IEEE Access
Multidisciplinary | Rapid Review | Open Access Journal

Received 20 November 2023, accepted 24 December 2023, date of publication 11 January 2024, date of current version 23 January 2024.

Digital Object Identifier 10.1109/ACCESS.2024.3352728

METHODS

The Complex Permittivity of Biological Tissues: A Practical Measurement Guideline

LOURDES FARRUGIA[1], EMILY PORTER[2], (Member, IEEE), RAQUEL C. CONCEIÇÃO[3], SIMONA DI MEO[4], (Member, IEEE), DANIELA M. GODINHO[3], JULIAN BONELLO[1], (Member, IEEE), MYKOLAS RAGULSKIS[5], ILJA OCKET[6], (Member, IEEE), LAURA FARINA[7], (Member, IEEE), MARTA CAVAGNARO[8], (Senior Member, IEEE), AND AZADEH PEYMAN[9]

[1]Department of Physics, University of Malta, MSD2080 Msida, Malta
[2]Department of Biomedical Engineering, Rue University, Montreal, QC H3A 2B4, Canada
[3]Instituto de Biofísica e Engenharia Biomédica, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisbon, Portugal
[4]Department of Electrical, Computer and Biomedical Engineering, University of Pavia, 27100 Pavia, Italy
[5]Keysight Laboratories, Keysight Technologies, 4040 Linz, Austria
[6]KU Leuven, Division ESAT-TELEMIC, 3000 Leuven, Belgium
[7]R&D, Endowave Ltd., Galway, H91 DCH9 Ireland
[8]Department of Information Engineering, Electronics, and Telecommunications, Sapienza University of Rome, 00184 Rome, Italy
[9]U.K. Health Security Agency (previously Public Health England), Chilton, OX11 0RQ Didcot, U.K.

Corresponding author: Lourdes Farrugia (lourdes.farrugia@um.edu.mt)

This work was developed within the Cooperation in Science and Technology (COST) CA17115 MyWAVE and supported in part by projects: Fundação para a Ciência e Tecnologia (UIDB/00645/2020 and https://doi.org/10.54499/UIDB/00645/2020); and 'CountMe' funded by the Malta Council for Science and Technology (MCST).

ABSTRACT Despite the significant number of studies published on the measurements of complex permittivity of biological tissues in the last thirty years, implementing a successful measurement program for dielectric measurements can still present a challenge for researchers. Most problems are not theoretical but of methodological or practical nature. In this article, lessons learned from experiences with goal-oriented measurements are presented by structuring them into practical guidelines for efficient and useful measurements of dielectric properties of biological tissues, aimed at addressing gaps in knowledge. Issues related to calibration, validation of the measurement system and data collection procedures are addressed from a practical perspective. This will help support reproducibility of measurements. In addition, guidelines for data analysis and data reporting are provided. The latter is also supported by a data analysis tool developed in MATLAB, made available as open source. This facilitates the harmonisation and merging of different datasets, ease of interpreting and re-using of data and comparison of data across studies. Additionally, a data repository is presented for uploading of dielectric data of biological tissues, along with the corresponding meta-data describing the experiments. These guidelines are the result of the work carried out by a dedicated working group in the project COST Action MyWAVE.

INDEX TERMS Complex permittivity, dielectric properties, electromagnetic medical devices, open-ended coaxial probe, tissues.

I. INTRODUCTION

One of the fastest growing areas in medical device research in Europe is emerging electromagnetic (EM) devices for a wide range of clinical conditions [1], [2], [3]. These devices provide a very attractive solution as they are based on non-ionising radiation sources, largely non-invasive and minimise hospitalisation time and costs, thus very appealing within the context of an ageing population in Europe and an exponential growth in healthcare costs. Example of medical applications using electromagnetic fields as a source, include microwave imaging (MWI) for the diagnosis of several

The associate editor coordinating the review of this manuscript and approving it for publication was Ali Karami Horestani.

diseases (e.g., breast tumour, brain stroke, axillary staging, etc. [4], [5], [6], [7], [8], [9]) and therapeutic techniques such as hyperthermia (HT) and thermal ablation (TA) [2], [10]. While these technologies are widely studied in several research institutions and some of them are already in use in the clinic, their spreading as alternative techniques to traditional ones (e.g., MWI in place of computed tomography – CT - or magnetic resonance imaging - MRI; TA in place of surgery) is not progressing at the same speed of the research.

The challenges undermining EM medical technologies are being synergistically addressed by a collaborative network, COST Action MyWAVE (CA17115) [11], which brings together engineers, scientists, medical professionals, and experts from the market-commercialisation community to further advance EM hyperthermic technologies. These technologies include radiofrequency (RF) and microwave (MW) ablation and hyperthermia and are proposed for treatment of several diseases including cancer, inflammation, and others, through modification of tissue temperature. This project aims to make significant advancements towards achieving electromagnetic (EM) therapies that are clinically effective, through identification of clinical needs, development of improved safety standards and development of novel therapeutic EM devices.

EM hyperthermic technologies heavily rely on the knowledge of dielectric properties of various tissues amongst patients, and how these properties change during the treatment. In fact, dielectric properties. dictate the interaction of the electromagnetic field with the human body. Dielectric properties of biological materials have been studied since 1950s [12]. Both theoretical approaches to model dependence of the dielectric properties from the frequency of the electromagnetic field [13], [14] and measurements to characterize the different tissues and differences between healthy and malignant tissues [15] were carried out. However, these initial works were carried out applying different methods, often looking at the dielectric properties over a limited frequency band and concentrating on a limited number of tissues [16]. Towards the last decade of the previous century, the spreading of cellular phones demanded the development of new dosimetry studies to evaluate the electromagnetic field absorbed by the human head when located in proximity of the radiating cellular phone. Availability of new, powerful computers and the development of numerical methods to solve Maxwell's equations allowed such evaluations, but the need of new knowledge on dielectric properties, both with reference to the frequency range and to the number of human tissues characterized, was clearly evidenced [16].

In this respect, the work performed by C. Gabriel and colleagues was of outmost importance [17], [18]. In their work, Gabriel et al., developed techniques to measure the dielectric properties of biological tissues across a wide frequency range from 10 Hz to 20 GHz; they measured human and animal tissues at body temperature, and provided mathematical fit of the measured data to a four-pole Cole-Cole model [19]. To cover such broadband frequency range, Gabriel et al. used three different measurement techniques and the results showed good agreement between data obtained from three experimental setups in the overlapping frequency ranges. The data were also largely in good agreement with the corresponding values in the literature and the results were put in the so called "1996 database" on an open web site where they can still be found (https://www.fcc.gov/general/body-tissue-dielectric-parameters). Since then, other website implemented the same Cole-Cole formulas (http://niremf.ifac.cnr.it/tissprop/; https://itis.swiss/virtual-population/tissue-properties/database/dielectric-properties/), and this data is now a point of reference in most of the studies devoted to the interaction of electromagnetic fields with the human body. Successive studies aimed to characterise the dielectric properties of biological tissues and their confounders were conducted [20], [21], [22], [23], [24], [25], [26]. Most of these studies addressed dosimetry concerns and this defined the experimental approach including the tissue types, measurement methods, and temperature of the sample, amongst many other experimental parameters.

Nowadays, given the increase in medical applications of EM fields, the needs evolved, and researchers require additional information from dielectric studies. This led to several studies devoted to the measurements of dielectric properties of tissues. However, very often the report of these studies is not complete, leading in difficulties in reproducing the data, difficulty which is of course increased by the great natural variability of biological tissues.

Moreover, recent studies show that there still exists substantial inconsistencies and conflicting datasets for the dielectric properties of biological tissues, and comparison across published data is challenging due to different measurement methods and limited reporting of experimental metadata [27]. Very often, the measurement protocol is briefly outlined in publications and very few studies capture all the relevant protocol details, limiting the reusability of data. In this respect, a general consensus on the measurement procedure, as well as on the reporting of the study (information to be reported), based on the knowledge to date, would be of great help to the community.

In this paper, we present a best-practice guideline for the dielectric measurement of homogeneous biological tissues at a single temperature using a reflection technique. We specifically cover several topics, ranging from the measurement itself, to measurement validation, calculating and reporting accuracy, and discuss numerous tissue-specific challenges and considerations. We further provide a data-analysis application that will help researchers within the community harmonise their method of data-analysis and reporting. Additionally, a data repository that highlights the confounders discussed in this guideline was designed (https://www.um.edu.mt/projects/mywave/data-repository/). This work is being proposed as a consensus work of the COST MyWAVE network.

II. BACKGROUND

The dielectric properties of biological tissues, i.e., the relative complex permittivity (ε_r) describe the electric polarizability of a material as a reaction to the presence of an external electric field and is defined mathematically by,

$$\varepsilon_r^*(\omega) = \varepsilon_r'(\omega) - j\varepsilon_r''(\omega) \quad (1)$$

where ε_r' is the real part of the relative complex permittivity (also called 'relative permittivity or dielectric constant'), ε_r'' is the imaginary part, and ω is the angular frequency of the external EM field. ε_r' represents the amount of energy stored in the material whilst ε_r'' represents the energy dissipated inside the material under test. Both ε_r' and ε_r'' are frequency- and tissue-dependent [28]. Accurate knowledge of these properties is important to designing and optimizing EM hyperthermic technologies, as well as developing appropriate treatment planning and monitoring procedures.

Dielectric properties of tissues can be measured through a variety of methods. These include resonant cavities, free-space methods, transmission methods and reflection techniques [29]. The latter using open-ended coaxial probes is a technique widely used to measure the dielectric properties of biological tissues and it was developed in 1994 by [30] and since then has been the preferred method for measurements of dielectric properties of biological tissues due to its relative non-destructiveness of the sample, the ability to measure in-vivo, and the ability to easily measure small samples (on the order of ∼4-5 mm). Since this method is by far the most common for measuring biological tissues, this document will focus on this approach [25], [31], [32].

When dielectric measurements of biological tissues are conducted using the open-ended coaxial probe method, the measurement system includes the probe itself located in contact with the material under test (MUT), and a vector network analyser (VNA) which transmits a signal to the probe and receives the reflected response. Then, a mathematical algorithm is needed to convert from the recorded reflection coefficient to the corresponding dielectric properties. Although the system is straightforward to operate, it is not as easy to achieve accurate and repeatable results when biological tissues are under measured, and different dielectric centers adopted different measurement procedures, often without consistency across centers [33], [34]. This, together with other random factors associated with the inherent variability of tissues, confounders in the measurements, and questions about how to deal with heterogeneous biological tissues, contribute to the large variation in reported dielectric properties.

Although the open-ended coaxial measurement technique is very well established and dielectric measurements of biological tissues have been measured for the past 50 years [16], [17], [35], [36], [37], [38], a systematic guideline for performing high accuracy dielectric measurements of biological tissues can be very useful for the scientific community. Therefore, this paper will promote a consistent approach to good measurement practice for accurate measurements of the complex permittivity of homogenous biological tissues using an open-ended coaxial technique.

Together with MINDER (which proposes a framework for reporting raw data and metadata in dielectric studies of biological tissues [27]), this work presents recommendations for the best practice in dielectric measurement of biological tissues by first describing the hardware and typical measurement setup and then providing a detailed description of the best-practices to be considered when conducting dielectric measurements. Each practice has at its basis a thorough consideration of the foundational aspects described in Section V. This guideline provides a best-practice method specifically for obtaining average dielectric properties of homogeneous and heterogeneous tissues and the best-practice methods proposed related to the measurement setup, calibration, and validation, are all applicable to heterogeneous samples.

To facilitate the implementation of these best-practices guidelines a data-analysis application is being made available for download at GitHub (https://github.com/lourdesfarrugia/MyWAVEapp). Additionally, the publication of a Data Repository encourages open science, through use of FAIR data principles, to make collected data Findable, Accessible, Interoperable and Re-usable [39]. This will harmonize on-going dielectric studies of biological tissues. Specifically, collecting and curating data in line with the FAIR principles supports research productivity and innovation, as it allows integration of knowledge across disciplines, institutions, researchers, and industry, and enables reliable re-use of data [40].

III. THE REFLECTIVE DIELECTRIC MEASUREMENT SETUP

A typical reflection measurement setup using an open-ended coaxial transmission line is presented in Fig. 1. It consists of a VNA connected to an open-ended coaxial transmission line via a high-stability cable or an elbow connector. The MUT is placed on a laboratory jack and is moved in contact with the open tip of the transmission line. The tip is either immersed or placed in contact with the MUT such that the fringing fields are all within the MUT.

