz current in phase. They determined SAR patterns theoretically and confirmed experimentally in phantoms. Since the distance between the antennae is less than half the wavelength ($\lambda/2$) the microwaves add in phase in-between the antennae and a much more homogenous SAR pattern results compared to the SAR of a single antenna.

In an effort to further improve uniformity of power deposition, different phase modulation patterns have been investigated. Phase modulation results in local minima and maxima of the SAR due to shift in locations of constructive and destructive interference of the waves. To create a uniform SAR pattern, the phase shift configuration is then cycled, similar to rapidly switched power application described in RF ablation. Trembly et al. [49] examined the four-antenna array described above where he applied current to two of the antennae shifted by 90° and showed more uniform power deposition. Subsequently, in an effort to create larger uniform temperature distributions, different phase modulation strategies have been investigated for four-antenna and hexagonal six-antenna arrays [47–49]. Currently commercially available microwave hyperthermia systems drive up to 24 antennae simultaneously (BSD 500, BSD Medical Corp., Salt Lake City, Utah).

Even though uniform power deposition patterns are not as important for ablative therapies as for hyperthermia, the methods described above may help develop more effective MW ablation devices which allow rapid treatment of large tumours and reduced susceptibility to vascular mediated cooling.

Conclusion

Certainly there is a need for increased research efforts on MW ablation devices, as so far most literature focuses on RF ablation. Many methods like phase modulated arrays and different antenna lengths and spacings have been studied extensively for hyperthermia applications, but have not yet been investigated for MW ablation. MW ablation devices still use comparably simple control algorithms (i.e. constant power) without any sort of feedback to adjust power according to requirements, compared to temperature or impedance feedback used in RF devices. Since dielectric tissue properties change significantly with temperature, tunable antennae may enable reduced reflection (and resultant heating of the feeding cable), especially at higher power settings. With larger ablation zones in RF devices and rising power requirements, avoiding grounding burns becomes a significant problem. This is not an issue for MW ablation devices. The main advantage of MW antenna arrays over RF electrode arrays is the possibility of using constructive interference in-between antennae to obtain more uniform SAR than possible with RF electrodes. This may enable treatment by placing antennae around the tumour without puncturing it, which may in turn reduce tumour seeding.

Future outlook

A major focus of current ablation research is on developing technologies to increase induced coagulation volume. The use of multiple applicators is one way to reach this target, which may help decrease the number of local tumour progressions that result when treating a large tumour with overlapping sequential ablations. In addition, multiple tumours could be treated simultaneously with multiple applicator devices and treatment time, anaesthetic complications and costs could potentially be decreased.

Currently, RF ablation devices are more technically advanced than MW ablation devices, likely because they received more attention. MW ablation devices, while not yet commercially available in the US, have the potential to become the superior treatment modality if they receive more attention from the research community. Microwaves provide deeper tissue heating compared to RF and multiple antenna arrays provide the advantage of constructive interference in-between antennae. This may eventually enable more rapid creation of large ablation zones and more effective treatment of tumours located close to vessels.

For both bipolar and rapidly switched RF ablation, several studies show the potential of these methods and it is conceivable that one will see either one in some of the commercial next generation RF devices. For multiple antenna MW ablation, comparably little literature is available, which concentrates on the use of coherently driven antennae. More information is available in the hyperthermia literature where other possible methods of driving antenna arrays have been investigated. Some of these methods may be applicable to MW ablation and could lead to improved MW ablation devices which will enable faster treatment of large tumours.

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Publisher's Apology

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Haemmerich and Lee

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