

MICROWAVE POWER AMPLIFIERS, RESONANT STRUCTURES AND THE RAPID DIAGNOSIS OF C-DIFFICILE AND OTHER ANTIBIOTIC RESISTANT BACTERIA

J Lees¹, H Choi¹, T L Joshi², A Porch¹

¹ School of Engineering, Cardiff University, UK, CF143AA

² School of Pharmacy, Cardiff University, UK, CF103NB

The spread of antibiotic resistance is a growing threat to our ability to treat infectious disease, due largely to the “blind” prescribing of antibiotics, and is in part a consequence of our inability to determine the antibiotic susceptibility of the infecting bacteria in real time. Current bacterial detection methods take typically several hours and sometimes days to process, and as a result, these tend to be used to confirm rather than to prevent infection. This paper describes the role of high-efficiency microwave amplifiers and microwave resonant cavities in enabling a prototype bacterial DNA detection system that is able to identify specific pathogens within minutes; a change that promises to reduce patient suffering and morbidity, and help extend the utility of the remaining effective antibiotics.

INTRODUCTION

Single-mode microwave resonant cavities driven by high-efficiency microwave power amplifiers are enabling many applications within research, industry, and healthcare related fields. Examples of these include polymer curing for the production of microcapsules for drug delivery, curing large-scale components for the aerospace industry, as well as the assisted curing of new types of environmentally friendly concrete. Developing research areas also include tumour ablation, disruption of bacterial biofilms, water sterilisation, additive manufacture monitoring, hydrogen storage and release, heavy-oil cracking and others. Most of these research are commercially interesting and all currently use resonant cavity structures capable of allowing almost all (typically >99 %) of the generated microwave power to be delivered into a sample or device. Each of these cavities typically needs to be driven by a high-efficiency microwave amplifier developing power between 1 W and 300 W, and due to the load-dependent resonant properties, these microwave power generators need to be frequency agile and able to operate over wide bandwidths.

Previous work in the area of microwave-assisted bacterial diagnostics has been limited to using conventional microwave ovens and metallic bow-tie structures deposited on glass to focus and intensify electric (E) field within a small sample. Due to the nature of magnetrons and multi-mode cavities, this approach proved unreliable, inefficient, physically large, imprecise and difficult to control, as well as requiring mains level voltage to operate.

In the microwave enhanced diagnostic application targeted in this work, high microwave field is generated within a circular cavity resonator and is used to disrupt, not only bacterial vegetative cell but also bacterial spore, such that bacterial DNA can be easily detected using patented, rapid, high-sensitivity and high-selectivity biochemical assays. For this portable and potentially field deployable apparatus; compactness, high power-efficiency, frequency agility, ease of integration and measurement accuracy are all critical aspects of the design.

Solid-state microwave generation for diagnostic and sensing systems have, over the years, attracted the attention of medical and engineering professionals alike. For example, beam focused annular arrays of microstrip patch antennas studied in [1]-[3] are currently in use for non-invasive treatment of tumours in the head, neck and pelvic region of human body. More recently, and associated with this work, rapid detection (≤ 4 min) of *C-difficile*, anthrax and tuberculosis using advanced DNA-detecting biochemical techniques have been patented in [4]. Similarly, in [5][6], a fully integrated solid-state microwave heating system is demonstrated in which a cavity resonator is directly presented to the LDMOS power transistor.

Achieving high power delivery and good power-efficiency when driving a resonant cavity is problematic because of the sensitivity of the resonant mode to any perturbations of the load. In other words, it is difficult to control the fundamental and harmonic load impedance environment presented by the cavity as it changes significantly when the volume, temperature and consistency of the sample is varied, as would likely be the case in a practical healthcare setting. This is compounded by the fact that in the optimized, adaptive system envisaged, the frequency of the excitation would need to be precisely adjusted to accommodate shifts in resonant frequency. In this work however, it is shown that the efficiency of a microwave heating system can be increased by designing a broadband matching network that can accommodate changes in the impedance environment of the cavity resonator due to such variations, through the adoption of continuous mode PA matching techniques [7].