The reflection coefficient (Γ) is measured using the VNA and then converted to the corresponding complex permittivity. Very often, the VNA and conversion algorithms are interfaced via an embedded software resulting in a quick measurement of Γ and conversion to the corresponding complex permittivity. The procedure to perform the measurements on biological MUTs foresees a calibration using three standards and then measurements of the MUT.

Several commercially available open-ended coaxial transmission lines (probes) are available on the market and are widely used for the measurement of the complex permittivity of biological tissues. Also, associated commercial software are available for the conversion of the measured reflection coefficient to the corresponding complex permittivity. These software feature in-calibration algorithms as well as allow for the use of different probes having different physical properties (e.g. flanged probes, different diameters, etc.).

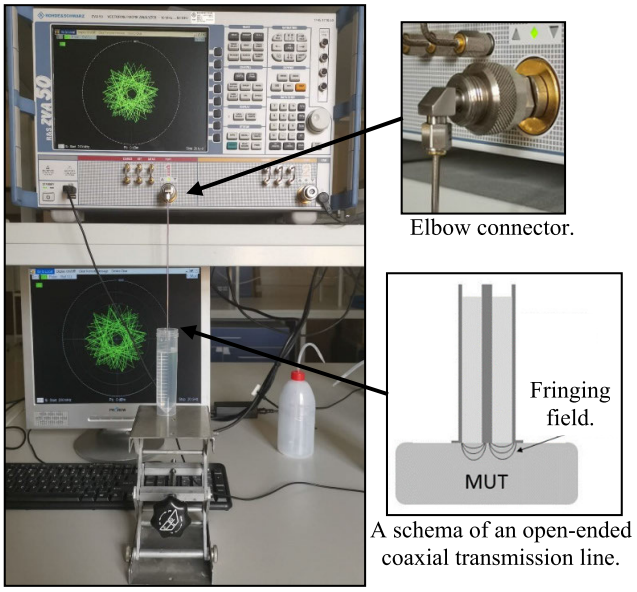


FIGURE 1. A typical reflection measurement system used for the measurement of the complex permittivity of biological tissues.

However, in many cases there is limited information on the conversion method employed in commercial software and thus very often it is treated as a black box. However, efforts have been put in the development of non-proprietary and transparent conversion algorithms [41], [42]. In some cases, there are also hardware compatibility issues between different VNA manufacturers and commercial probes, limiting their use. To date, most of these conversion methods are based on either full-wave analysis which is computationally intensive, approximating the probe as an ideal TEM guide [43] or through the use of equivalent circuit methods which calculates the permittivity from the probe input admittance [30], [44], [45]. Alternatively, a recent method was published in [46] based on the use of an Artificial Neural Network which provides a solution for most of the compatibility issues between the conversion algorithm software and VNAs, as well as translating the calibration plane to the VNA port, thus making the measurement process more straightforward.

IV. A DIELECTRIC MEASUREMENT BEST-PRACTICES GUIDELINE

This guideline is sectioned into five steps which cover from the system preparation of a typical setup described in Section III, up to reporting of results. The different steps are summarised in Fig. 2, with the first two relating to the system preparation and calibration, the third to the measurements of the complex permittivity of the MUT (including rigorous sample considerations) and finally, the last two discussing the data analysis and reporting of the measured data. A detailed flow diagram of the measurement procedure is presented in Appendix I which summarises the best-practices outlined in the following sections. Additionally, for ease of use, a table

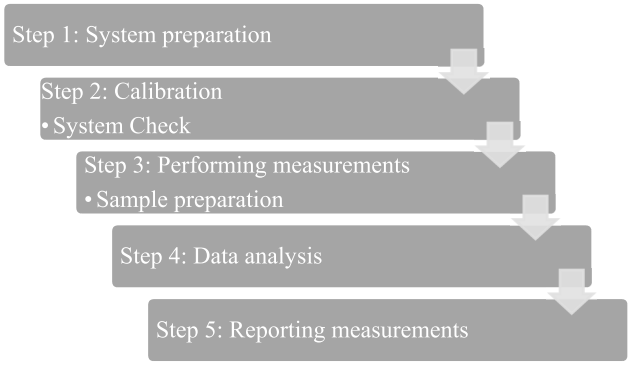


FIGURE 2. A block diagram breaking down the measurement process of complex permittivity in five main steps: system preparation, calibration, measurements, data analysis and final reporting of the measured data.

summarising the data proposed for reporting is presented in Appendix II.

In the following sections, the different steps required to setup and conduct dielectric measurements using an open-ended reflection technique are outlined and then discussed in detail step by step.

1. Cable movements significantly influence the measurement of the reflection coefficient and thus, the cables used to connect the open-ended coaxial transmission line with the VNA should be carefully fixed. Elbow connectors, being rigid structures, minimize such an issue, so their use is strongly recommended. Also, the use of torque wrenches is recommended to ensure that all connections are tight and secure and that connections are repeatable and consistent each time the system is set up. These minimize VNA measurement errors due to reflectivity, directivity and tracking. Using torque wrenches will also maximize connector lifetime.
   In case of using a cable, the quality of cable should be very high precision and rigorous movements should be avoided.
2. The use of a laboratory jack is recommended so that only the MUT is moved to make contact with the probe. This will eliminate any phase errors introduced by movements of the setup, after calibration is completed.
3. For most of the VNAs on the market, it is recommended that any calibration/measurements are done after at least 30 minutes of warm-up time. This time is required so that all electronics reach thermal equilibrium.
4. The probe tip should be cleaned well prior to calibration and in between measurements during the experiment. It can be wiped using alcohol or rinsed with water/alcohol and then wiped with a dry lint-free paper towel. This will ensure that no residues are present at the sample-probe tip surface.
5. Before starting with the calibration step, the following points need to be considered: frequency range to be investigated; data resolution and the scale (whether log/linear) to be used; the physical characteristics of

the probe which will be used (this will determine the frequency range to be investigated, sensing volume etc.) and desired temperature at which measurements are to be conducted. It is important to consider the scale well prior measurements especially when planning to fit the measured data to mathematical models such as Debye or Cole-Cole. When data points are more distributed across frequency (linear scale), the fit is more representative of each frequency across the range instead of heavily focused on one region of the range (log scale) [47].

6. The choice of probe depends on the frequency of interest, sample size, measurement sensitivity and compatibility between different hardware. Small sample sizes require the use of probes having a small diameter of the outer conductor. Larger, flanged probes are used when large sample sizes are available. Refer also to points 18 & 19 of this guideline [29], [48], [49].
The size of the probe is also related to the sensitivity of its performance across the frequency range, as smaller probes have higher performance sensitivity at higher frequencies and vice versa [37], [38].

A. STEP 2: PERFORMING THE CALIBRATION

7. Calibration requires the measurement of at least three well-characterised loads. The number and typology of the loads depend on the model used to reconstruct the dielectric properties from the measured reflection coefficient. The loads can include Open circuit, Short circuit and any other calibration load or any other three well-characterised loads. A calibration load can be any standard material of which the dielectric properties are well-known. Typically, deionized water or 0.1N NaCl is used for this purpose, since their dielectric properties have been thoroughly characterized and traceable data is available [50], [51], [52]. For highly lossy materials such as high-water content tissues (eg. liver and muscle) the use of a 0.15N NaCl is recommended, as the latter has similar conductivity to that of most tissues. Otherwise, other highly-characterized materials may also be used if desired (e.g., ethanol, methanol) [53], [54], [55]. Alternatively, the calibration plane can also be defined at the VNA output port. This can be done either using mechanical standards or electronic calibration kits (e.g. eCAL by Keysight), however, this would require compensation for the phase delay introduced by the open-ended coaxial transmission line used and thus the calibration plane needs to be translated to the tip of the probe.

1) MEASURING LOAD STANDARD

8. If a liquid is used as a calibration load, its temperature should be accurately recorded because the calibration parameters (reflection coefficients which eventually translate to dielectric properties) are highly temperature dependent. Measurements are to be conducted in a temperature-controlled laboratory to avoid extreme temperature drifts. The use of a water bath for warming or cooling MUT to a certain temperature is recommended, ensuring that the MUT is placed in a sealed bag/container so that no sample contamination occurs. Additionally, it must be ensured that the liquid volume is larger than the sensing volume of the probe. This can be validated by covering the sample holder with Aluminium foil and check for any changes in the reflection coefficient.
9. The complex permittivity of the calibration load should be known a priori, and it is important that it is recorded at the desired measurement temperature. Ideally, the temperature of the calibration load is similar to that of the MUT [56].
10. It is important that the probe tip is in good contact with the calibration materials. In the case of a liquid, it must be ensured that no air bubbles are present at the tip of the probe or within the sensing volume.

2) MEASURING THE SHORT STANDARD

11. Replicating a perfect Short circuit can be very challenging and this standard measurement is a source of a number of erroneous calibrations. There are various ways to produce a Short standard and different labs use different techniques, e.g. use of liquid metal, use of special jigs that are made to produce almost perfect contact between metal and the probe tip and using a soft material covered with Aluminium foil which is pressed against the probe tip. In the latter case, there should be a balance of pressure as too much pressure will damage the connections and too little will result in a bad short contact. The Aluminium foil should be in contact with both inner and outer conductor of the probe.
12. Once any standard is connected to the probe tip, it is recommended to wait for a few seconds to ensure that the setup is stable and free from any vibrations, before conducting the measurement. This is particularly applicable when using special jigs as the Short circuit standard.
13. Being a challenging standard to produce, the Short circuit standard could be verified post calibration, as outlined below in the verification section, see point 17.

3) MEASURING THE OPEN STANDARD

14. Very often, the Open circuit standard is produced by measuring air, ensuring that nothing stands within the sensing volume of the probe whilst conducting the measurement.
15. At this point, it is recommended that the time at which calibration is completed is recorded. This will be used to evaluate drift errors in the measurements in the data reporting/data analysis section.

Measuring the above three standards will complete the system calibration and user can proceed with the verification of the calibration.

16. In the meantime, it is important that no physical changes occur to the system or the surrounding environment that could influence the electronics of the system after performing calibration.

4) SYSTEM CHECK

17. The verification of calibration (referred to as System Check) is a two-step process:
    a. The Short and Open circuit standards are re-measured and compared such that the difference between the phase of the open and short is about 180°.
    b. A well-characterised validation liquid (different than that used for calibration), with well-known and with wide consensus dielectric data, is measured and compared[1] to published data. Very often different concentrations of Sodium Chloride (NaCl) are used for such a material, due to the non-toxic nature, ease of availability, and properties near to the range of expected tissue properties. In the case of measurements of biological tissues, 0.1 NaCl is widely used [55], [57], [58], [59].

    The measured complex permittivity is to be compared to previously reported/published data (e.g. [55], [60]). Differences between the dielectric measurement of the verification liquid and the corresponding published data are calculated and the lower the differences the better. In general, a difference of 5% in either relative permittivity or conductivity is acceptable, however this depends on the MUT and frequency range. In the case of well characterised standard liquids, 5% may be too high and a lower value should be obtained.[2]

B. STEP 3: SAMPLE CONSIDERATIONS AND MEASUREMENTS

1) SAMPLE CONSIDERATIONS

18. The size of the sample holder depends on the dielectric properties of the MUT and the frequency of operation, thus it should be big enough to ensure that no reflections occur from the boundaries [61]. This could be verified by monitoring the reflection coefficient (S11) or measuring the complex permittivity of the sample holder with and without Aluminium foil fitted on the inner walls/surface of the sample holder. If differences are detected, then a larger sample holder should be considered.
19. In the case of biological tissues, the sample under test should be of sufficient thickness and width. This could be verified using the same technique as described in 18.
20. It is recommended that biological samples are not put in saline solutions or preserving agent. It has been shown that some preserving agents significantly alter the complex permittivity of the sample under test [62].
21. Sample preparation and manipulation should always be kept at a minimum prior taking measurements.
22. In the case of heterogeneous tissues, samples can be homogenised to obtain a mean value of the dielectric properties of the MUT [63], ensuring that in the process of homogenisation no loss of hydration occurs. Accurate histology sampling may support the accurate characterisation of the tissue components composing the heterogeneity in the measured volume [64], [65].
23. In the case of ex-vivo measurements at microwave frequencies, sample hydration should be preserved as much as possible. This is due to the direct relationship between γ dispersion and water content of the sample (polarisation of the water molecules). At β and α dispersion regions this has less effect. Preservation of tissue's water can be done by considering the following:
    a. Samples should be transported in sealed containers/bags.
    b. The time between excision and measurements should be always kept at a minimum. Very often time between excision is ambiguously used to refer to both to the time from when the sample is excised from source of origin and to the time from when a large sample is dissected into smaller samples. It is recommended that both are clearly distinguished and reported.
    c. Prolonged exposure of the measurement area to air should be avoided as this can cause dehydration at the measurement point.
    d. It is important to preserve any biological fluid in the sample whilst excising biological tissue. Fluid seeping out can easily occur if you apply excessive pressure when preparing the sample for measurements.
24. The issue of preservation of hydration levels when it comes to dielectric measurements of biological samples is of critical importance and has been investigated with further detail by many research groups [34], [59], [66]. A more detailed section on this point is presented in the Section 5.1.
25. It is recommended that the temperature at the measurement point is recorded both before and after a measurement is performed. Ideally, temperatures are equal.
26. In case of in-vivo or in-vitro measurements:
    a. Exposure of the measurement area to air should be minimized, especially if animal/sample is kept

[1]Comparison of data should be done on the basis of like with like, i.e. calculated data with calculated data and/or experimental data with experimental data. Calculated data refers to data derived from mathematical models such as Debye and Cole-Cole, the parameters of which are usually published in studies reporting wideband measurements of the complex permittivity.