Continuous mode amplifier design is a relatively new concept, and the 'normal' application is transmitter design for wireless communication systems. The approach is attractive in that it is able to tolerate and even exploit the varying impedances presented by a fixed matching network, and deliver consistently high power and efficiency over wide or very wide operational bandwidths. This bio-medical application is different in that the load is not a matched load or antenna, but is a single-mode resonant cavity containing a biological sample, with significant fundamental and harmonic impedance change caused by variations in key sample parameters including volume, consistency and temperature. The impedance variation at the fundamental frequency for example manifests itself as a shift in the cavity's resonant frequency, which can change significantly with variation in these parameters. It is important to stress that to ensure high efficiency in terms of delivering generated RF power into the cavity, the frequency of excitation needs to change in response to the resonant frequency of the cavity, minimizing the reflection coefficient.

This technique significantly reduces the complexity and physical size of matching networks typically required for broadband amplifiers. For example, conventional broadband class-F⁻¹ power amplifiers typically use complicated and physically large output matching networks

together with the built-in transistor package network to match fundamental impedance to 50 Ω and harmonic impedances to open or short circuits.

In this work, a broadband class-F⁻¹ matching network, consisting of a transistor package network together with series microstrip lines has been designed to accommodate the temperature or volume dependent changes in the impedance environment of the circular cavity. The integrated matching network ensures the reflection coefficient of the cavity at the intrinsic plane of the RF transistor and allows continuous mode operation to be achieved. Unlike conventional 50 Ω continuous class-F⁻¹ PA design approaches [7][8], this method relies on a direct integration approach and eliminates the need for the additional, and physically large harmonic tuning networks connecting the PA to the resonator, together with their associated loss. Further integration has been considered by introducing a directional coupler into the output stage of the PA in order to monitor the delivered and reflected power, to enable some degree of performance analysis as well as to ultimately provide a means of adaptive control.

Highly Efficient Integrated Microwave Power Delivery System Design

A. A Prototype Microwave Power Delivery System

A schematic of the prototype microwave delivery system is shown in Figure 1. The microwave generator (1, Telemakus TEG27006) provides a single-tone output at a power level of 1 dBm. The switch (2, Telemakus TES6000-30) directs the signal either to the input of the microwave power amplifier (MPA, 3, Mini-circuits ZHL-30W-262) for cavity excitation, or into a 50 Ohm matched load for cavity excitation.

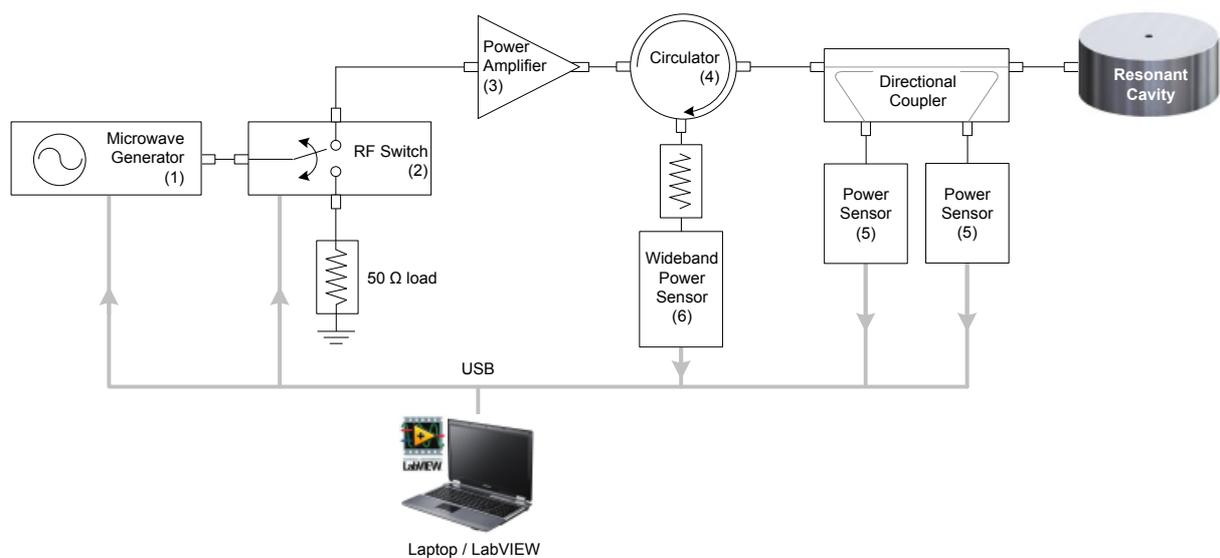


Fig 1. Schematic of the microwave delivery system

The MPA provides a maximum output power of 46 dBm and a gain of approximately 50 dB. Transmitted and reflected powers are measured using the combination of the directional coupler (4, Mini-circuits ZABDC20-322H) and the precision power sensors (5, Telemakus TED6000-50). A broadband power sensor (Rhode & Schwarz NRP-Z81) is included for detailed measurement of the power profile of the reflected pulses. The instruments are controlled using National Instruments LabVIEW software, which also records all power readings.

The bacterial spores were suspended in suitable buffer solution within small plastic (300 μ l) Eppendorf tubes, in the centre of the circular resonant cavity where the *E*-field was maximum. Figure 2 shows a COMSOL Multiphysics simulation of the normalised *E*-field distribution within the cavity when excited at resonance, both empty and when loaded with the sample.

Photographs of spores of strain DS1813 were imaged under SEM before and after microwaving at a range of duty cycles (DC) between 100%- 0.3% for 5 seconds. A total of 40 spores were imaged for each DC at x82000 magnification. Figure 3(a) - a spore of DS1813 which has not been exposed to microwave treatment (control), Figure 3(b) DS1813 exposed to constant microwaves at 100% DC. Damage to the spore structure and debris is clearly visible and Figure 3(c) DS1813 exposed to pulsed microwaves at 10% DC. Some damage to the spore structure is visible at its terminal end. Figure 3(d) shows DS1813 exposed to pulsed microwaves at 1% DC, where there is no visible damage to spore structure (image scale bar = 200 nm).

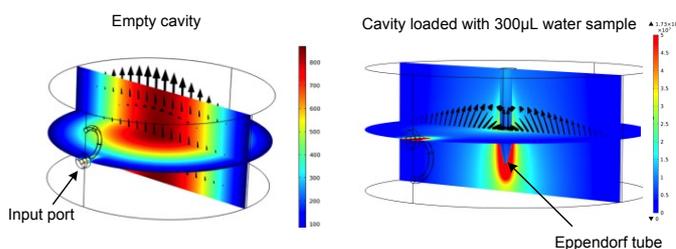


Fig 2. E-field distribution (V/m) - simulated using COMSOL multiphysics package at 2.5GHz.

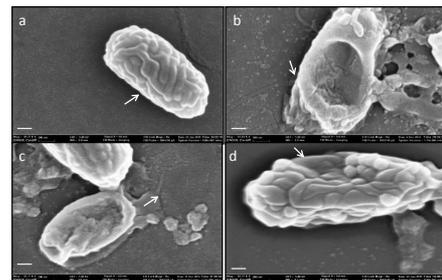


Fig 3. Scanning Electron Microscopy of *C. difficile* spores before (a) and after (b-d) microwave exposure

It is clear from the images in Figure 3 that the microwave exposure is having an effect, not only on the vegetative bacteria, but also the bacterial spore. The microwave assisted release of bacterial DNA was further evidenced by the the ability of the bio-chemical DNA detection assay to detect the presence of *C*-difficile in human faeces at levels as low at 800 spores per gram.