[2]Some dielectric centres allow for ensure for smaller tolerance on the percentage difference. In some cases, it can be as low as 1%.

under a heating source. It is common practice that small animals such as rodents are kept under UV/heat source to help the animal thermoregulate. However, the presence of a heating source could dehydrate the area, leading to erroneous measurements.

b. Pat drying/draining any excessive fluid present in the measurement area is not recommended as this can alter the amount of fluid typically found in that area. In the case of excessive blood in a measurement area, then it is recommended that another measurement site is considered [67]. The effect of blood contamination on measurements is significant, especially in highly perfused tissues such as liver. Ideally, no small vessels are present in the measurement area.

c. Measurements are to be conducted as fast as possible with the probe placed in good contact with the MUT.

27. For in-vivo, ex-vivo or in-situ measurements, in some cases, it might be necessary to perforate slightly the surface of the material under test and guide the probe deeper in the material. This should be done without applying excessive pressure to avoid contaminating the measurement area with biological fluid. If confounders are well-controlled, the difference between surface and deep measurements at the time of excision are within experimental uncertainty [67].
28. It is recommended that the temperature at the measurement point is recorded both before and after a measurement is conducted.

2) REPEATED MEASUREMENTS

29. Several independent repeated measurements should be considered for each sample. An independent measurement is defined as re-initiating the entire measurement procedure, that is disengaging the probe tip from the MUT, clean the probe and re-measure. This should be done even if measurement is conducted at the same location.
30. Three independent repeated measurements are usually conducted for each location and multiple locations should be considered for each sample.
31. The number of measurements/samples to be conducted depends on the 'expected' variation of the mean value. It has been shown that a sample/tissue with high water content has less variation in the mean compared to tissues with low percentage of water content or with high heterogeneity [68].
32. When conducting measurements on heterogeneous tissues many measurements on various sites are recommended. This will result in a mean value of the dielectric properties representing the tissues within the sensing volume of the probe [54], [69].

3) CLEANING THE PROBE

33. In the case of measurements on biological tissues, it is recommended that the probe is cleaned initially with water and then followed by alcohol. Water will dissolve any blood residue at the tip of the probe and the alcohol will disinfect the probe. In some cases, autoclaving the probe may be required. In [70], the dielectric properties of a standard material before and after probe autoclave were compared, illustrating that in the case of Slim Form Probe (Keysight) no statistically significant difference was observed.
34. At the end of each measurement session, the standard liquid used for the system check is to be re-measured and compared to the initial measurement obtained in 17b.

C. STEP 4: DATA ANALYSIS

1) EXPERIMENTAL OUTLIERS

35. The system check measured before (point 17b) and after (point 32) measuring the MUT should be compared to ensure that no deviations in the system occurred.
36. When conducting measurements over a wide frequency band, experimental outliers can be identified using a selection method based on Kramers Kronig (KK) relationships.[3]

    Generally, when measuring the complex permittivity of biological tissue using open-ended coaxial transmission lines, measurements are conducted as a function of frequency and then modelled mathematically using a Cole-Cole equation together with a conductivity term [18].

    This equation satisfies KK relations, given that the dielectric response of the MUT is both linear and causal.[4] Therefore, knowing the dispersion law a priori, a pre-defined threshold on the residuals could be used as an identifier of experimental outliers. This data selection criteria is also implemented in the MyWAVE data-analysis application.
37. The measurement uncertainty must be calculated, and the method used to evaluate the uncertainty should be clearly explained and reported. Different labs use different methods. However, it is recommended that these methods include a detailed analysis and quantification of both Type A and B errors, as described in the GUM guidelines.) [71]. Following that, an average measurement uncertainty is to be reported for different frequency ranges.

[3] Kramer's Kronig relations are bidirectional mathematical relations, relating the real and imaginary parts of any complex function that is analytic in a half-plane.

[4] Both conditions are generally satisfied since the amplitude of the applied electric-field is low and ε' increases when σ decreases.

In the MyWAVE dielectric data analysis application, a tool to evaluate the measurement uncertainty has been published and the method is based on the pragmatic approach published in [54].

D. STEP 5: REPORTING THE MEASURED DATA

38. It is recommended that the range of temperatures or the mean temperature recorded during several measurements as specified in point 28 is reported.
39. The difference in the measured data of the validation liquid (for system check) as obtained in points 17b should be clearly reported. In the case of multiple calibrations, it is recommended that either the mean difference across all calibrations is calculated and reported, otherwise the upper and lower bounds of the measured data of the validation liquid should be clearly specified.
40. The standard deviation in the measured complex permittivity of the MUT is to be reported along with the mean value.
41. It is recommended that whenever wideband measurements of the complex permittivity are conducted, these are modelled mathematically using dispersion laws, such as Debye and Cole-Cole. This will facilitate re-usability of the results and support the incorporation of the reported data into numerical simulations. Depending on the frequency range of the measurements, multi-pole Cole-Cole or Debye equations can be considered which constitute multiple dispersions.
42. If the measured data is reported in the form of models, the fitting algorithm used to obtain the model parameters needs to be reported, together with the accuracy of the fitting technique.
43. When fitting measured data to mathematical models, it is recommended that both the confidence interval of each fitted parameter and the root mean square error of the model are reported. Any other parameter indicating the goodness of fit could be used to further support the results [13], [18], [72].
44. A table with the recommended data to be reported is presented in Appendix I.
45. As per EU recommendations and best practices in scientific research, experimental data and metadata should be made open source [27], [39], [40], [73].

V. MYWAVE DATA ANALYSIS APPLICATION

In order to harmonise the data-analysis technique presented in this paper, a MyWAVE dielectric data analysis application is being published. The application is developed in MATLAB following the best-practices guideline detailed in Section IV. It includes four tabs: 1) load data tab, 2) filtering tab, 3) mathematical model and 4) uncertainty calculation tab.

The load tab requires the data to be uploaded in the application in the format: frequency (Hz), real and imaginary part of the complex permittivity, with the imaginary part being < 0 as per definition presented in Equation 1.

The filtering tab corresponds to the data filtering technique outlined in point 36. In this step all the individual measurements are fitted to different mathematical models (Cole-Cole + conductivity term, Cole-Cole, Debye + conductivity term, Debye) and the corresponding root mean square error (RMSE) is plotted. The equations implemented in the code are summarised in Appendix III. The fitting algorithm is based on a non-linear regression fit implemented in MATLAB and requires a set of initial conditions. In this case, a threshold on the RMSE can be set and any dataset which is fitted and results in a RMSE that exceeds the threshold is discarded. Finally, the average of the remaining datasets is presented, and the corresponding fitted parameters are tabulated in third tab ''Mathematical model'', together with the 95% confidence interval of each parameter and the RMSE of the model.

Finally, the last tab implements the pragmatic approach for the uncertainty calculation as published in [54].

VI. MYWAVE OPEN-ACCESS DATA REPOSITORY

An open-access data repository of dielectric and thermal properties of biological tissues was designed and published on COST MyWAVE Action's website [74]. This repository is an outcome of the best practices outlined in Section IV and highlights the importance of reporting all metadata. The data repository can be a useful tool for 1) researchers searching for measurements of a specific biological tissue under certain conditions, and 2) researchers who want to share their work and report their measurements following the recommended guidelines. This allows for the merging and replication of dielectric studies, thus promoting the complementarity of various measurement campaigns across different research centres.

A search page is available to all visitors of the repository, which shows all approved entries of both dielectric and thermal properties measurements with filtering options. Visitors can switch between dielectric and thermal properties, filter by frequency band and metadata related to the sample and hardware. The filtering options for the sample metadata include the type of tissue, its origin (e.g. human, bovine, etc), its pathology (e.g. healthy or diseased), its state (e.g. in-vivo, in-vitro, ex-vivo), the method of sample preservation and temperature of samples, temperature of the samples during measurement, number of samples measured, and volume of the samples. The filtering options for the hardware metadata include the type of measurement method (e.g. open-ended coaxial probe, transmission line) and its model and brand and similarly for the other equipment, and the type of calibration performed and the relevant details as outlined in Section IV. Each entry can be analysed in more detail with a full list of the metadata and associated data. The associated data can be made available in raw form (all measurements or mean/median curves), through models (Debye or Cole-Cole models) or fitted parameters of mathematical models. Both dielectric/thermal data and metadata can be downloaded in CSV files.

Researchers who want to upload their own data to the repository can register to the repository and have access to an upload form and a dashboard with their submitted entries. Besides the metadata mentioned above, the upload form requests the time between measurement and excision of the sample (if applicable), time since slaughter (if applicable), number of measurements per sample, number of subjects, and conversion method used to retrieve the properties. This metadata is reported in Appendix I. Not all fields of the form are mandatory, ensuring the best balance between the amount of requested and essential information. An additional field is available for observations which researchers believe are important to report. Researchers are encouraged to download the executable file of the data analysis tool (presented in Section V) to process the data before uploading. They are not obliged to submit the raw data along with the metadata to the repository and can indicate their published paper and/or e-mail contact instead. After uploading, the entry will be reviewed before made available in the repository.

VII. FUNDAMENTAL CONFOUNDERS FOR THE GUIDELINES

These guidelines were developed taking account the current knowledge about a number of confounders and give particular importance to practices that can impact the accuracy of the dielectric measurements due to these confounders, which are related to both the MUT and measurement system. Specifically, hydration, temperature of the calibration load and sample size requirements have been identified as points that need to be highlighted and supported with additional information. Thus, this section will review the current knowledge related to each of these confounders and outline any open questions that still need to be considered.

A. HYDRATION

Hydration variation is without any doubt a determining confounder for dielectric measurements at microwave frequencies. This is because the interaction occurring in the GHz range is mainly due to the vibrations of polar molecules that oscillate with the changing field, mainly related to the presence of water in the biological tissue, also referred to as γ – dispersion [36]. In [20], a comparison of in-vivo and in-situ dielectric measurements was reported. The impact of tissue dehydration on the dielectric properties of excised tissue samples was further investigated in [67]. The effect of dehydration on the tissue surface has been characterized as a function of time after excision on freshly excised mouse liver, showing a change of more than 25% in both the real and imaginary parts of complex permittivity over 3.5 h after excision. Additionally, the correlation between the dielectric properties of biological tissues and their different states of hydration was investigated by Pollacco et al. [66]. Measurements were conducted on rat muscle and fat tissues both in vivo and ex vivo, observing which dehydration fractions fall within in vivo values, it was deduced that, for tissues with high water content, ex vivo samples can be used as a representation of the dielectric parameters of in vivo samples, if hydration loss does not exceed 10%. A similar observation was reported in [59], which in turn also compared dielectric measurements for tissues obtained from the same organ (referred to as intra-organ) and measurements on samples having same water content but obtained from different organs (inter-organ). It has been shown that the variation (% standard deviation) in the measured dielectric properties decreases with increasing sample hydration level and thus further analysis is required for tissue characterized by low water content.

All these studies indicate that the impact of tissue hydration on dielectric properties are significant and thus it is imperative to consider controls in the experimental design of both ex vivo and in vivo dielectric measurements to preserve tissue hydration. Whilst systematic differences are not anticipated at microwave frequencies when care is taken to avoid drying of excised tissue samples, this is not the case at lower frequencies, in the range of the α and β dispersions in view of the sensitivity of their causal mechanism to the physiological state of the tissue [75], [76].

B. TEMPERATURE OF CALIBRATION LOAD

The temperature of the calibration load is very important when conducting dielectric measurements that characterise temperature-dependent dielectric properties of biological tissues. In some studies, this temperature is recorded and used in the calibration procedure to compensate for any temperature-dependent errors whilst in some others this is not considered even though in studies might cover a very wide range of temperatures, starting from body temperature going up to ablative temperatures (80°C to 100°C). Recent experiments and manufacturers guidelines [56], show that more attention is required as this can have a significant impact on the measured data. When conducting temperature-dependent dielectric measurements, the MUT is heated using external sources and this can trigger thermal effects on both the MUT and the coaxial probe, which ideally are compensated for during the calibration procedure. To further show the impact of these thermal effects on dielectric measurements, a series of reflection measurements using an open-ended coaxial technique as explained in Section III was conducted for 0.1N NaCl from 500 MHz to 30 GHz, at 55 °C, using a R&S ZVA-50 VNA and Slim Form probe (Keysight). The best-practices guidelines outlined in Section IV were followed, as applicable, and calibration of the measurement setup was done at the tip of the probe using three standards: air, short circuit and deionized water. The calibration procedure was repeated for three calibration load temperatures 23 °C, 55 °C and 80 °C, respectively. The 0.1N NaCl data obtained when the calibration load temperature was set to 55 °C was considered as the reference datum and then the difference between the measured dielectric data of 0.1N NaCl at 55 °C made with the two other calibration temperatures were evaluated. Fig. 3 presents the percentage difference between the dielectric properties of 0.1N NaCl at 55 °C with the temperature of calibration

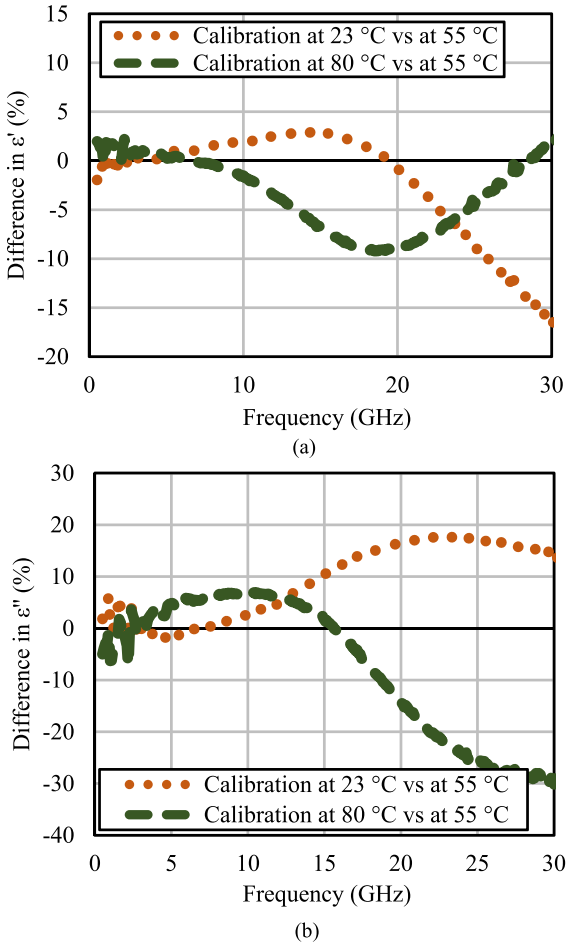


FIGURE 3. Percentage differences between the real (a) and imaginary (b) parts of the complex permittivity as a function of frequency for 0.1 M NaCl at 55 °C with calibration load temperature set at 23 °C and 80 °C, and 55 °C.

load set to 55 °C and the corresponding measurements for temperature of calibration loads set to 23 °C and 80 °C.

It can be observed that, for frequencies below 5 GHz, dielectric measurements at high temperatures are acceptable. The variability with respect to measurements at room temperatures were lower than 2% for ε' and lower than 7% for ε'', even with system calibration made at room temperature. However, at higher frequencies (> 5 GHz), the maximum percentage difference was 10 % at 18 GHz for ε' and 30% at 30 GHz for ε''.

Up to authors' knowledge only a few dielectric studies have reported on the temperature-dependence of the calibration load, and these focus on shorter frequency ranges (up to 3 GHz) and different materials [77], [78]. Therefore, a direct comparison with previous studies is difficult to conduct.

In order, to establish whether this variability in the dielectric measurements of the 0.1N NaCl solution for different calibration temperatures was only due to the difference between the calibration temperature of the setup and the temperature of the sample, or due to a change in the composition of the sample during heating, another set of measurements were conducted. In particular, dielectric measurements of 0.1 N NaCl were performed at 23 °C (setup calibrated at same temperature, 23 °C), then after heating the solution to 80 °C, it was cooled down to 23 °C again. In the latter the setup was calibrated at 23 °C. The calculated percentage difference between these two sets of measurements were calculated, obtaining a maximum difference of 0.2% on ε' and 4% on ε'' for frequencies less than 5 GHz and a maximum difference of 0.7% on ε' and 1.6% on ε'' for frequencies greater than 5 GHz.

Nevertheless, based on observations from these preliminary results, the quantification of the impact of the setup calibration temperature on dielectric measurement data at high temperature merits attention from the scientific community and is still to be investigated further in future studies.

C. SAMPLE SIZE REQUIREMENTS

The minimum homogenous sample size required to obtain an accurate measurement depends on the sensing volume of the probe. The sensing volume is typically defined by the sensing radius (in the radial direction from the probe tip center) and the sensing depth (in the axial direction). While conservative sample size requirements can often be found on the probe data sheet (if using a commercial probe, e.g. [79]), due to the number of parameters that can affect the minimum homogeneous sample size and the typically small size of tissue samples, it is always useful to verify the sample size requirement for each type of tissue sample in each experiment. Notably, some studies suggest that the functional sensing volume can be an order of magnitude less than such conservative estimates [80], [81], [82]. The minimum required homogeneous sample size is probe and scenario-dependent, and depends on the probe dimensions and materials, along with the dielectric properties of the sample under test (and their relative contrasts), and the frequency [48], [81], [82], [83], [84].

The minimum homogeneous sample size can be determined by: i) positioning a flat high-contrast material layer behind a sample that has dielectric properties close to those which are the target of the experimental campaign, and increasing the sample thickness until the high-contrast material is not detectable in the reflection measurements (i.e., the measurements reach steady values even with increasing thickness), and ii) positioning a cylindrical high-contrast material layer around a cylindrical inner sample that has dielectric properties close to those which are the target of the experimental campaign, and increasing the sample radius until the high-contrast material is not detectable in the reflection measurements [85]. (Note that a low-contrast material could also be used in these steps, particularly if it is of a similar contrast to tissue heterogeneities that would be expected to exist in the region surrounding the homogeneous tissue region that is the measurement target). The definition of 'not detectable'; however, is experiment-dependent and varies across studies [84]. It should be chosen with the target uncertainty in mind. It should also be noted that the sensing volume is

best determined by restricting the sensing radius and the sensing depth simultaneously, as thresholds for change in one dimension are not consistent with simultaneous volume changes in both dimensions [85].

VIII. OPEN CHALLENGES

Despite the fact that this best-practices guideline outlines in detail the most commonly used measurement method for dielectric properties of biological tissues, there still exist a number of issues that still need to be studied further. These are particularly related to the measurement method for temperature-dependent dielectric properties, how to deal with measuring the dielectric properties of heterogenous tissues and conducting accurate low-frequency dielectric measurements. Each of this is discussed into more detail in the following sections.

A. TEMPERATURE-DEPENDENT DIELECTRIC MEASUREMENTS

Several studies investigating the dielectric properties as a function of temperature have been reported in recent years [86], [87], [88]. This data is becoming even more in demand in the light of recent advancements in therapeutic applications using EMFs, particularly for MW hyperthermia and ablation. In most of these studies, the dielectric properties of ex-vivo biological tissues at ablative temperatures are reported. using an experimental setup similar to that outlined in Fig. 4, which typically consists of an ablation antenna fed by high-power signals together with an open-ended reflection probe, set perpendicular to the antenna and connected to a VNA. Often, the antenna is used as a heating source and dielectric measurements are retrieved from the reflection measurements performed using the VNA, very often following the method outlined in Section III. We note that although both the dielectric measurement probe and heating source may contain metal elements, the measurement probe is at a sufficient distance away that measurements are not impacted by the presence of these elements.

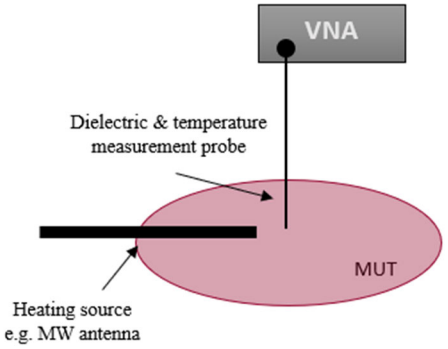


FIGURE 4. Typical measurement setup for temperature-dependent dielectric measurements using mw antenna and an open-ended coaxial probe.

Very often, temperature-dependent dielectric properties are characterised at a single frequency (e.g. 2.45 GHz and 915 MHz) using a relationship between the dielectric properties and temperature, with the gradient being referred to as the temperature coefficient [89]. When temperature is below 80 ^{o}C, a linear relationship between temperature and dielectric properties was used [89]. However, following other studies characterising tissues at higher temperatures, $>$ 80 °C, a non-linear dependence was used to characterise this relationship. The latter is attributed to changes in the tissue composition and the irreversible loss of water content [86], [87].

In recent years, there have been studies comparing different heating sources and their impact on the measured temperature-dependent dielectric properties. In [87] the dielectric properties of ex-vivo bovine liver as a function of the temperature were measured at 2.45 GHz during a thermal ablation procedure, utilising a setup similar to Fig. 2. These measurements were then compared to measurements on liver heated in a thermostatic bath. Results showed good agreement between the two datasets. Additionally, [57] compared another heating modality, a microwave oven, to an ablation system by conducting measurements on ex-vivo ovine lung tissues at 2.45 GHz and again no difference in the temperature-dependent dielectric properties was observed. This illustrates that for ex-vivo samples the measured properties do not depend on the heating modality and given the polarisation mechanism relevant at these frequencies, more importance should be given to the changes in the water content and changes in the composition of the tissue.

With the heating of the MUT, there are different factors that come into play, some are related to the measurement setup and others to the MUT. The temperature of calibration load, if conducted accurately, should be accounted by the calibration algorithm, however the temperature of the coaxial probe can cause some of the materials to expand as the temperature increase and thus a slight change in length could influence the dielectric measurements at higher frequencies ($>$ 3 GHz). Additionally, the temperature of MUT can impact the measured results because the probe is heated or cooled by the MUT and therefore measured data is a combination of the probe temperature and MUT temperature. This is also related to the discussion in Section V.

Moreover, when utilising a setup similar to Fig. 4, the rate of heating can be considered as a determining factor that can possibly change the composition of the tissue fluids in the area surrounding the open-ended coaxial probe, leading to variation in the measured dielectric properties. As the temperature around the antenna starts to increase, the tissue fluids are displaced from the region surrounding the antenna towards the open-ended coaxial probe, disturbing the micro-environment of the tissue close to the probe, leading to an ill-conditioned system. This problem is mostly observed when the rate of heating is slower compared to that used in ablation in which case the drying of tissue occurs almost instantaneously.

Therefore, these points highlight the importance that the characterisation of temperature-dependent dielectric

properties requires further work prior establishing a measurement guideline which could be adopted for biological tissues.

B. DEALING WITH HETEROGENEOUS TISSUES

Spectroscopy has the effect of averaging the dielectric properties throughout the sensing volume of the coaxial probe. Therefore, measuring the dielectric properties of highly heterogeneous tissues presents significant challenges over measuring the properties of homogeneous tissues. Specifically, the measurement at one site might not be representative of the whole tissue sample, and even if it is, it is difficult to interpret the dielectric measurement because it is unclear which tissue types contributed to it. In general, two approaches have been taken for dealing with heterogeneous tissues. The first and most straightforward is to take measurements from multiple measurement sites and then report the mean and standard deviation across all measurements, as recommended by [31], [54]. Or otherwise samples can be homogenised to obtain a mean value of the dielectric properties of the MUT [46], ensuring that in the process of homogenization that no loss of hydration occurs. Both methods provide an indication of the properties of the whole sample. The second approach is to use histology to identify tissue content and distribution within the sample, and to use this information to interpret the dielectric data [32], [64], [65], [90], [91], [92], [93]. This method is site-specific and provides information on the sample properties at one specific location on the sample.