Once the approach had been successfully demonstrated on the bench, the motivation was then to move toward a more compact PA design that supported miniaturisation and integration of the PA into the cavity itself. Figure 4(a) shows a conventional, independent arrangement, as is the case for the system shown in Figure 1 and in all the previously reported works to date, where the signal generator, amplifier and resonator are all separate 50 Ω impedance entities [9]-[11]. Figure 4(b) shows the focus and ambition of this work, where we use the natural impedance environment of the cavity itself to present the required 'high efficiency' impedance environment, reducing the need for matching circuit complexity.

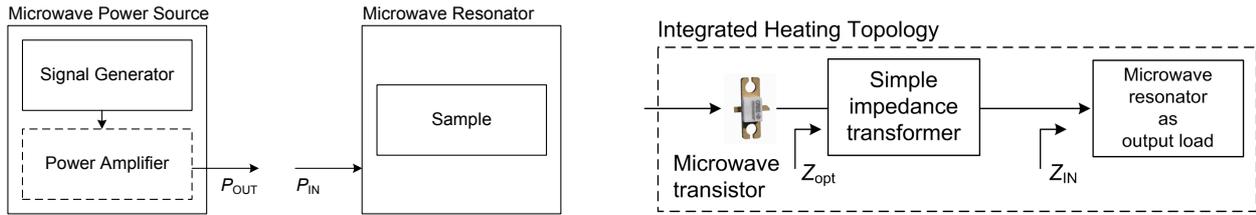


Fig 4. Schematic diagram of the (left) dependent and (right) integrated microwave heating approach

B. Characterisation of Microwave Cylindrical Cavity Resonator

Commercial microwave ovens comprise large, multimode resonant cavities excited by a relatively broadband (20 MHz) microwave source (magnetron). Although highly effective for domestic cooking and a wide variety of industrial applications, the complex impedance environment and unpredictable field distribution within these cavities restrict their use for precision microwave heating and disruption purposes where the controlled delivery and dosage is critical. In contrast, single mode cavity resonators having well-defined impedance environments, well-defined resonant modes and uniform and predictable E and magnetic (H) field distribution offer many possibilities in both industry and academia.

Excellent spatial separation and uniformity of the E and H fields can be achieved by exciting a cylindrical cavity's TM₀₁₀ mode. The inner radius of the cylindrical aluminium cavity used in this work is 46 mm, giving a resonant frequency of approximately 2.5 GHz when empty. The inner height is 40 mm, which is long enough to ensure high uniformity of the axial E -field (i.e. it is ostensibly not affected by the sample holes) but short enough to ensure that the TM₀₁₀ mode is spectrally well separated from other modes (the next nearest mode is TM₁₁₀ at 4 GHz). Excitation of the TM₀₁₀ mode is provided by a loop-terminated N-type connector, which couples to the H -field around the perimeter of the cavity. The unloaded quality factor (Q) is measured to be 3000. The coupling loop can be both rotated and moved in and out of the cavity to achieve critical coupling, whereby virtually all incident power is absorbed by the cavity (and its contents).

In order to understand if the cavity's natural impedance could be exploited in high-efficiency PA design, a detailed characterisation under normal, expected loading conditions was needed. The cavity was initially loaded with a plastic Eppendorf tube containing 100 μ l of water ($\epsilon_r=74$). Critical coupling into the H -field was achieved by careful adjustment of the position and orientation of the coupling loop. The microwave cavity loaded with the water was placed in controlled temperature environment. The 1st measurement was taken at 50°C with the resonator critically coupled by adjusting the coupling loop rotational position. Further measurements were then taken when varying the temperature in 2.5° steps between 27.5 to 70°C.

Segmented frequency spans were selected to cover fundamental, 2nd, and 3rd harmonic loads; fundamental from 2.2-2.6 GHz, 2nd from 4.4-5.2 GHz and 3rd from 6.6-7.8 GHz. To capture the resonance and impedance change, the temperature of the cavity was varied linearly from 27.5

to 70°C and three discrete sets of temperature dependent S-Parameters were recorded. To allow PA-Cavity analysis offline, the measured S2P files were separately arranged into three discrete MDIF files containing S-Parameters of fundamental, 2nd and 3rd harmonic frequency spans respectively over specified temperature range. The measured data files were combined and imported into nonlinear circuit simulator to allow the cavity to be used as passive load in power amplifier design simulations. The measured data for the fundamental band is shown in Figure 5.

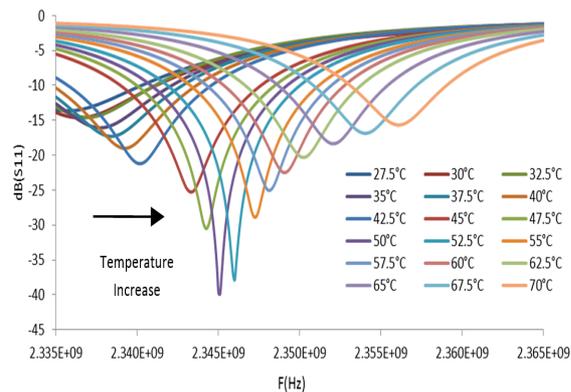


Fig 5. Measured reflection coefficients for the temperature between 27.5 – 70 degree C for a fixed volume of water

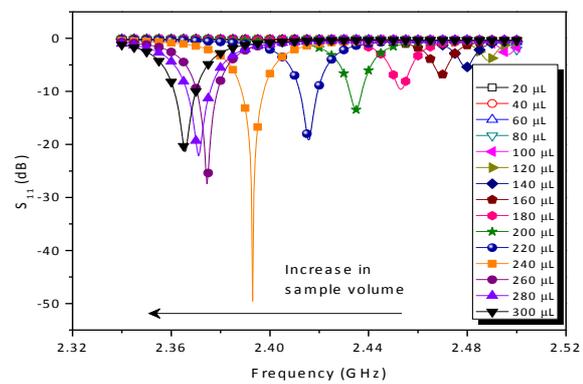


Fig 6. Measured TM010 mode circular cavity response showing resonant shift due to varying water volume at a fixed temperature of 20 degrees C

A similar experiment was then conducted where the water volume was varied whilst holding the temperature constant. The water volume was reduced in 20 µl steps from 20 µl to 300 µl, at which point, for a fixed coupling position, the cavity became excessively reflective (insertion loss > 3dB). This experiment resulted in 15 discrete S1P data files with each file containing the one-port S-parameters of the cavity corresponding to a specific water volume. The measured data for the fundamental band is shown in Figure 6.

Achieving very high performance in power amplifiers requires specific fundamental and harmonic impedances to be presented to the transistor. For example, a narrow-band class-F⁻¹ mode can be achieved by presenting optimum fundamental, 2nd harmonic open and 3rd harmonic short-circuit impedances at the I_{GEN}-plane of the transistor [12]. Conventional high-efficiency mode power amplifiers, although practical in many applications, are limited due to narrowband operation. These limitations extend to the biomedical applications discussed here, where the excitation frequency needs to be continually adjusted to track resonant frequency change due to volume and temperature changes in the sample.

Continuous mode theory, targeted almost exclusively so far at mobile communications applications, provides a solution for achieving high efficiency wideband operation [13]. Continuous class-F⁻¹ mode is an extended version of the narrow-band class-F⁻¹ mode [14]. This mode of operation is achieved by ideally short circuiting the 3rd harmonic and presenting specific fundamental admittance and 2nd harmonic susceptance to the intrinsic plane of the transistor. This results in a second harmonic peaking half wave rectified sinusoidal voltage waveform and an ‘allowed’ set of current waveforms which, starting as a square waveform, can

change in phase, shape and amplitude, but importantly retain power and efficiency performance.