Different strategies for using histology with dielectric measurements have been examined, which has led to data that are difficult to compare, especially for key tissues (such as the breast) [29]. Further, using histology requires identifying a histology region (on the image of the sample slice) that contains tissues that contributed to the dielectric measurement. To achieve the most representative histology region requires knowledge of both the sensing volume of the probe and how tissue samples shrink or deform during histology [94]. Many studies have examined the sensing volume of the probe, under conditions of different tissue types present, different tissue distributions, and different frequency ranges [48], [80], [81], [84], [95], [96], [97], [98], [99]. However, the definitions used for defining the sensing volumes have varied, and no standard method has gained consensus [84]. Additionally, it is known that tissues closest to the probe tip contribute dominantly to the dielectric measurement [96]; therefore, understanding how tissues in different locations contribute to the dielectric measurement could be of interest [99]. Again, these questions have not yet reached a consensus, and are active areas of interest.

Due to the challenges associated with using histology, and the fact that it is a destructive and expensive process, alternate strategies for dealing with dielectric measurements of heterogeneous tissues are of interest. One method that has been proposed that may support measurement of heterogeneous tissues is to use a transmission measurement approach, instead of a reflection measurement approach [100], [101], [102]. This enables measurement of bulk sample properties without having to take multiple measurements at multiple sites on the sample. Another method that has been proposed is to use microCT instead of histology, since it enables sample imaging in a less destructive manner and imaging may be able to be done at the same time as the dielectric measurement [103], [104]. However, these methods both require further studies to examine if they can be useful for the dielectric measurement of heterogeneous tissues.

C. LOW FREQUENCY DIELECTRIC MEASUREMENTS

The urgent need for high quality dielectric data of biological tissues at low frequencies and improvements in dosimetric tools has been highlighted in recommendations of the International Commission on Non-Ionising Radiation Protection and the World Health Organization (ICNIRP 2010 and WHO 2007). It is also a requirement for many low frequency medical applications. At low frequencies, the dielectric data for body tissues are difficult to determine due, at least partly, to the dependency of the dielectric properties on the physiological state of the tissues and changes occurring after death. In practice, there is at least one other major source of error that is a phenomenon referred to as ''electrode polarisation'', which originates from chemical interactions between sample and probe and interferes with the measurement. This was highlighted as one of the shortcomings of the 1996 database [16], [17], [18]. It only provides a 'best estimate' of dielectric data at frequencies below 1MHz based on available knowledge. Thus, using the open-ended coaxial probe technique, as discussed in this guideline at low frequencies becomes a challenge as polarization effects are more dominant and therefore alternative methods need to be explored.

This was addressed in a critical review of data for the conductivity of tissues at frequencies below 1 MHz with emphasis on the data published following post 1996 data base to highlight their usefulness and limitations [105]. Additionally, the same study included the development of a probe comprising a rectilinear array of four pin electrodes. The probe was used to produce a coherent set of capacitance and conductance values for water and low concentration saline solutions, down to 1 Hz. Measurements were also carried out on a selection of porcine tissues under in -vivo conditions to produce new tissue conductivity data to complement the literature reviewed. The effect of electrode polarisation at low frequencies, and some other high-frequency effects were identified as measurement artefacts that made the capacitive part of the permittivity data unreliable. Gabriel et al 2009, concluded that further work is needed to correct the problems identified in the study. On the positive side, it pointed out given the regularity and reproducibility of artefacts, there is a possibility of their avoidance or correction and hence for the opportunity of making error-free low-frequency permittivity and conductivity measurement in future [106].

IX. CONCLUSION

This paper outlines the work initiated by a network of researchers participating in COST Action MyWAVE and these guidelines are based on expertise of scientists and observations resulted from discussions during meetings and results from short-term scientific missions/visits of members of the network. It presents a consensus between network members on the best-practices for the accurate measurement

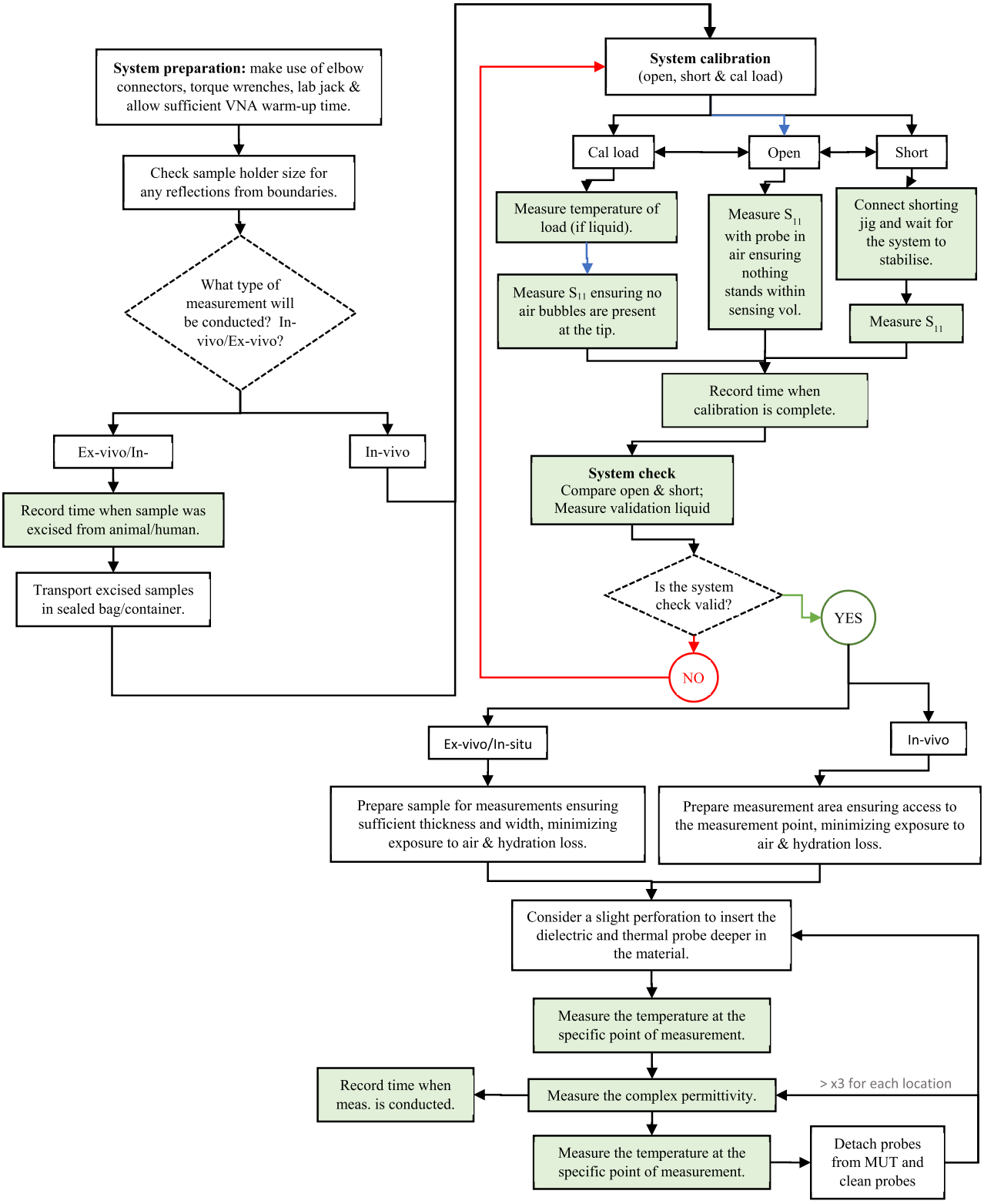


FIGURE 5. A detailed flow diagram of the protocol following best-practices to accurately measure the complex permittivity of liquids and biological tissues using an open-ended coaxial probe technique.

of dielectric properties of homogenous biological tissues at a constant temperature and the method for reporting. The latter is important as it facilitates the usability of the published data for other studies. This guideline addresses fundamental issues associated with the current state of knowledge of dielectric properties and the large variability in published data which is highly attributed to the variations in the measurement protocols adopted across different dielectric centers. It presents a detailed description of a typical reflection method using an open-ended coaxial line, widely used for the dielectric property measurements of biological tissues. Then a step-by-step guideline towards accurate measurements is provided

TABLE 1. A table with a list of recommend data to be reported for each study. an asterisk (*) marks the mandatory fields in the data repository.

	Recommended limit (if applicable)	Data to be reported
Preliminary sample & system information		
Description of the hardware (model and brand of the measurement equipment; measurement method*; model and brand of the measurement method) and the conversion algorithm* used to compute the complex permittivity from the reflection coefficient.		
Frequency range* of interest incl. information on step-size, log/linear scale, etc…		
Physical characteristics of the probe (e.g., outer diameter, flanged probe, etc…).		
Type of sample (origin*, e.g., human, bovine, etc…; pathology*, e.g., healthy, benign, malignant; state*, e.g., ex-vivo, in-vivo, in-vitro).		
Detailed characterization of sample (age of animal; info on hydration of sample if available; homogenous/heterogenous).		
Calibration & System Check		
Time the equipment was on prior to measurement	> 120 minutes	
Identify standard materials including load material* and its temperature of calibration*, if applicable.		
Record the time when calibration is completed.		
% Difference between the measured data in the system check and published data (17 ii) *.	< 5%	
Sample considerations & measurements		
Description of the sample collection procedure, preservation (storage*, e.g. fridge, freezer, etc…; temperature*) and preparation.		
For ex-vivo measurements, report the time of excision* of tissue from source of origin, if known, and the time since slaughter* (if applicable). For in-vivo/in-vitro measurements, report the time at which measurement session is initiated and time from exposure of the measurement site.		
The time of dissection into smaller samples (if applicable).		
Information on sample size* (e.g., approximate length, width and height) or volume* considered for measurements.		
Sample average temperature including the standard deviation in measurements conducted before and after each measurement. Sample minimum and maximum temperature* during measurements.		
The number of independent repeated measurements*, number of calibrations, number of subjects* and number of samples* considered.		
Any drift in measurements when comparing standard in system check and that at the end of each measurement session.		
Data analysis		
Description of data filtering process in determining experimental outliers, if applicable.		
For wideband measurements, the fitted models and parameters* including confidence interval and root mean square error* of the model or any other parameter indicating the goodness of fit.		
Description of the measurement uncertainty calculations.		
Complex permittivity of the MUT* including the corresponding uncertainty in the measurement.		

and covers dielectric measurements of liquids and homogenous biological tissues, as measured in vivo, ex vivo and in situ. Detailed considerations of the important confounders on which the best practices were developed is presented, highlighting the importance of controlling hydration, temperature of the calibration load and sample size. Finally, pertinent fundamental open challenges that have been identified within the network that need further efforts to be addressed are discussed.

APPENDIX I

A detailed flow diagram of the protocol following best-practices to accurately measure the complex permittivity of liquids and biological tissues using an open-ended coaxial probe technique. See Fig. 5.

APPENDIX II

A table with a list of recommend data to be reported for each study. an asterisk (∗) marks the mandatory fields in the data repository. See Table 1.

APPENDIX III

Debye equation

$$\varepsilon_r = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + j\omega\tau}$$

Debye equation with a conductivity term

$$\varepsilon_r = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + j\omega\tau} + \frac{\sigma}{j\omega\varepsilon_o}$$

Cole-Cole equation

$$\varepsilon_r = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + j\omega\tau^{1-\alpha}}$$

Cole-Cole equation with a conductivity term

$$\varepsilon_r = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + j\omega\tau^{1-\alpha}} + \frac{\sigma}{j\omega\varepsilon_\infty}$$

REFERENCES

[1] J. Redr, T. Pokorny, T. Drizdal, O. Fiser, M. Brunat, J. Vrba, and D. Vrba, "Microwave hyperthermia of brain tumors: A 2D assessment parametric numerical study," *Sensors*, vol. 22, no. 16, p. 6115, Aug. 2022.

[2] A. Radosevic et al., "Microwave versus radiofrequency ablation for the treatment of liver malignancies: A randomized controlled phase 2 trial," *Sci. Rep.*, vol. 12, no. 1, pp. 1–10, Jan. 2022.

[3] M.-O. Mattsson and M. Simkó, "Emerging medical applications based on non-ionizing electromagnetic fields from 0 Hz to 10 THz," *Med. Devices, Evidence*, vol. 12, pp. 347–368, Jan. 2019.

[4] E. C. Fear and M. A. Stuchly, "Microwave system for breast tumor detection," *IEEE Microw. Guided Wave Lett.*, vol. 9, no. 11, pp. 470–472, Nov. 1999.

[5] S. C. Hagness, A. Taflove, and J. E. Bridges, "Three-dimensional FDTD analysis of a pulsed microwave confocal system for breast cancer detection: Design of an antenna-array element," *IEEE Trans. Antennas Propag.*, vol. 47, no. 5, pp. 783–791, May 1999.