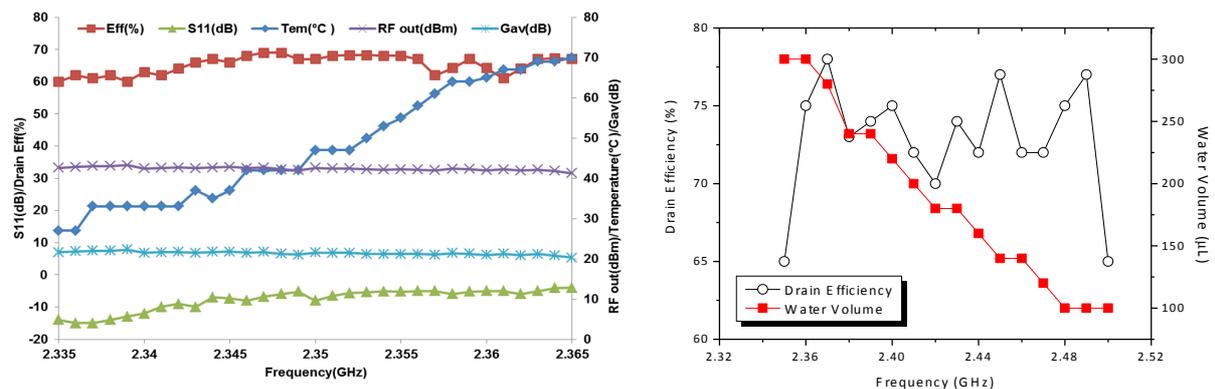
Observing and experimenting with the natural behaviour of the measured cavity wideband impedance environment under normal loading conditions led to an idea: Could continuous mode theory be applied to the design of a PA in this application to realise high performance over operational bandwidth, whilst at the same time, reduced output matching complexity? The answer to this question was ‘yes’!

C. Integrated Microwave Power Delivery System

As already discussed, a correct impedance matching network is a critical requirement for realizing high efficiency PA modes. Low-pass filtering methods using multistage low-pass networks or stepped-impedance transformer approaches can be used to present the required loading conditions for high efficiency PA modes designed in 50 Ω environments.

To be able to present the required continuous class-F⁻¹ loading conditions over the cavity bandwidth, some very simple series transmission lines were used in conjunction with the transistor’s package parasitics. Line dimensions were adjusted until the fundamental and 2nd harmonic loads were as close as possible to their optimum locations. It is possible to transfer the discrete cavity loads to the optimum points of the transistor, as identified in the load-pull measurements, allowing an integrated continuous mode PA structure to be realized.

Figure 7 shows two separate sets of measurement results for (a) fixed sample volume while the sample is heated from 27.5 °C to 70 °C, and (b) fixed temperature while sample volume is varied from 100 μl to 300 μl. Although some variation is observed, the efficiency of the PA is maintained over 60% for different sample temperature or volume, respectively.



(a) PA performance when varying sample temperature between 27.5 °C to 70 °C

(b) Measured results according to varying sample volume

Fig 7. Measurement results showing high efficiency operation of PA independent of sample (a) temperature and (b) volume

CONCLUSION

In this paper, an application of microwave power amplifiers and resonant structure in the rapid diagnosis of antibiotic resistant bacteria is presented. The integrated microwave heating apparatus has been targeted for portable and field deployable diagnostic healthcare applications. The applicability is proven with the prototype heating system, and the integrated design method is proposed to further integrate the system to make it portable. The proposed structure is capable of accommodating (heating) water samples of different volumes whilst guaranteeing high-efficiency operation of the power amplifier and minimizing the reflections from the cavity resonator. Under continuous F^{-1} loading conditions, the apparatus demonstrated a high RF performance over the functional bandwidth of the cavity (2.37 to 2.49 GHz) over varying sample temperature and volume. The integrated design also contains a directional coupler that offers impedance matching as well as continuous performance monitoring mechanism and adds to the further compactness of the system. Due to its small size, flexibility and light weight, this apparatus can be installed and operated bedside for sample diagnosis.