[6] R. C. Conceição, J. J. Mohr, and M. O'Halloran, *An Introduction to Microwave Imaging for Breast Cancer Detection*. Cham, Switzerland: Springer, 2016.

[7] L. Crocco, I. Karanasiou, M. L. James, and R. C. Conceição, *Emerging Electromagnetic Technologies for Brain Diseases Diagnostics, Monitoring and Therapy*. Cham, Switzerland: Springer, 2018.

[8] D. O. Rodriguez-Duarte, J. A. T. Vasquez, R. Scapaticci, L. Crocco, and F. Vipiana, "Assessing a microwave imaging system for brain stroke monitoring via high fidelity numerical modelling," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 5, no. 3, pp. 238–245, Sep. 2021.

[9] D. M. Godinho, J. M. Felício, C. A. Fernandes, and R. C. Conceição, "Experimental evaluation of an axillary microwave imaging system to aid breast cancer staging," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 6, no. 1, pp. 68–76, Mar. 2022.

[10] M. Ijff, J. Crezee, A. L. Oei, L. J. A. Stalpers, and H. Westerveld, "The role of hyperthermia in the treatment of locally advanced cervical cancer: A comprehensive review," *Int. J. Gynecologic Cancer*, vol. 32, no. 3, pp. 288–296, Mar. 2022.

[11] *European Network for Advancing Electromagnetic Hyperthermic Medical Technologies*. Accessed: Jan. 16, 2024. [Online]. Available: http://www.um.edu.mt/projects/mywave

[12] M. A. Stuchly and S. S. Stuchly, "Coaxial line reflection methods for measuring dielectric properties of biological substances at radio and microwave frequencies—A review," *IEEE Trans. Instrum. Meas.*, vol. IM-29, no. 3, pp. 176–183, Mar. 1980.

[13] K. S. Cole and R. H. Cole, "Dispersion and absorption in dielectrics I. Alternating current characteristics," *J. Chem. Phys.*, vol. 9, no. 4, pp. 341–351, Apr. 1941.

[14] K. R. Foster and H. P. Schwan, "Dielectric properties of tissues and biological materials: A critical review," *Critical Rev. Biomed. Eng.*, vol. 17, no. 1, pp. 25–104, 1989.

[15] K. R. Foster and J. L. Schepps, "Dielectric properties of tumor and normal tissues at radio through microwave frequencies," *J. Microw. Power*, vol. 16, no. 2, pp. 107–119, Jan. 1981.

[16] C. Gabriel, S. Gabriel, and E. Corthout, "The dielectric properties of biological tissues: I. Literature survey," *Phys. Med. Biol.*, vol. 41, no. 11, pp. 2231–2249, 1996.

[17] S. Gabriel, R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz," *Phys. Med. Biol.*, vol. 41, no. 11, pp. 2251–2269, Nov. 1996.

[18] S. Gabriel, R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues," *Phys. Med. Biol.*, vol. 41, no. 11, pp. 2271–2293, Nov. 1996.

[19] S. Gabriel, and C. Gabriel. (May 2019). *Compilation of the Dielectric Properties of Body Tissues at RF and Microwave Frequencies*. [Online]. Available: http://niremf.ifac.cnr.it/docs/DIELECTRIC/Report.html

[20] A. Peyman, S. J. Holden, S. Watts, R. Perrott, and C. Gabriel, "Dielectric properties of porcine cerebrospinal tissues at microwave frequencies: In vivo, in vitro and systematic variation with age," *Phys. Med. Biol.*, vol. 52, no. 8, pp. 2229–2245, Apr. 2007.

[21] A. Peyman, C. Gabriel, H. R. Benedickter, and J. Fröhlich, "Dielectric properties of human placenta, umbilical cord and amniotic fluid," *Phys. Med. Biol.*, vol. 56, no. 7, pp. N93–N98, Apr. 2011.

[22] A. Peyman and C. Gabriel, "Dielectric properties of rat embryo and foetus as a function of gestation," *Phys. Med. Biol.*, vol. 57, no. 8, pp. 2103–2116, Apr. 2012.

[23] A. Peyman and C. Gabriel, "Dielectric properties of porcine glands, gonads and body fluids," *Phys. Med. Biol.*, vol. 57, no. 19, pp. N339–N344, Oct. 2012.

[24] A. Peyman, A. A. Rezazadeh, and C. Gabriel, "Changes in the dielectric properties of rat tissue as a function of age at microwave frequencies," *Phys. Med. Biol.*, vol. 47, no. 12, pp. 2187–2188, Jun. 2002.

[25] A. Peyman, "Dielectric properties of tissues; variation with age and their relevance in exposure of children to electromagnetic fields; state of knowledge," *Prog. Biophys. Mol. Biol.*, vol. 107, no. 3, pp. 434–438, Dec. 2011.

[26] A. Peyman and C. Gabriel, "Cole–cole parameters for the dielectric properties of porcine tissues as a function of age at microwave frequencies," *Phys. Med. Biol.*, vol. 55, no. 15, pp. 413–419, Aug. 2010.

[27] E. Porter, A. La Gioia, S. Salahuddin, S. Decker, A. Shahzad, M. A. Elahi, M. O'Halloran, and O. Beyan, "Minimum information for dielectric measurements of biological tissues (MINDER): A framework for repeatable and reusable data," *Int. J. RF Microw. Comput.-Aided Eng.*, vol. 28, no. 3, Mar. 2018, Art. no. e21201.

[28] C. Gabriel and A. Peyman, "Electric and magnetic properties of biological materials," in *Bioengineering and Biophysical Aspects of Electromagnetic Fields*. Boca Raton, FL, USA: CRC Press, 2018, pp. 101–159.

[29] A. La Gioia, E. Porter, I. Merunka, A. Shahzad, S. Salahuddin, M. Jones, and M. O'Halloran, "Open-ended coaxial probe technique for dielectric measurement of biological tissues: Challenges and common practices," *Diagnostics*, vol. 8, no. 2, pp. 1–38, Jun. 2018.

[30] C. Gabriel, T. Y. A. Chan, and E. H. Grant, "Admittance models for open ended coaxial probes and their place in dielectric spectroscopy," *Phys. Med. Biol.*, vol. 39, no. 12, pp. 2183–2200, Dec. 1994.

[31] L. Farrugia, P. S. Wismayer, L. Z. Mangion, and C. V. Sammut, "Accurate in vivo dielectric properties of liver from 500 MHz to 40 GHz and their correlation to ex vivo measurements," *Electromagn. Biol. Med.*, vol. 35, no. 4, pp. 365–373, Oct. 2016.

[32] M. Lazebnik, D. Popovic, L. McCartney, C. B. Watkins, M. J. Lindstrom, J. Harter, S. Sewall, T. Ogilvie, A. Magliocco, T. M. Breslin, W. Temple, D. Mew, J. H. Booske, M. Okoniewski, and S. C. Hagness, "A large-scale study of the ultrawideband microwave dielectric properties of normal, benign and malignant breast tissues obtained from cancer surgeries," *Phys. Med. Biol.*, vol. 52, no. 20, pp. 6093–6115, Oct. 2007.

[33] L. Farrugia, J. Bonello, and C. V. Sammut, "Dielectric properties of breast: A review," in *Proc. 12th Eur. Conf. Antennas Propag. (EuCAP)*, Apr. 2018, pp. 1–3.

[34] G. Maenhout, A. Santorelli, E. Porter, I. Ocket, T. Markovic, and B. Nauwelaers, "Effect of dehydration on dielectric measurements of biological tissue as function of time," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 4, no. 3, pp. 200–207, Sep. 2020.

[35] R. Pethig, "Dielectric properties of biological materials: Biophysical and medical applications," *IEEE Trans. Electr. Insul.*, vol. EI-19, no. 5, pp. 453–474, Oct. 1984.

[36] H. P. Schwan and K. R. Foster, "RF-field interactions with biological systems: Electrical properties and biophysical mechanisms," *Proc. IEEE*, vol. 68, no. 1, pp. 104–113, Feb. 1980.

[37] C. Gabriel, "Numerical modelling of fringing fields and their use for complex permittivity measurements at high frequencies," Brooks Air Force Base, San Antonio, TX, USA, Tech. Rep. AL/OE-TR-1993-0068, 1993.

[38] B. J. Klauenberg and D. Miklavčič, *Radio Frequency Radiation Dosimetry and Its Relationship to the Biological Effects of Electromagnetic Fields* (Nato Science Series). Dordrecht, The Netherlands: Kluwer, 2000, pp. 73–84.

[39] H2020 Programme. *Guidelines on FAIR Data Management in Horizon 2020*. Accessed: Jan. 16, 2024. [Online]. Available: http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/oa_pilot/h2020-hi-oa-data-mgt_en.pdf

[40] M. D. Wilkinson et al., "The FAIR guiding principles for scientific-data management and stewardship," *Sci. Data.*, vol. 3, Jan. 2016, Art. no. 160018.

[41] G. Ruvio, M. Vaselli, V. Lopresto, R. Pinto, L. Farina, and M. Cavagnaro, "Comparison of different methods for dielectric properties measurements in liquid sample media," *Int. J. RF Microw. Comput.-Aided Eng.*, vol. 28, no. 3, Mar. 2018, Art. no. e21215.

[42] G. Ruvio, L. Farina, A. Bottiglieri, J. Eaton-Evans, M. A. Elahi, M. O'Halloran, R. Pinto, V. Lopresto, and M. Cavagnaro, "Comparison of coaxial open-ended probe based dielectric measurements on ex-vivo thermally ablated liver tissue," Presented at the Eur. Conf. Antennas Propag. (EuCAP), 2019.

[43] D. Misra, M. Chabbra, B. R. Epstein, M. Microtznik, and K. R. Foster, "Noninvasive electrical characterization of materials at microwave frequencies using an open-ended coaxial line: Test of an improved calibration technique," *IEEE Trans. Microw. Theory Techn.*, vol. 38, no. 1, pp. 8–14, Mar. 1990.

[44] T. E. Hodgetts, *The Calculation of the Equivalent Circuits of Coaxial-Line Step Discontinuities*. Malvern, U.K.: RSRE, 1981.

[45] T. P. Marsland and S. Evans, "Dielectric measurements with an open-ended coaxial probe," *IEE Proc. H Microw., Antennas Propag.*, vol. 134, no. 4, pp. 341–349, 1987.

[46] J. Bonello, A. Demarco, I. Farhat, L. Farrugia, and C. V. Sammut, "Application of artificial neural networks for accurate determination of the complex permittivity of biological tissue," *Sensors*, vol. 20, no. 16, p. 4640, Aug. 2020.

[47] S. Salahuddin, E. Porter, P. M. Meaney, and M. O'Halloran, "Effect of logarithmic and linear frequency scales on parametric modelling of tissue dielectric data," *Biomed. Phys. Eng. Exp.*, vol. 3, no. 1, Feb. 2017, Art. no. 015020.

[48] D. M. Hagl, D. Popovic, S. C. Hagness, J. H. Booske, and M. Okoniewski, "Sensing volume of open-ended coaxial probes for dielectric characterization of breast tissue at microwave frequencies," *IEEE Trans. Microw. Theory Techn.*, vol. 51, no. 4, pp. 1194–1206, Apr. 2003.

[49] D. Popovic, L. McCartney, C. Beasley, M. Lazebnik, M. Okoniewski, S. C. Hagness, and J. H. Booske, "Precision open-ended coaxial probes for in vivo and ex vivo dielectric spectroscopy of biological tissues at microwave frequencies," *IEEE Trans. Microw. Theory Techn.*, vol. 53, no. 5, pp. 1713–1722, May 2005.

[50] U. Kaatze, "Complex permittivity of water as a function of frequency and temperature," *J. Chem. Eng. Data*, vol. 34, no. 4, pp. 371–374, Oct. 1989.

[51] C. Ronne, L. Thrane, P.-O. Åstrand, A. Wallqvist, K. V. Mikkelsen, and S. R. Keiding, "Investigation of the temperature dependence of dielectric relaxation in liquid water by THz reflection spectroscopy and molecular dynamics simulation," *J. Chem. Phys.*, vol. 107, no. 14, pp. 5319–5331, Oct. 1997.

[52] W. J. Ellison, "Permittivity of pure water, at standard atmospheric pressure, over the frequency range −25 THz and the temperature range −100 °C," *J. Phys. Chem. Reference Data*, vol. 36, no. 1, pp. 1–18, Mar. 2007.

[53] A. P. Gregory, R. N. Clarke, and M. G. Cox, "Traceable measurement of dielectric reference liquids over the temperature interval 10–50 °C using coaxial-line methods," *Meas. Sci. Technol.*, vol. 20, no. 7, Jul. 2009, Art. no. 075106.

[54] C. Gabriel and A. Peyman, "Dielectric measurement: Error analysis and assessment of uncertainty," *Phys. Med. Biol.*, vol. 51, no. 23, pp. 6033–6046, Dec. 2006.

[55] A. Peyman, C. Gabriel, and E. H. Grant, "Complex permittivity of sodium chloride solutions at microwave frequencies," *Bioelectromagnetics*, vol. 28, no. 4, pp. 264–274, May 2007.

[56] Keysight. *Technical Support: N5242B PNA-X Microwave Network Analyzer, 900 Hz/10 MHz to 26.5 GHz*. Accessed: Jan. 16, 2024. [Online]. Available: https://na.support.keysight.com/materials/help/WebHelp/Opt.004_Common_Problems_and_Solutions.htm

[57] J. Bonello, M. A. Elahi, E. Porter, M. O'Hollaran, L. Farrugia, and C. V. Sammut, "An investigation of the variation of dielectric properties of ovine lung tissue with temperature," *Biomed. Phys. Eng. Exp.*, vol. 5, no. 4, Jun. 2019, Art. no. 045024.

[58] S. Salahuddin, A. L. Gioia, A. Shahzad, M. A. Elahi, A. Kumar, D. Kilroy, E. Porter, and M. O'Halloran, "An anatomically accurate dielectric profile of the porcine kidney," *Biomed. Phys. Eng. Exp.*, vol. 4, no. 2, Feb. 2018, Art. no. 025042.

[59] S. Di Meo, J. Bonello, I. Farhat, L. Farrugia, M. Pasian, M. T. C. Podesta, S. Suleiman, J. Calleja-Agius, and C. V. Sammut, "The variability of dielectric permittivity of biological tissues with water content," *J. Electromagn. Waves Appl.*, vol. 36, no. 1, pp. 48–68, Jan. 2022.

[60] R. N. Clarke, A. P. Gregory, D. Cannell, M. Patrick, S. Wylie, I. Youngs, and G. Hill, "A guide to the characterisation of dielectric materials at RF and microwave frequencies," Inst. Meas. Control/Nat. Phys. Lab., London, U.K., Tech. Rep., 2003.

[61] M. Cavagnaro and G. Ruvio, "Numerical sensitivity analysis for dielectric characterization of biological samples by open-ended probe technique," *Sensors*, vol. 20, no. 13, p. 3756, Jul. 2020.

[62] J. Bonello, L. Farrugia, P. Schembri Wismayer, I. L. Alborova, and C. V. Sammut, "A study of the effects of preservative solutions on the dielectric properties of biological tissue," *Int. J. RF Microw. Comput.-Aided Eng.*, vol. 28, no. 3, Mar. 2018, Art. no. e21214.

[63] A. Peyman, B. Kos, M. Djokić, B. Trotovšek, C. Limbaeck-Stokin, G. Sersa, and D. Miklavcic, "Variation in dielectric properties due to pathological changes in human liver," *Bioelectromagnetics*, vol. 36, no. 8, pp. 603–612, Dec. 2015.

[64] A. Bottiglieri, A. Shahzad, P. Donlon, M. C. Dennedy, A. Lowery, M. O'Halloran, and L. Farina, "Dielectric characterization of ex vivo ovine and human adrenal glands for microwave thermal ablation applications," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 5, no. 3, pp. 254–261, Sep. 2021.

[65] M. Guardiola, S. Buitrago, G. Fernández-Esparrach, J. M. O'Callaghan, J. Romeu, M. Cuatrecasas, H. Córdova, M. Á. González Ballester, and O. Camara, "Dielectric properties of colon polyps, cancer, and normal mucosa: Ex vivo measurements from 0.5 to 20 GHz," *Med. Phys.*, vol. 45, no. 8, pp. 3768–3782, Aug. 2018.

[66] D. A. Pollacco, L. Farina, P. S. Wismayer, L. Farrugia, and C. V. Sammut, "Characterization of the dielectric properties of biological tissues and their correlation to tissue hydration," *IEEE Trans. Dielectr. Electr. Insul.*, vol. 25, no. 6, pp. 2191–2197, Dec. 2018.
[67] A. Shahzad, S. Khan, M. Jones, R. M. Dwyer, and M. O'Halloran, "Investigation of the effect of dehydration on tissue dielectric properties in ex vivo measurements," *Biomed. Phys. Eng. Exp.*, vol. 3, no. 4, Jun. 2017, Art. no. 045001.
[68] S. Di Meo, P. F. Espín-López, A. Martellosio, M. Pasian, G. Matrone, M. Bozzi, G. Magenes, A. Mazzanti, L. Perregrini, F. Svelto, P. E. Summers, G. Renne, L. Preda, and M. Bellomi, "On the feasibility of breast cancer imaging systems at millimeter-waves frequencies," *IEEE Trans. Microw. Theory Techn.*, vol. 65, no. 5, pp. 1795–1806, May 2017.
[69] K. Vidjak, L. Farina, G. Ruvio, M. O'Halloran, and M. Cavagnaro, "Dielectric properties of healthy ex-vivo ovine lung tissue at microwave frequencies," *IEEE Trans. Dielectr. Electr. Insul.*, vol. 30, no. 3, pp. 1162–1169, Jun. 2023.
[70] D. Sladden, L. Farrugia, R. Scicluna, J. Bonello, and C. Sammut, "Preliminary study on in-vivo dielectric properties of tissues in the human oral cavity at microwave frequencies," in *Proc. IEEE Int. Conf. Microw., Antennas, Commun. Electron. Syst. (COMCAS)*, Nov. 2021, pp. 140–145.
[71] *Evaluation of Measurement Data—Guide to the Expression of Uncertainty in Measurement*, document JCGM 100:2008, Working Group 1 of the Joint Committee for Guides in Metrology (JCGM/WG 1), GUM 1995 with minor corrections, 2008.
[72] J. Clegg and M. P. Robinson, "A genetic algorithm for optimizing multipole Debye models of tissue dielectric properties," *Phys. Med. Biol.*, vol. 57, no. 19, pp. 6227–6243, Oct. 2012.
[73] S. A. Sansone et al., "Toward interoperable bioscience data," *Nat Genet.*, vol. 44, no. 2, pp. 121–126, 2012.
[74] *MyWAVE COST Action: Open-Access Repository of Dielectric and Thermal Properties of Biological Tissues*. Accessed: Jan. 16, 2024. [Online]. Available: https://www.um.edu.mt/projects/mywave/data-repository
[75] A. Kraszewski, M. A. Stuchly, S. S. Stuchly, and A. M. Smith, "In vivo and in vitro dielectric properties of animal tissues at radio frequencies," *Bioelectromagnetics*, vol. 3, no. 4, pp. 421–432, Jan. 1982.
[76] W. Kuang and S. O. Nelson, "Low-frequency dielectric properties of biological tissues, a review with some new insights," *Trans. ASAE*, vol. 41, no. 1, pp. 173–184, 1998.
[77] J. Chen, K. Pitchai, S. Birla, D. D. Jones, J. Subbiah, and R. Gonzalez, "Development of a multi-temperature calibration method for measuring dielectric properties of food," *IEEE Trans. Dielectr. Electr. Insul.*, vol. 22, no. 1, pp. 626–634, Feb. 2015.
[78] D. C. Campos, J. C. A. Santos, and L. E. P. Borges, "Investigation of thermal effects in coaxial probe method and dielectric characterization of glycerol up to 140 °C," *J. Microw., Optoelectron. Electromagn. Appl.*, vol. 18, no. 1, pp. 1–17, Mar. 2019.
[79] Keysight Technologies. *N1501A Dielectric Probe Kit, Technical Overview*. Accessed: Jan. 16, 2024. [Online]. Available: https://www.keysight.com/us/en/assets/7018-04631/technical-overviews/5992-0264.pdf
[80] P. M. Meaney, A. P. Gregory, J. Seppälä, and T. Lahtinen, "Open-ended coaxial dielectric probe effective penetration depth determination," *IEEE Trans. Microw. Theory Techn.*, vol. 64, no. 3, pp. 915–923, Mar. 2016.
[81] A. La Gioia, M. O'Halloran, and E. Porter, "Modelling the sensing radius of a coaxial probe for dielectric characterisation of biological tissues," *IEEE Access*, vol. 6, pp. 46516–46526, 2018.
[82] A. L. Gioia, A. Santorelli, M. O'Halloran, and E. Porter, "Predicting the sensing radius of a coaxial probe based on the probe dimensions," *IEEE Trans. Antennas Propag.*, vol. 68, no. 9, pp. 6704–6716, Sep. 2020.
[83] C. Aydinalp, S. Joof, and T. Yilmaz, "Towards accurate microwave characterization of tissues: Sensing depth analysis of open-ended coaxial probes with ex vivo rat breast and skin tissues," *Diagnostics*, vol. 11, no. 2, p. 338, Feb. 2021.
[84] E. Porter and M. O'Halloran, "Investigation of histology region in dielectric measurements of heterogeneous tissues," *IEEE Trans. Antennas Propag.*, vol. 65, no. 10, pp. 5541–5552, Oct. 2017.
[85] A. Farshkaran and E. Porter, "Coaxial probe-based measurements of biological tissues: Inaccuracies in sensing volume when calculated from sensing radius and sensing depth," in *Proc. Int. Conf. Electromagn. Adv. Appl. (ICEAA)*, Aug. 2021, pp. 110–113.
[86] C. L. Brace, "Temperature-dependent dielectric properties of liver tissue measured during thermal ablation: Toward an improved numerical model," in *Proc. 30th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, Aug. 2008, pp. 230–233.
[87] V. Lopresto, R. Pinto, G. A. Lovisolo, and M. Cavagnaro, "Changes in the dielectric properties of ex vivo bovine liver during microwave thermal ablation at 2.45 GHz," *Phys. Med. Biol.*, vol. 57, no. 8, pp. 2309–2327, Apr. 2012.
[88] M. Lazebnik, M. C. Converse, J. H. Booske, and S. C. Hagness, "Ultrawideband temperature-dependent dielectric properties of animal liver tissue in the microwave frequency range," *Phys. Med. Biol.*, vol. 51, no. 7, pp. 1941–1955, Apr. 2006.
[89] C. Rossmanna and D. Haemmerich, "Review of temperature dependence of thermal properties, dielectric properties, and perfusion of biological tissues at hyperthermic and ablation temperatures," *Crit. Rev. Biomed. Eng.*, vol. 42, no. 6, pp. 467–492, 2014.
[90] R. J. Halter, T. Zhou, P. M. Meaney, A. Hartov, R. J. Barth, K. M. Rosenkranz, W. A. Wells, C. A. Kogel, A. Borsic, E. J. Rizzo, and K. D. Paulsen, "The correlation of in vivo and ex vivo tissue dielectric properties to validate electromagnetic breast imaging: Initial clinical experience," *Physiolog. Meas.*, vol. 30, no. 6, pp. S121–S136, Jun. 2009.
[91] M. Lazebnik, L. McCartney, D. Popovic, C. B. Watkins, M. J. Lindstrom, J. Harter, S. Sewall, A. Magliocco, J. H. Booske, M. Okoniewski, and S. C. Hagness, "A large-scale study of the ultrawideband microwave dielectric properties of normal breast tissue obtained from reduction surgeries," *Phys. Med. Biol.*, vol. 52, no. 10, pp. 2637–2656, May 2007.
[92] T. Sugitani, S.-I. Kubota, S.-I. Kuroki, K. Sogo, K. Arihiro, M. Okada, T. Kadoya, M. Hide, M. Oda, and T. Kikkawa, "Complex permittivities of breast tumor tissues obtained from cancer surgeries," *Appl. Phys. Lett.*, vol. 104, no. 25, Jun. 2014, Art. no. 253702.
[93] A. Martellosio, M. Pasian, M. Bozzi, L. Perregrini, A. Mazzanti, F. Svelto, P. E. Summers, G. Renne, L. Preda, and M. Bellomi, "Dielectric properties characterization from 0.5 to 50 GHz of breast cancer tissues," *IEEE Trans. Microw. Theory Techn.*, vol. 65, no. 3, pp. 998–1011, Mar. 2017.
[94] A. La Gioia, M. O'Halloran, and E. Porter, "Challenges of post-measurement histology for the dielectric characterisation of heterogeneous biological tissues," *Sensors*, vol. 20, no. 11, p. 3290, Jun. 2020.
[95] D. Popovic, M. Okoniewski, D. Hagl, J. H. Booske, and S. C. Hagness, "Volume sensing properties of open-ended coaxial probes for dielectric spectroscopy of breast tissue," in *Proc. IEEE Antennas Propag. Soc. Int. Symp., Dig., USNC/URSI Nat. Radio Sci. Meeting*, Jul. 2002, pp. 254–257.
[96] P. M. Meaney, A. P. Gregory, N. R. Epstein, and K. D. Paulsen, "Microwave open-ended coaxial dielectric probe: Interpretation of the sensing volume re-visited," *BMC Med. Phys.*, vol. 14, no. 1, Dec. 2014.
[97] E. Porter, A. L. Gioia, A. Santorelli, and M. O'Halloran, "Modeling of the dielectric properties of biological tissues within the histology region," *IEEE Trans. Dielectr. Electr. Insul.*, vol. 24, no. 5, pp. 3290–3301, Oct. 2017.
[98] A. La Gioia, S. Salahuddin, M. O'Halloran, and E. Porter, "Quantification of the sensing radius of a coaxial probe for accurate interpretation of heterogeneous tissue dielectric data," *IEEE J. Electromagn., RF Microw. Med. Biol.*, vol. 2, no. 3, pp. 145–153, Sep. 2018.
[99] A. L. Gioia, M. O'Halloran, A. Elahi, and E. Porter, "Investigation of histology radius for dielectric characterisation of heterogeneous materials," *IEEE Trans. Dielectr. Electr. Insul.*, vol. 25, no. 3, pp. 1064–1079, Jun. 2018.
[100] P. M. Meaney, T. Rydholm, and H. Brisby, "Transmission-based dielectric probes for surgical applications," in *Proc. 13th Eur. Conf. Antennas Propag. (EuCAP)*, Mar. 2019, pp. 1–2.
[101] P. Meaney, T. Rydholm, and H. Brisby, "A transmission-based dielectric property probe for clinical applications," *Sensors*, vol. 18, no. 10, p. 3484, Oct. 2018.
[102] M. Savazzi, E. Porter, M. O'Halloran, J. R. Costa, C. Fernandes, J. M. Felicío, and R. C. Conceição, "Development of a transmission-based open-ended coaxial-probe suitable for axillary lymph node dielectric measurements," in *Proc. 14th Eur. Conf. Antennas Propag. (EuCAP)*, Mar. 2020, pp. 1–5.
[103] S. Etoz and C. L. Brace, "Tissue permittivity measurement with concurrent CT imaging: Analysis of heterogeneity effects," in *Proc. 13th Eur. Conf. Antennas Propag. (EuCAP)*, Mar. 2019, pp. 1–5.
[104] A. La Gioia, "Accurate dielectric characterisation of biological tissues in the microwave range using the open-ended coaxial probe technique," Ph.D. dissertation, Dept. Elect. Electron. Eng., College Eng. Inform., Nat. Univ. Ireland Galway, Galway, Ireland, 2019.