REFERENCES

- [1] H. D. Trefna and M. Persson, "Antenna array design for brain monitoring," in *Proc. IEEE Int. Symp. Antennas Propag. Soc. (APSURSI)*, San Diego, CA, USA, July 2008, pp. 1 – 4.
- [2] M. A. Khorshidi, *et al*, "Classification of Microwave scattering data based on a subspace distance with application to bleeding stroke," in *Proc. Computational Advances in Multi-Sensor Adaptive Processing (CAMSAP), 2009 3rd IEEE Int. Workshop on*, Aruba, Dutch Antilles, December 2009, pp. 301-304.
- [3] H. D. Trefna, A. Imtiaz, H. Lui, and M. Persson, "Evolution of an UWB antenna for hyperthermia array applicator," in *Proc. 6th European Conf. Antennas Propag. (EuCAP)*, Prague, Czech Republic, March 2012, pp. 1046-1048.
- [4] Y. Abed, *et al*, "Efficient discrimination of mycobacterium tuberculosis strains by 16S-23S spacer region based random amplified polymorphic DNA analysis," *J. Microbiology and Biotechnology*, no. 33, vol. 5, pp. 1418-1420, November 1995.
- [5] A. Imtiaz, Z. A. Mokhti, J. Cuenca, and J. Lees, "An integrated inverse-F power amplifier design approach for heating applications in a microwave resonant cavity," in *Proc. Microw. Conf. (APMC), 2014 Asia Pacific*, Sendai, Japan, November 2014, pp. 756-758.
- [6] A. Imtiaz, J. Hartley, H. Choi, and Jonathan Lees, "A high power high efficiency integrated solid-state microwave heating structure for portable diagnostic healthcare applications", in *Proc. RF and Wireless Technol. for Biomedical and Healthcare Applications (IMWS-Bio), 2014 IEEE MTT-S Int. Microw. Workshop Series on*, London, United Kingdom, December 2014, pp. 1-3.
- [7] K. Chen and D. Peroulis, "Design of broadband high-efficiency power amplifier using in-band class- F^{-1}/F mode transferring technique," in *Proc. Microw. Symp. Digest (MTT), 2012 IEEE MTT-S Int.*, Montreal, QC, Canada, June 2012, pp. 17-22.
- [8] K. Chen and D. Peroulis, "Design of broadband highly efficient harmonic-tuned power amplifier using in-band continuous class (F^{-1}/F) mode transferring," *IEEE Trans. Microw. Theory Techn.*, vol. 60, no. 12, pp. 4107-4116, December 2012.
- [9] J. M. Osepchuk, "A history of microwave heating applications," *IEEE Trans. Microw. Theory Techn.*, vol. 32, no. 9, pp. 1200-1224, Sep. 1984.
- [10] A. Mashal, *et al*, "Toward carbon-nanotube-based thernostic agents for microwave detection and treatment of breast cancer: enhanced dielectric and heating response of tissue-mimicking materials," *IEEE Trans. Biomed. Eng.*, vol. 57, no. 8, pp. 1831-1835, Aug. 2010.

- [11] J. M. Catala-Civera, *et al.*, "Dynamic measurement of dielectric properties of materials at high temperature during microwave heating in a dual mode cylindrical cavity," *IEEE Trans. Microw. Theory Techn.*, vol. 63, no. 9, pp. 2905-2915, Sep. 2015.
- [12] A. Grebennikov, "Load network design techniques for class-F and inv.F PAs," *High Frequency Electronics*, pp. 58-76, May 2011.
- [13] V. Carubba, A. L. Clarke, M. Akmal, J. Lees, J. Benedikt, P. J. Tasker, and S.C. Cripps "The continuous class-F mode power amplifier," *Microw. Integrated Circuits Conf. (EuMIC), 2010 European*, Paris, France, September 2010, pp. 432-435.
- [14] V. Carubba, A. L. Clarke, M. Akmal, J. Lees, J. Benedikt, S. C. Cripps, and P. J. Tasker, "The continuous inverse-F mode power amplifier with resistive second harmonic impedance," *IEEE Trans. Microw. Theory Techn.*, vol. 60, no.6, pp. 1928-1936, June 2010.