[105] C. Gabriel, A. Peyman, and E. H. Grant, "Electrical conductivity of tissue at frequencies below 1 MHz," *Phys. Med. Biol.*, vol. 54, no. 16, pp. 4863–4878, Aug. 2009.
[106] C. Karina, N. Chopra, M. Capstick, A. Peyman, S. Hashemizadeh, and N. Kuster, "Challenges in four-electrode probe measurement—Data acquisition system and probe hardware for low frequency dielectric spectroscopy," Presented at the Joint Annu. Meeting Bioelectromagn. Soc. Eur. BioElectromagn. Assoc., 2021.

LOURDES FARRUGIA was born in Malta. She received the M.Sc. and Ph.D. degrees in physics from the University of Malta, in 2008 and 2016, respectively.

She is currently a Senior Lecturer and the Head of the Physics Department, University of Malta. She has published over 70 journal articles and conference proceedings. Her research interests include the aspects of instrumentation and measurement of dielectric properties, in particular those of biological tissues, as relevant to the microwave medical device community. She is a member of the Technical Advisory Committee of URSI Commission K and a member of the ASME Thermal Medicine Committee. She was the Chair of COST Action CA17115 MyWAVE. She is also the Principal Investigator of Hyper4B: Microwave Hyperthermia for breast cancer and CountMe: personalized blood monitor sensor.

EMILY PORTER (Member, IEEE) received the B.Eng., M.Eng., and Ph.D. degrees in electrical engineering from McGill University, Montreal, QC, Canada, in 2009, 2010, and 2015, respectively.

Then, she was an NSERC Postdoctoral Fellow and an EU Marie-Curie Fellow with the Translational Medical Device Laboratory, National University of Ireland Galway, before becoming an Assistant Professor with The University of Texas at Austin, Austin, TX, USA, in 2019. She is currently an Assistant Professor with McGill University. Her research interests include the measurement of dielectric properties of biological tissues, the development novel technologies for therapeutic, and the diagnostic applications of electromagnetic waves. She was a recipient of the IEEE Lot Shafai Mid-Career Distinguished Achievement Award, in 2021.

RAQUEL C. CONCEIÇÃO was born in Lisbon, Portugal, in 1984. She received the integrated master's degree in biomedical engineering from Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal, in 2007, and the Ph.D. degree in electrical and electronic engineering from the National University of Ireland Galway (now University of Galway), in 2011. She is currently an Assistant Professor with Faculdade de Ciências, Universidade de Lisboa. She is the Coordinator of the Instituto de Biofísica e Engenharia Biomédica, and also the Coordinator of the master's degree of Biomedical Engineering and Biophysics. She is an Editor of two books: *An Introduction to Microwave Imaging for Breast Cancer Detection* (Springer International Publishing, Switzerland, 2016) and *Emerging Electromagnetic Technologies for Brain Diseases Diagnostics and Monitoring* (Springer International Publishing, Switzerland, 2018). She has published over 90 journal articles and conference proceedings. Her main research interests include developing microwave imaging techniques to detect and classify breast cancer and axillary lymph nodes. She is a member of MTTs TC-28 Biological Effects and Medical Applications Committee, an URSI Individual Member (appointment for life), since 2017, and the Vice-President of URSI Commission K in Portugal, since 2023.

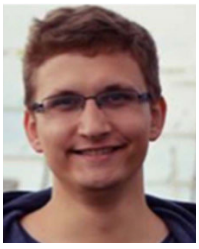
SIMONA DI MEO (Member, IEEE) received the M.Sc. degree (cum laude) in electronic engineering and the Ph.D. degree in electronics and computer science from the University of Pavia, in 2016 and 2020, respectively.

She is currently a Postdoctoral Researcher with the Microwave Laboratory, Department of Electrical, Computer, and Biomedical Engineering, University of Pavia. Her current research interest includes innovative techniques for early breast cancer detection. She was the Co-Principal Investigator (Co-PI) with the University of Pavia funding BlueSky Research Project MULTIWAVE.

Dr. Meo is a member of the IEEE AP-S, MTT-S, EMB-S, WiE, and the Italian Society on Electromagnetism (SIEm), and a member of the National Group of Bioengineering (GNB). She was a recipient of several awards and recognitions, including the IEEE AP-S Eugene F. Knott Memorial Pre-Doctoral Research Award, in 2015, the IEEE AP-S Doctoral Research Grant, in 2018, the IEEE AP-S Fellowship, in 2022, and several Young Scientist Awards in the framework of URSI conferences. She was the Education and Research Cooperation Committee Chair and a member of the Technical Program Committee for the Mediterranean Microwave Symposium 2022. She was the Student Activity Chair for the European Microwave Week 2022. She is an Associate Editor of *Healthcare Technology Letters* (IET) and an Editorial Board Member of IEEE Open Journal of Engineering in Medicine and Biology.

DANIELA M. GODINHO was born in Fundão, Portugal, in 1994. She received the integrated master's degree in biomedical engineering from Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal, in 2016, and the Ph.D. degree in biomedical engineering and biophysics from Faculdade de Ciências, Universidade de Lisboa, Portugal, in 2022. She is currently an invited Assistant Professor and a Postdoctoral Researcher with Faculdade de Ciências, Universidade de Lisboa. In the last five years, she has been working on microwave imaging to aid breast cancer diagnosis and staging. Her research interests include medical imaging, signal and image processing, and machine learning.

JULIAN BONELLO (Member, IEEE) received the Bachelor of Science (Hons.) degree in physics and computing, the Master of Science degree in physics from the University of Malta in 2012 and 2015, respectively, and the Ph.D. degree from the University of Malta, in 2020, focused on investigating the temperature and frequency-dependent variations of complex permittivity. In 2015, he became a Researcher within the Physics Department. His primary research interest includes revolve around the instrumentation and measurement of dielectric properties, with a specific emphasis on those related to biological tissues.



MYKOLAS RAGULSKIS received the B.Sc. degree in biomedical electronics from the Kaunas University of Technology, Kaunas, Lithuania, in 2014, and the M.Sc. degree in biomedical engineering and informatics from Aalborg University, Aalborg, Denmark, in 2016.

Since 2015, he has been working with Keysight Technologies, starting as a Student Worker, and in 2016, he became a Research and Development Engineer. His main research interests include impedance measurements and calibration.

ILJA OCKET (Member, IEEE) received the M.Sc. and Ph.D. degrees in electrical engineering from KU Leuven, Leuven, Belgium, in 1998 and 2009, respectively. He is currently the Program Manager in neuromorphic sensor fusion with IMEC, Leuven, Belgium. His research interests include the all aspects of heterogeneous integration of highly miniaturized millimeter wave systems, spanning design, technology, and metrology. He is also involved in research on using broadband impedance sensing and dielectrophoretic actuation for lab-on-chip applications.

LAURA FARINA (Member, IEEE) received the M.Sc. degree in biomedical engineering and the Ph.D. degree in information and communication technology—applied electromagnetism from the Sapienza University of Rome, in 2013 and 2017, respectively.

From 2018 to 2020, she was a Marie Skłodowska-Curie MedTrain Fellow with the CÚRAM, Translational Medical Device Laboratory, National University of Ireland, Galway. She is currently a Senior Clinical Engineer with Endowave Ltd., where she dedicates her research effort in developing preclinical studies for the next generation transbronchial, fully flexible microwave ablation treatment for lung cancer. Over the years, her research activity has been focused on the characterization of the electromagnetic, thermal and physical changes undergone by tissues treated with microwave ablation procedures, and on the use of these information to better develop electromagnetic-based medical technologies.

Dr. Farina received the Latmiral Prize, in 2018, from the Italian Society of Electromagnetism. She has been the Young Scientist Awardee at PIERS 2019 and IEEE COMCAS 2021. She is a recipient of the 2021 Royal Irish Academy Charlemont Grant. She edited IEEE JOURNAL OF ELECTROMAGNETICS, RF AND MICROWAVES IN MEDICINE AND BIOLOGY Special Issue on Developments in Electromagnetic-Based Medical Technologies, in 2021. She is a member of the ASME Thermal Medicine Committee, co-leading the Thermal Properties Subgroup.

MARTA CAVAGNARO (Senior Member, IEEE) received the degree (cum laude) in electronic engineering and the Ph.D. degree in electronic engineering from the Sapienza University of Rome, Rome, Italy. She is currently an Associate Professor with the Department of Information Engineering, Electronics and Telecommunications, Sapienza University of Rome. Her research interests include the dosimetric aspects of the interaction between electromagnetic fields and biological systems, as medical applications, the measurements of the dielectric properties of tissues, and the environmental impact of mobile communication systems. She serves as an anonymous reviewer for several scientific journals. She is a member of the Thermal Medicine Standard Committee of ASME (The American Society of Mechanical Engineers), and a member of the Italian CEI TC106 devoted to standardization issues related to human exposure to electromagnetic fields. She has participated in several EU funded COST action related to medical applications of electromagnetic fields (EMFMED, MiMed, and MyWAVE). She is the author or coauthor of more than 200 scientific articles. She is an Associate Editor of the *Bioelectromagnetics* journal.

AZADEH PEYMAN received the B.Sc., M.Sc., and Ph.D. degrees from Kings College London.

She is currently an internationally known expert in the field of interaction mechanisms of electromagnetic fields (EMF) with biological tissues and communicating information on exposure to radiation and risk in areas of public concern. She has more than 20 years of scientific research and a solid track record of peer reviewed publications. Her work on the dielectric properties of ageing tissues has been one of the key contributors to the debate on the extent to which children's exposure to EMF may be different from adults. She has served as a Consultant to the independent Advisory Group on Non-ionising Radiation. She also serves as part of the Secretariat for U.K. Government's Committee on Medical Aspects of Radiation in the Environment (COMARE). She is also a Consultant for WHO's International EMF Project and the President-Elect of the BioEM Society and a Visiting Fellow with the Department of Electronic Engineering, Queen Mary University of London. She also serves as an Associate Editor for the *Radiation Protection Dosimetry* journal.